

# Cyclodextrins in biotechnology



#### The Cyclodextrin Company What are cyclodextrins (CDs)?

• Composed of sugar units

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- Cyclic, doughnut-shaped molecules
- Naturally occurring compounds produced from plants (no animal origin!)
- Used in food, pharmaceuticals, drug delivery, chemical industries, agriculture, etc.



**Reversible inclusion complex formation** 

- CDs enhance the solubility of complexed substrates (substitute detergents and co-solvents)

- CDs do not damage the microbial cells or the enzymes

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- CDs intensify the enzymatic conversion of lipophilic substrates
- CDs improve the yield of product-inhibited fermentations

- Organic toxic compounds are tolerated by microbes in higher concentrations

- Compounds in small amounts can be isolated simply from complicated mixtures

- CDs complexes can substitute for mammalian serum in tissue cultures

- Unstable and/or insoluble proteins can be dissolved and stabilized in aqueous solution



**CycloLab is the world's only all-around Cyclodextrin Service Provider** 

**Our services include:** 

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- Supplying cyclodextrins for commercial products and product development;
- Screening cyclodextrin derivatives to find the right candidate for the request of customers;
- Providing formulation development services, composition optimization, stability assessment;
- Offering analytical services to characterize complexes and products;
- Preparing pilot-scale amounts for cyclodextrin complexes under GMP for development purposes;
- Assisting in compilation of regulatory documentation.

# For more information please click <u>here</u>



# **Biosynthesis by fermentation**



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Streptomyces rochei volubilis



Macrolides Antitumor-Antibiotic



- Enhanced
   production of
   antibiotics
- Diminished byproducts formation
- Decreased product inhibition

Sawada et al.: Appl. Microbiol. Biotechnol. 1990, 32, 556559



Palmitic acid

	Bordetella pertussis cell growth						<b>Complexation of</b>
	Inoculum size cells in 5 µL	0	α	β	Y	DIMEB	fatty acids (growth
	10 <sup>3</sup>	-	-	-	-	++	inhibitors)
	104	-	-	-	-	+++	results in
	10 <sup>5</sup>	-	-	-	-	+++	
	10 <sup>6</sup>	-	++	+	+	+++	enhanced cell
-	10 <sup>7</sup>	-	+++	++	++	+++	growth and
	- no growth	+ < 100 colonies	++ 10 <sup>2</sup> to 10 <sup>3</sup> colonies	+++ full growth			toxin production

DIMEB (dimethyl beta-cyclodextrin) increases pertussin toxin production 100-fold

Imaizumi et al.: Infect. Immun. 1983, 41, 1138-1143



# Serum-free culture media



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Mycobacterium leprae

#### Water-soluble lipid/CD complexes:

Cultivation of non-cultivable Mycobacterium leprae; Serum substitutes for lymphoblast cells; Non-cholesterol interacting fatty acid/CD complexes



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
Rajnavölgyi *et al.* Beilstein J.
Org. Chem. 2014, 10, 3152–3160

# **Cyclodextrin in artificial fertilization**

- Improvement of the quality of semen by cholesterol supplementation with cholesterol loaded methyl BCD (cryopreservation)
- Enhancement of capacitation and fertility rate by preincubation of thawed sperms with methyl BCD



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#### Polyphenol oxidase



chlorogenic acid (and other polyphenols)

Browning

• Complete inhibition of browning by soluble CDs

# $\alpha$ CD > maltosyl $\beta$ CD > $\beta$ CD

Hicks *et al.*: J. Agric. Food Chem. 1996, 44, 2098-2101 Lopez-Nicholas *et al.*: J. Agric. Food Chem. 2007, 55, 5312-5319

### **CD-assisted purification of waste water and soil**

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Improved solubility/ bioavailability of the pollutants
Improved cell growth
Protection of the biological sludge in the waste water plants
Enhanced microbial

decomposition of contaminants





Yoshii *et al.* Biol. J. Armenia, 2001, 18, 226-236 Fenyvesi *et al.* Land Contam. Reclam. 2009, 17, 585-597

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