CYCLOLAB

PIONEERS IN CYCLODEXTRIN-BASED INNOVATION

GETTING THE BEST OUT OF CYCLODEXTRINS

Custom Cyclodextrin

Synthesis under cGMP

THE USES OF CYCLODEXTRINS

- Enables formulation of water-insoluble APIs in all dosage forms (mainstream use in pharma industry)
  - Significant solubility enhancement
  - Improvement of chemical stability
  - Taste and odor masking of APIs
  - Increased bioavailability, facilitated delivery

- Chiral resolving agents (main analytical application)
- Intensify the enzymatic conversion of lipophilic substrates (main biotech application)
- Reduced aggregation (formulation of biologics)
- Potential APIs (emerging field, new application)

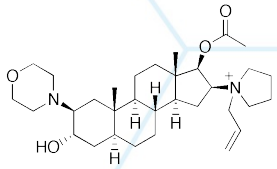
THE USES OF CYCLODEXTRINS
THE CHALLENGE

Cyclodextrin-based APIs are typically derivatives that

- Are not commercially available
- Do not have optimized synthesis process
- Do not have well-established analytical background

CycloLab has both the capabilities and the expertise to overcome these challenges and support such development

CYCLODEXTRINS AS APIs
SUGAMMADEX



Rocuronium

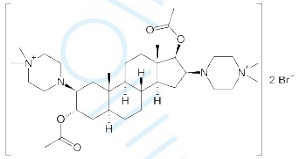
The 1st selective relaxant binding agent to reverse NMBA induced neuromuscular blockade

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

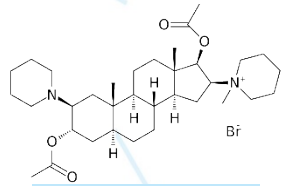
One of the strongest fits among CDs and gues[illegible] rocuronium is unavailable to bind the receptor

Reduced/eliminated adverse effects compared to neostigmine

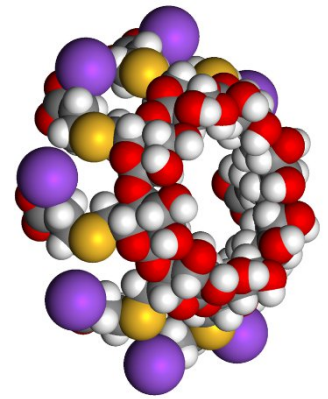
Somewhat lower affinity for vecuronium, pipecuronium and pancuronium, yet still working clinically



