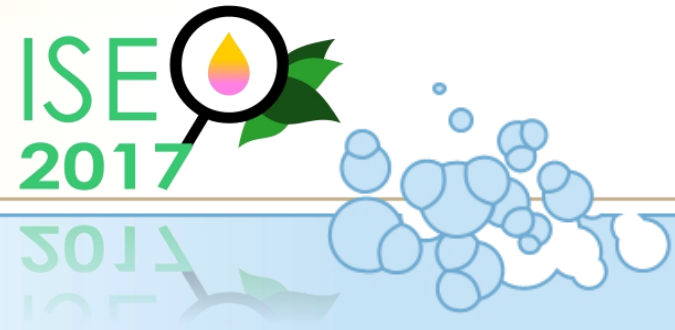


**CYCLOLAB**



*The Cyclodextrin Company*



# Cyclodextrin-based Molecular Coating for the Protection of Sensitive Essential Oils

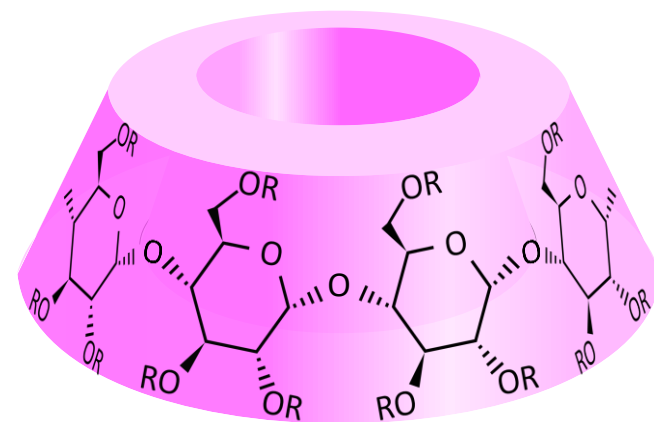
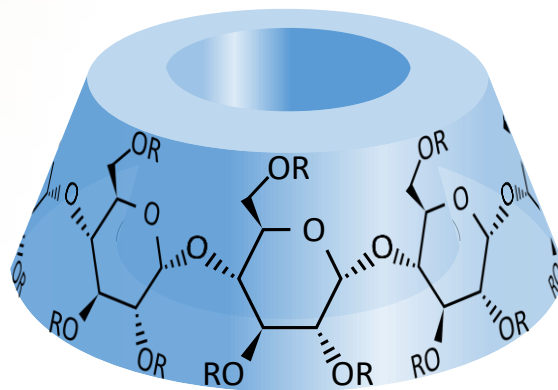
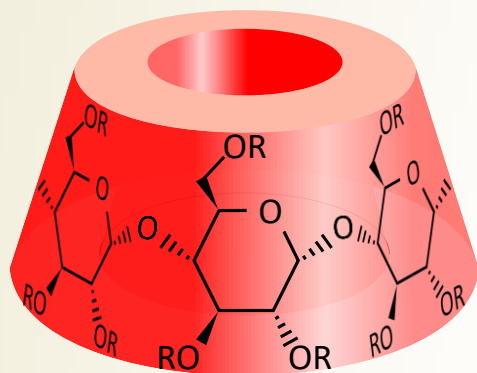
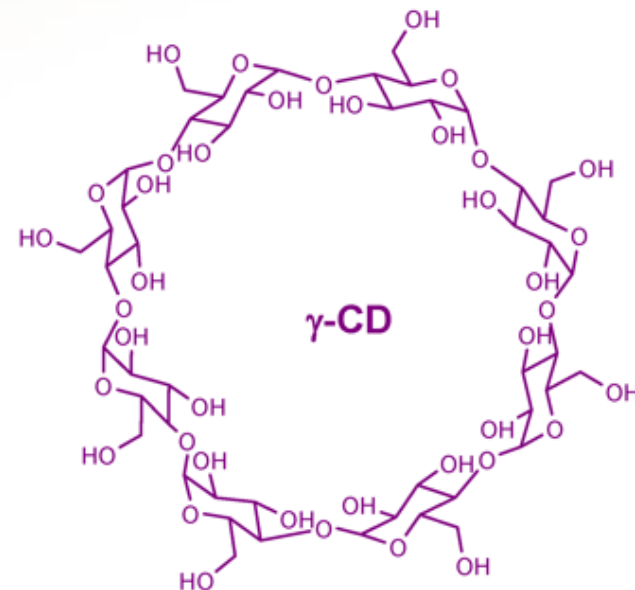
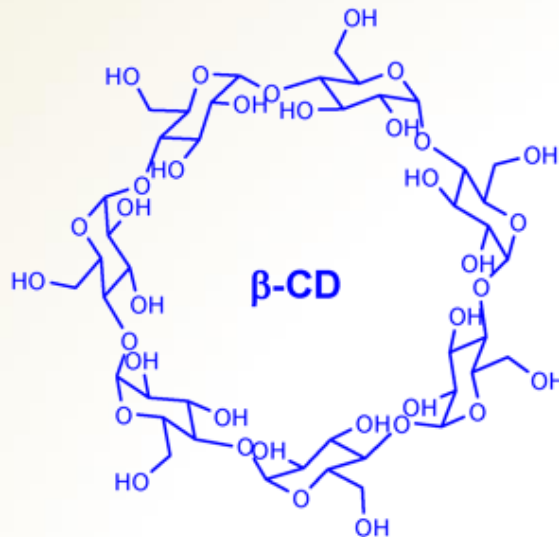
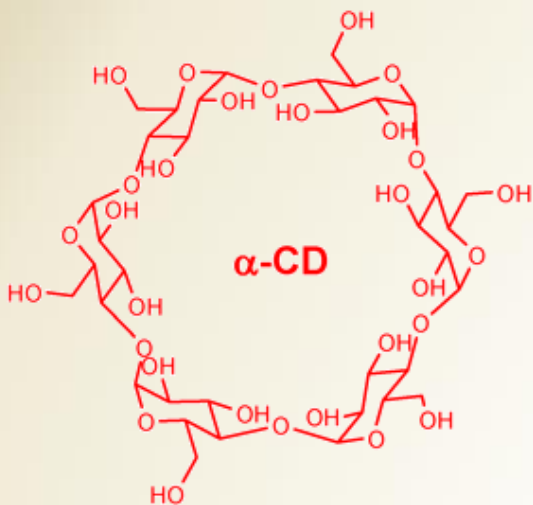


