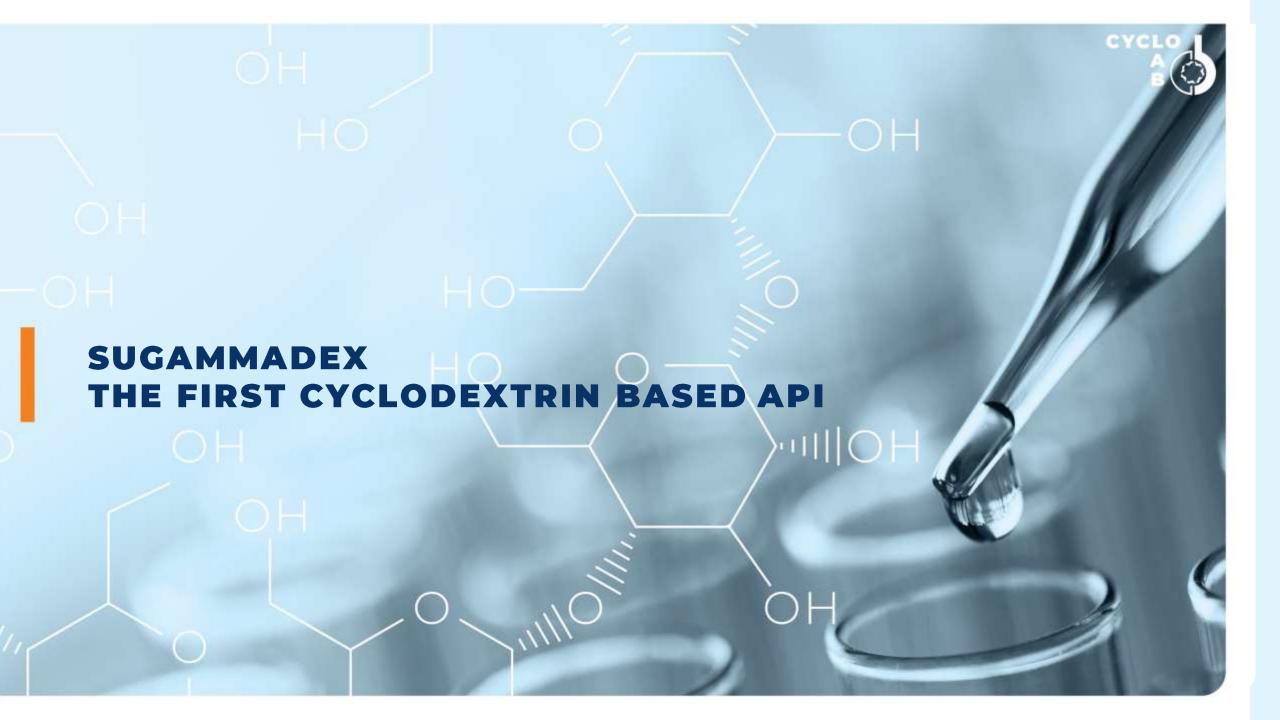


GETTING THE BEST OUT OF CYCLODEXTRINS

Technology presentation





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



SUGAMMADEX CONTRACT SERVICES AND IMPURITY STANDARDS



Contract services:

synthesis

process and formulation development

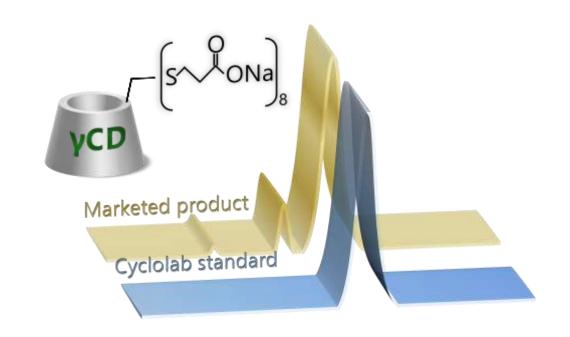
contract analysis

IP/FTO search and evaluation

Standards:

process intermediates

process impurities





SUGAMMADEX BACKGROUND



Sugammadex (SGM) is one of the greatest successes in the history of cyclodextrins.