Pipecuronium

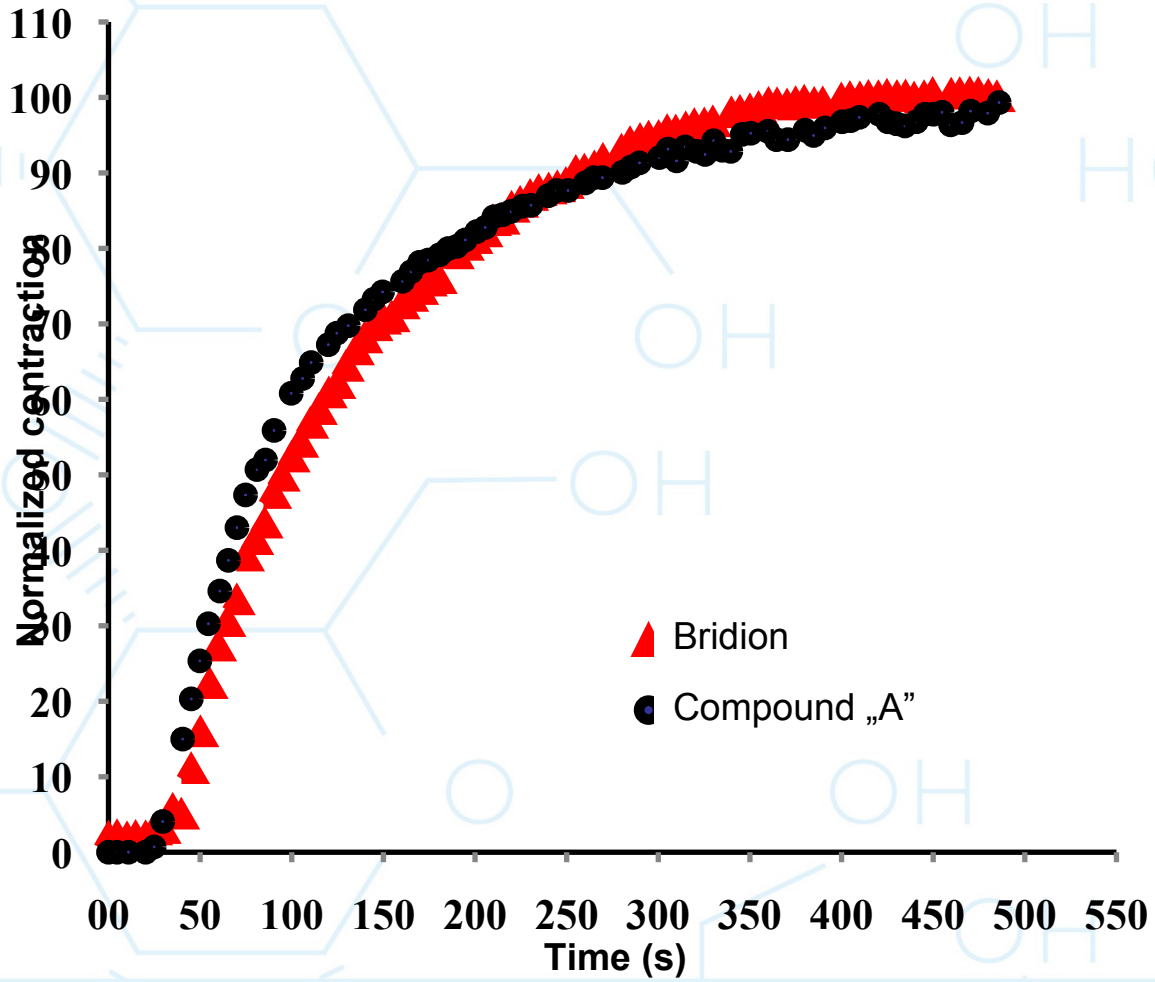


Vecuronium



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

CYCLODEXTRINS AS APIs
NEURODEGENERATIVE DISEASES

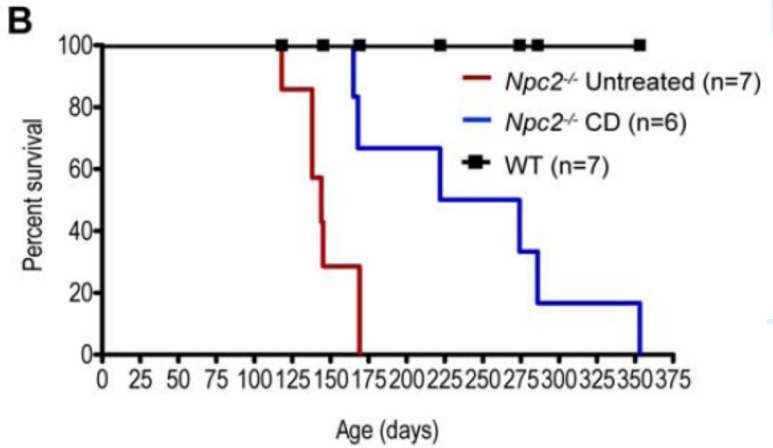
PNAS

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

Lina Abi-Mosleh, Rodney E. Infante, Arun Radhakrishnan[1], Joseph L. Goldstein[2], and Michael S. Brown[2]

Department of Molecular Genetics, University of Texas Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, TX 75390-9046

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



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
ONGOING EVALUATIONS

CNS diseases

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

Cardiovascular diseases

Atherosclerosis

Oncology

Anticancer agents

Infectious diseases

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

Respiratory diseases

- Asthma
- COPD
- Cystic fibrosis

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 papers

Expertise & Technology

Custom synthesis

Drug solubilization and stabilization

Further industrial applications

Cyclodextrin-related analytics

Stability testing

GMP-conform manufacturing

Feasibility studies

DEXOLVE™

CYCLOLAB'S EVOLUTION

Research and development studies, exploring potential in CDs (1975-)

Spin-off company, establishment (1989)

ISO 9001 certificate

Establishment of a smaller GMP facility (2002)

Audited and approved by the Hungarian Pharmaceutical Regulatory Authority (2007)

Development of a proprietary technology for SBECD production (2006-2008)

DMF accepted by the FDA (2008)

Dedicated GMP plant established for the SBECD production (2010)

EudraGMDP registration (2014), annual capacity for SBECD is over 15,000 kg (2017)