**Mihály Bálint**

ISEO 2017, Pécs, Hungary, 12 September 2017

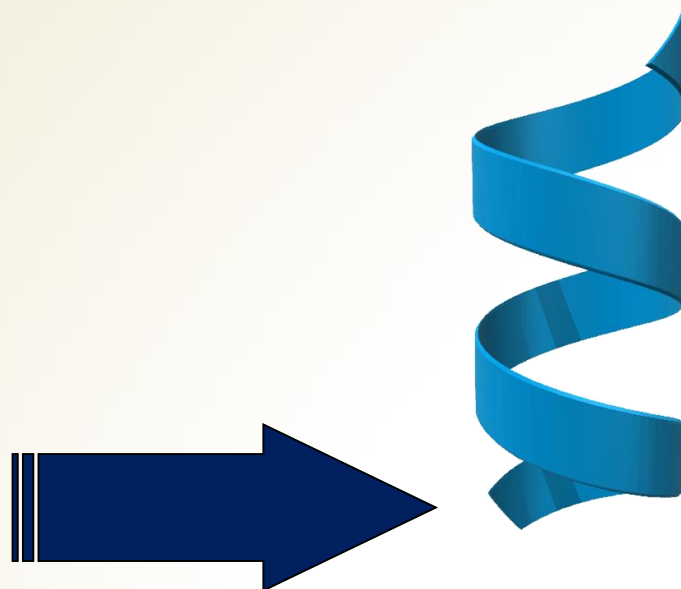
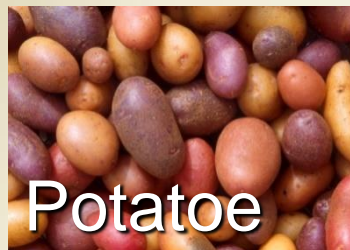