There is an increasing interest for this product and for the development of Sugammadex, since the approval of Bridion, a blockbuster drug, by the FDA.

SGM is used in anesthesia as an injectable antidote for rocuronium and similar neuromuscular blocking agents.

CycloLab has vast experience in the production of Per-6-halogeno-gamma-CD intermediates and has developed Sugammadex via various process routes and related compounds, supported by sensitive analytical tools to characterize the products.



SUGAMMADEX WHAT DOES CYCLOLAB OFFER?



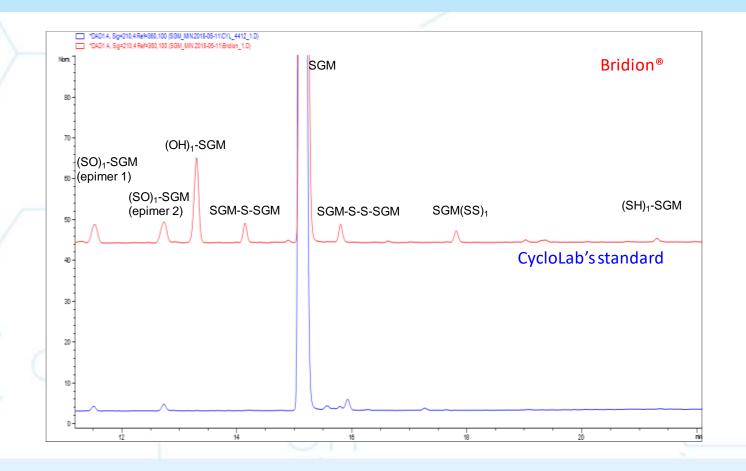
- Supplying the key intermediates (Per-6-halogeno-gamma-CDs) for the synthesis of the API (on commercial scale)
- Assisting in the optimization of the API production (from chemical and purification perspectives)
- Comparing samples (both API and final formulations) using sensitive analytical methods (capable of separating 20-30 potential impurities in the API)
- Providing high purity standards (intermediates, Sugammadex, key process impurities) to quantify the true and accurate purity of the compounds
- Providing formulation development and analytical services for the final product
- Conducting literature- and patent search for FTO/IP evaluation



SUGAMMADEX TECHNOLOGY AND ANALYSIS



Using CycloLab's technology, a standard material with exceptional quality outperforming the originator's in all aspects can be achieved.

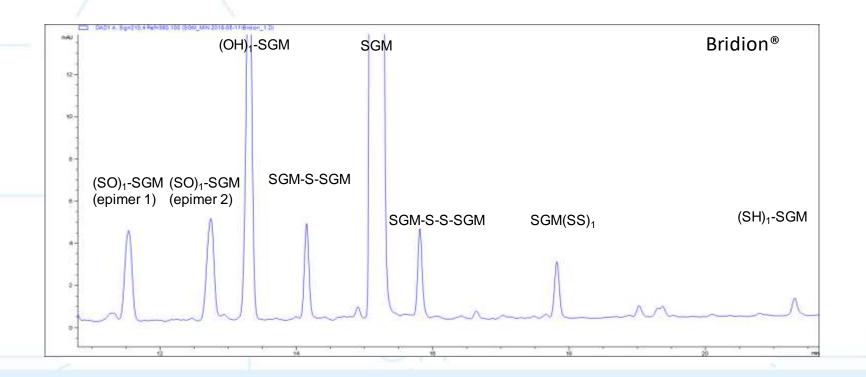




SUGAMMADEX TECHNOLOGY AND ANALYSIS



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.





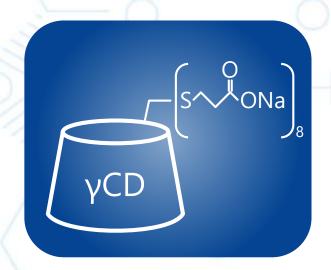
SUGAMMADEX RAW MATERIAL AND PRODUCT STANDARDS





Gamma-cyclodextrin Working Standard:

Declaration by CycloLab



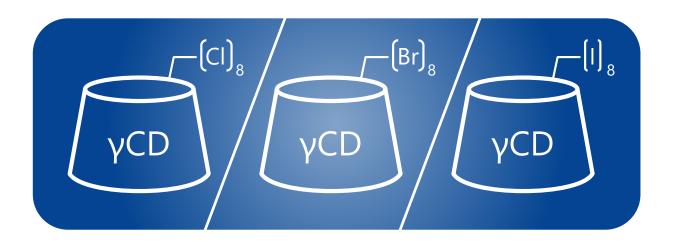
Sugammadex Primary reference standard:

- >99.0% purity (on dry substance)
- Identification by NMR, IR, HPLC and HPLC-MS



SUGAMMADEX PROCESS INTERMEDIATE STANDARDS





Per-6-halogeno-gamma-cyclodextrin primary standards:

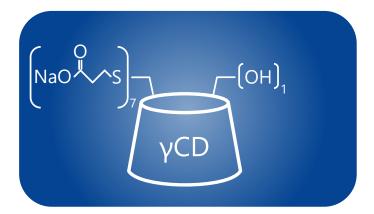
- Available for any chosen synthetic route (chloro-, bromo- or iodo derivative)
- >90% content
- Identification by NMR, IR

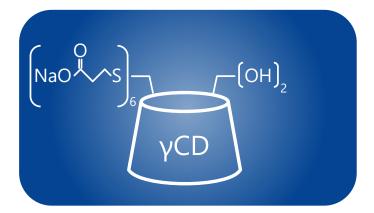




Mono-OH- and Di-OH-Sugammadex:

- >95% (Area%) with proprietary HPLC method, DAD detection, peak purity proven by LC-MS
- Identification by NMR, IR, HPLC-MS
- Residual solvents by TGM-MS and residual salts by CE



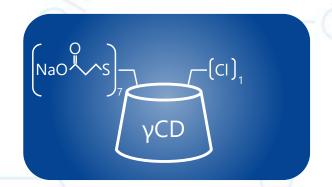


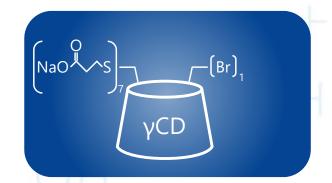


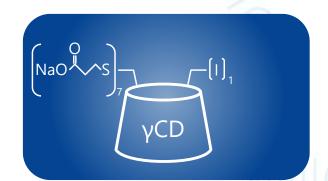


Mono-halogeno-Sugammadex:

- Available for all synthetic routes
- Minimum >90% (Area%) with proprietary HPLC method, DAD detection, peak purity proven by LC-MS
- Identification by NMR, IR, HPLC-MS
- Residual solvents by TGM-MS and residual salts by CE















Typical analysis:

- Minimum >90% (Area%) with proprietary HPLC method, DAD detection, peak purity proven by LC-MS
- Identification by NMR, IR, HPLC-MS
- Residual solvents by TGM-MS and residual salts by CE