Successful regulatory inspection (OGYÉI) and obtaining cGMP license for Dexolve™ (2018 and 2022)

DEXOLVE™

TEAM AND RESOURCES

Team

18 qualified cyclodextrin scientists

7 PhDs

2 MBAs

3 members in the QA

By profession:

- chemists
- chemical engineers
- biologists
- pharmacists

14 qualified technicians and operators

sales, business dev, logistics, admin

Resources

2,000 m2 (own property) facility

2 galenic/technology labs

4 analytical labs (GC, HPLC, MS and CZE)

2 synthetic chemistry labs

150 m2 cGMP compliant clean room

350 m2 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

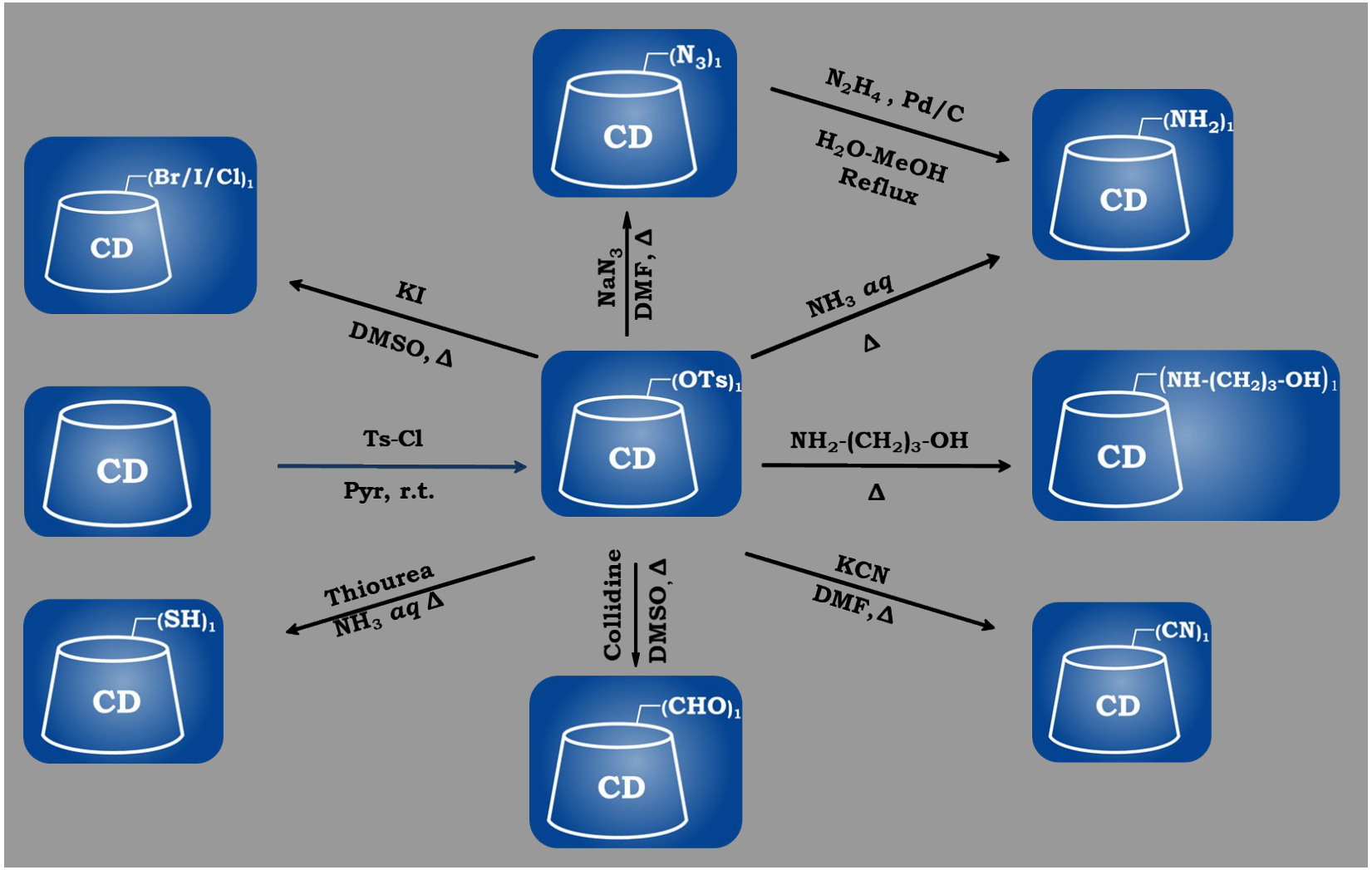
Products

- 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

DEXOLVE™

ABOUT CYCLOLAB

EXAMPLES ON THE FLEXIBILITY OF DERIVATIZATION



ABOUT CYCLOLAB
CUSTOM cGMP MANUFACTURING

GMP Synthesis

Regulatory license for manufacture of APIs and clinical investigational products

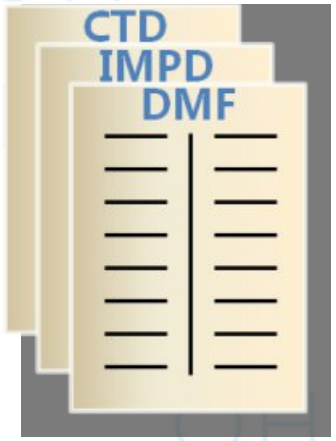
Process optimization

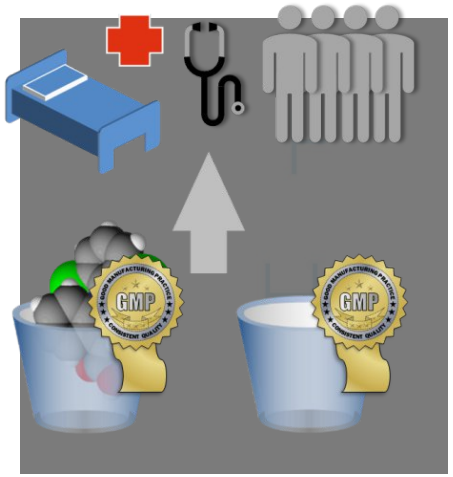
Scale-up

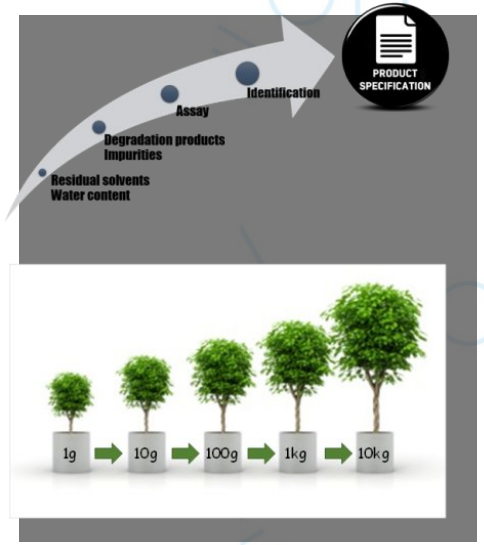
Record with CDs as APIs

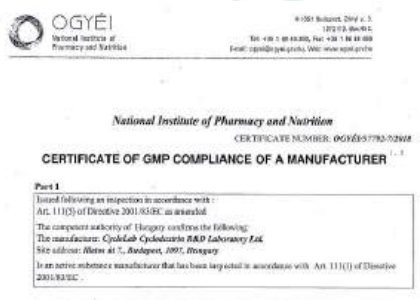
Regulatory support

cGMP license









OGYÉI

National Institute of Pharmacy and Nutrition

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER

DEXOLVE™

PAT-controlled semi-industrial reactor at Cyclolab Ltd.

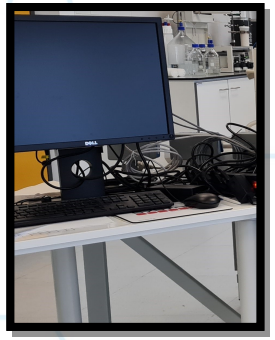
5 l addition funnel

automated burette

20 l glass reactor

thermostat

special overhead



controlling PC

weight-based liquid dosing pump

mechanical stirrer

- liquid thermometer
- air thermometer
- pressure sensor

CRITICAL PROCESS PARAMETERS

Critical parameters are dependant on the specific process/reaction.

Usual critical parameters:

- temperature
- speed of reagent dosage
- pressure
- reaction-time
- concentration
- stirring
- etc.

We can control:

- temperature of reactor
- stirring speed
- weight-based liquid addition with pump
- precise liquid addition with burette
- sensors

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

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

CD-guest interaction studies
CD-based chiral separations
Assay, impurity tests
Bioanalytical investigations

DEXOLVE™

COMPANY CONTACTS

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