- **Cyclodextrins**
- **Cyclodextrin / essential oil inclusion complexes**
- **Regulatory status of cyclodextrins**
- **Marketed product examples**
- **Future prospects**

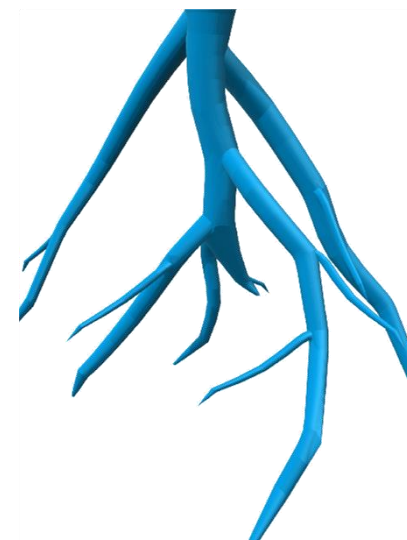
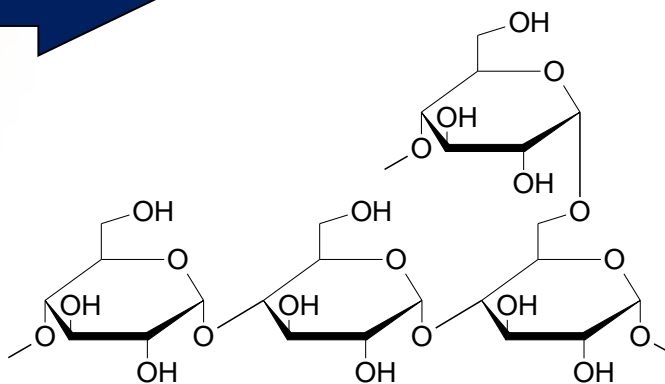
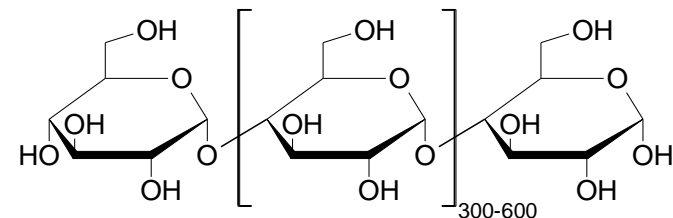




# Cyclodextrins

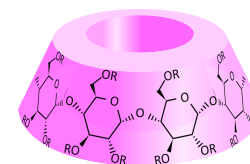
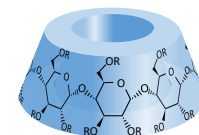
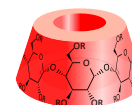
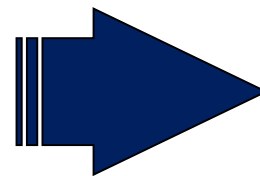
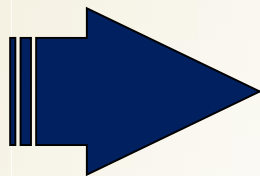
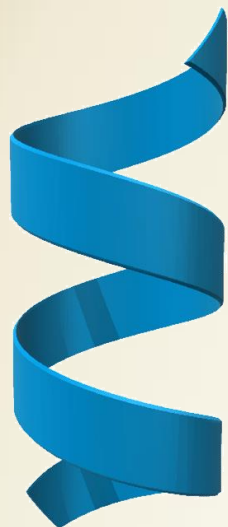