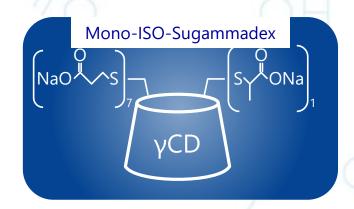












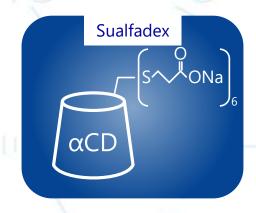


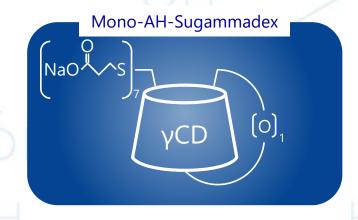


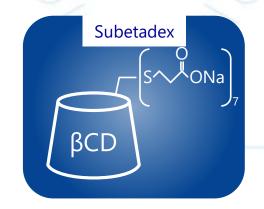
For typical analysis see slide 12

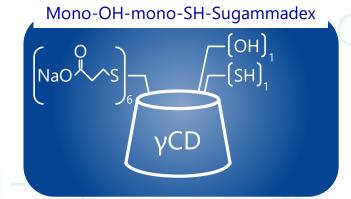


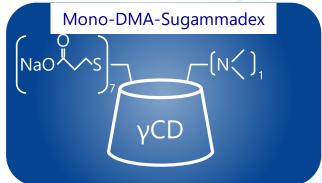










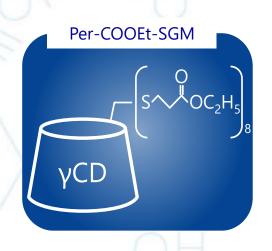


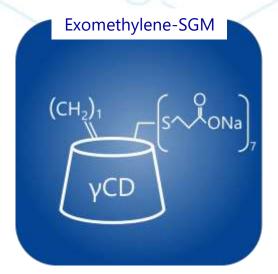






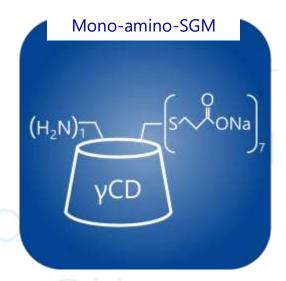








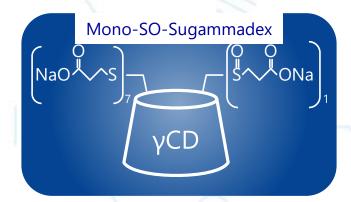




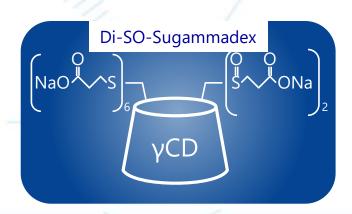




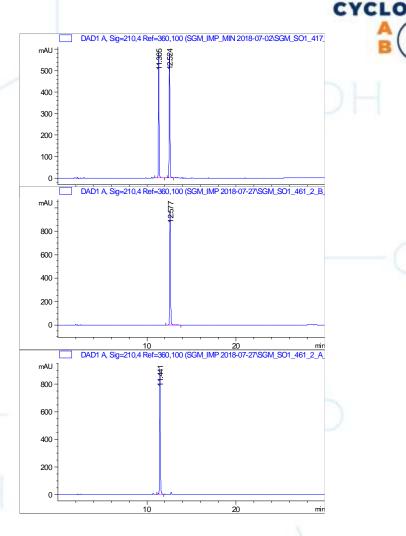
For typical analysis see slide 12



This compound is a mixture of two epimers. With our purification method these epimers were separated. The epimer mixture and the separate epimers are commercial available.



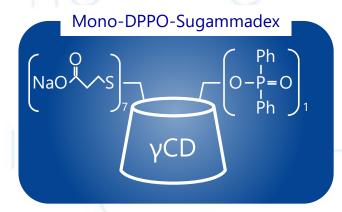
The disulfoxide derivative has also been prepared as mixture of several isomers.





SUGAMMADEX PROCESS IMPURITIES UNDER DEVELOPMENT

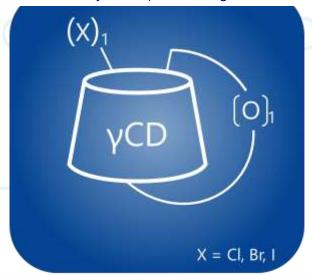






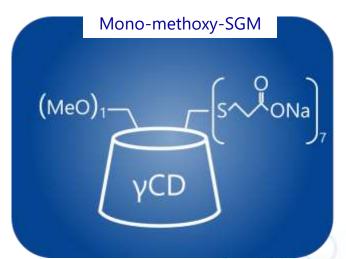


Mono-anhydro-heptakis-halogeno-GCD



Contact us for any other impurities you identified in your generic Sugammadex!







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



SUGAMMADEX

COMPANY CONTACTS

CYCLOLAB CYCLODEXTRIN RESEARCH & DEVELOPMENT LABORATORY LTD.

Budapest, P.O. Box 435, H-1525 Hungary

Location: Illatos út 7., Budapest, H-1097- Hungary

Tel: (+36) 1-347-60-70

E-mail: info@cyclolab.hu

Web: http://www.cyclolab.hu

CONTACT PERSON

Sales department

E-mail: commerce@cyclolab.hu

István Puskás

Scientific Director

E-mail: istvan.puskas@cyclolab.hu