Amylose



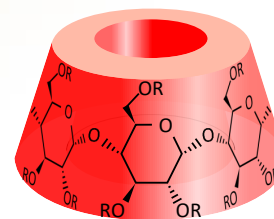
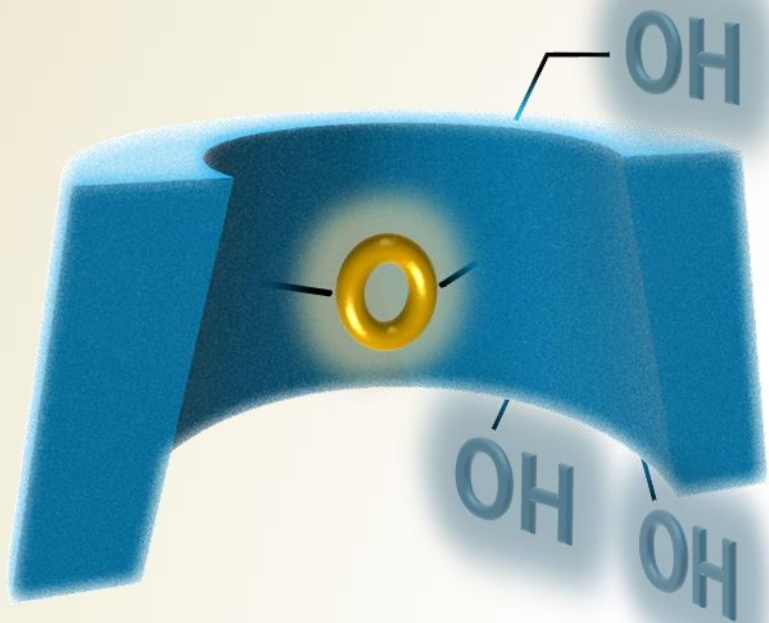
Amylopectin

Starch

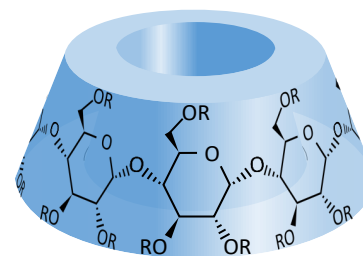


## CD Glycosyltransferase (Bacillus Macerans)

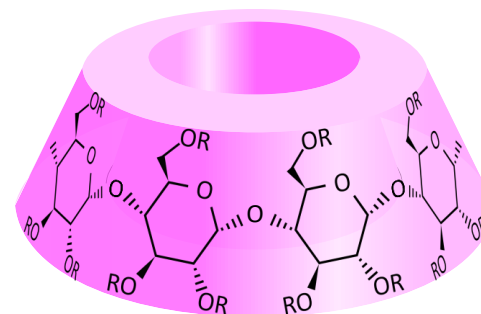
Conversion mixture



**α-CD**



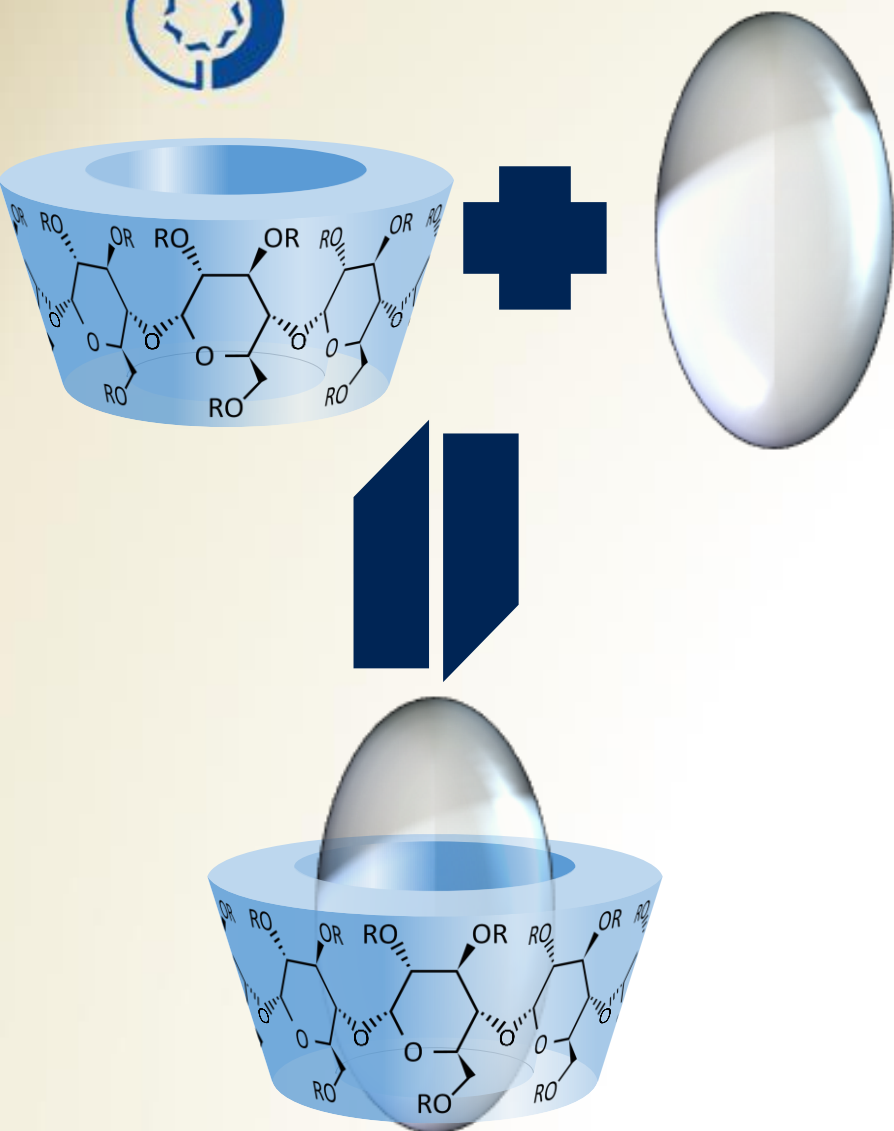
**β-CD**



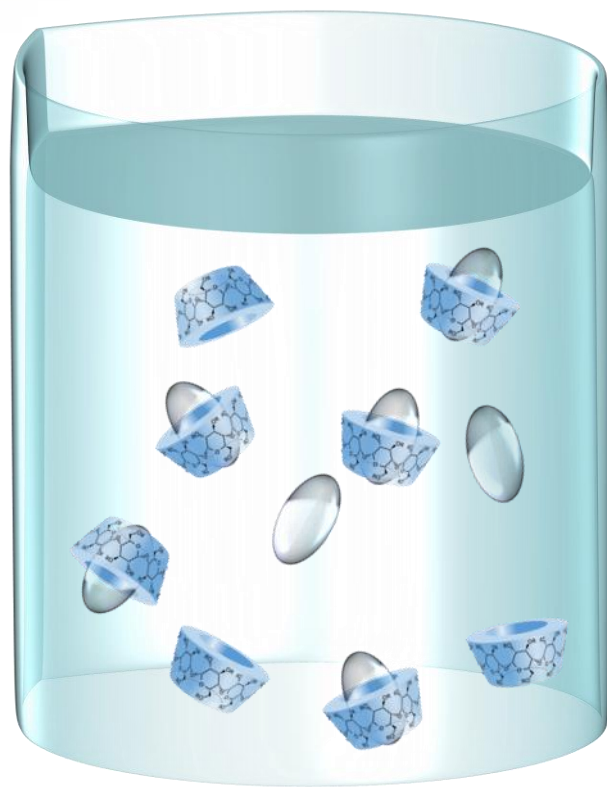
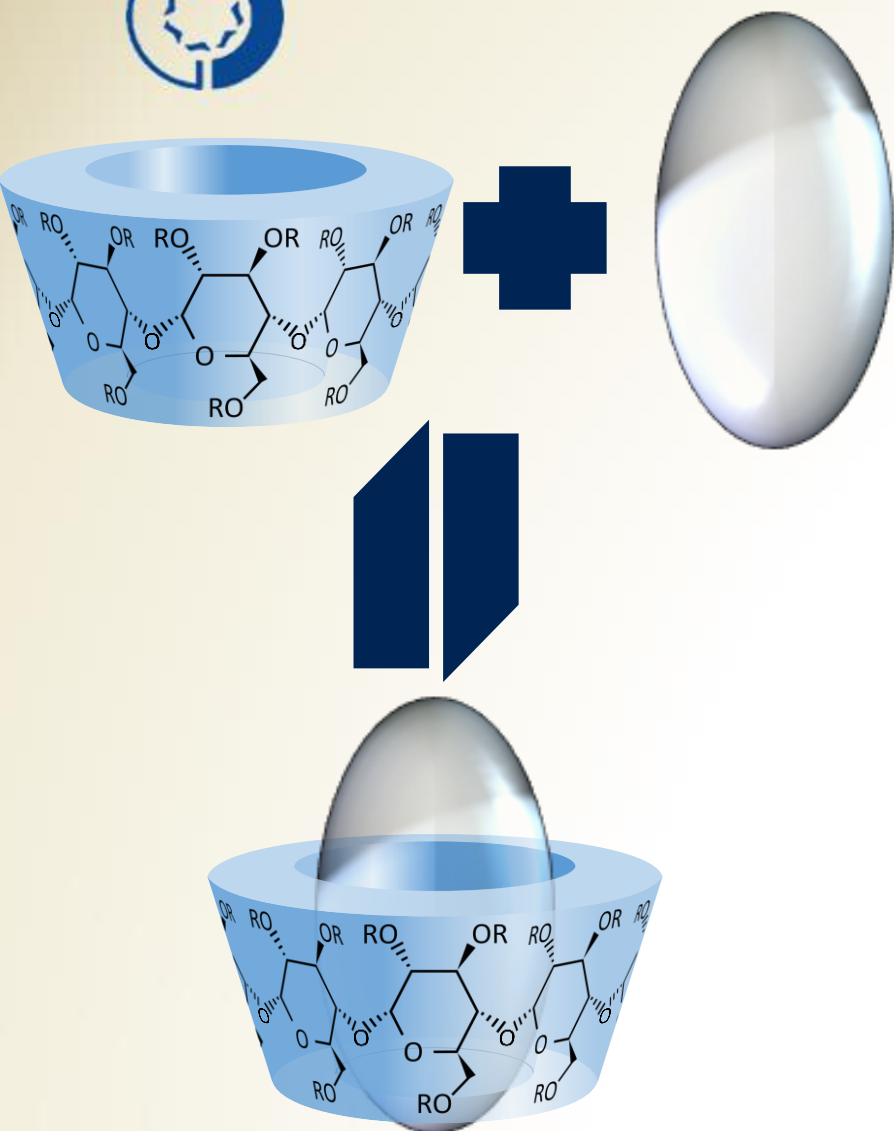
**γ-CD**



# Inclusion complexes

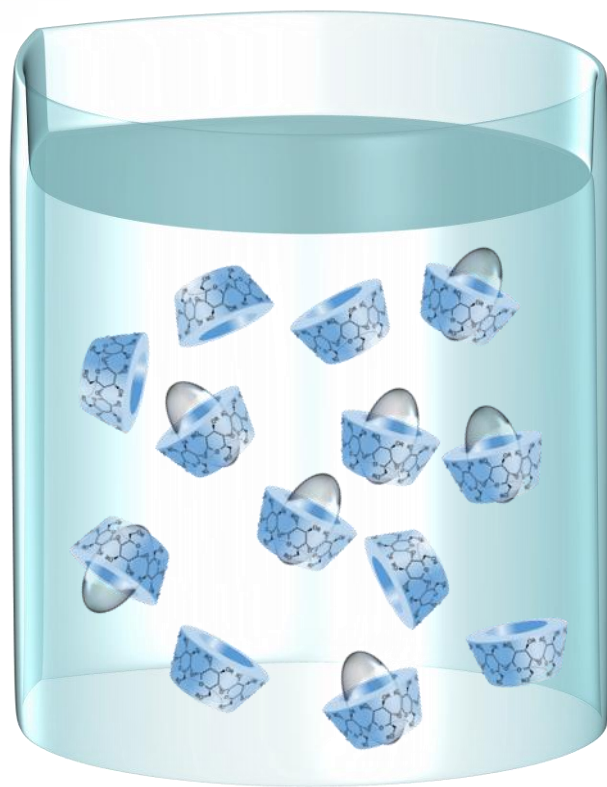
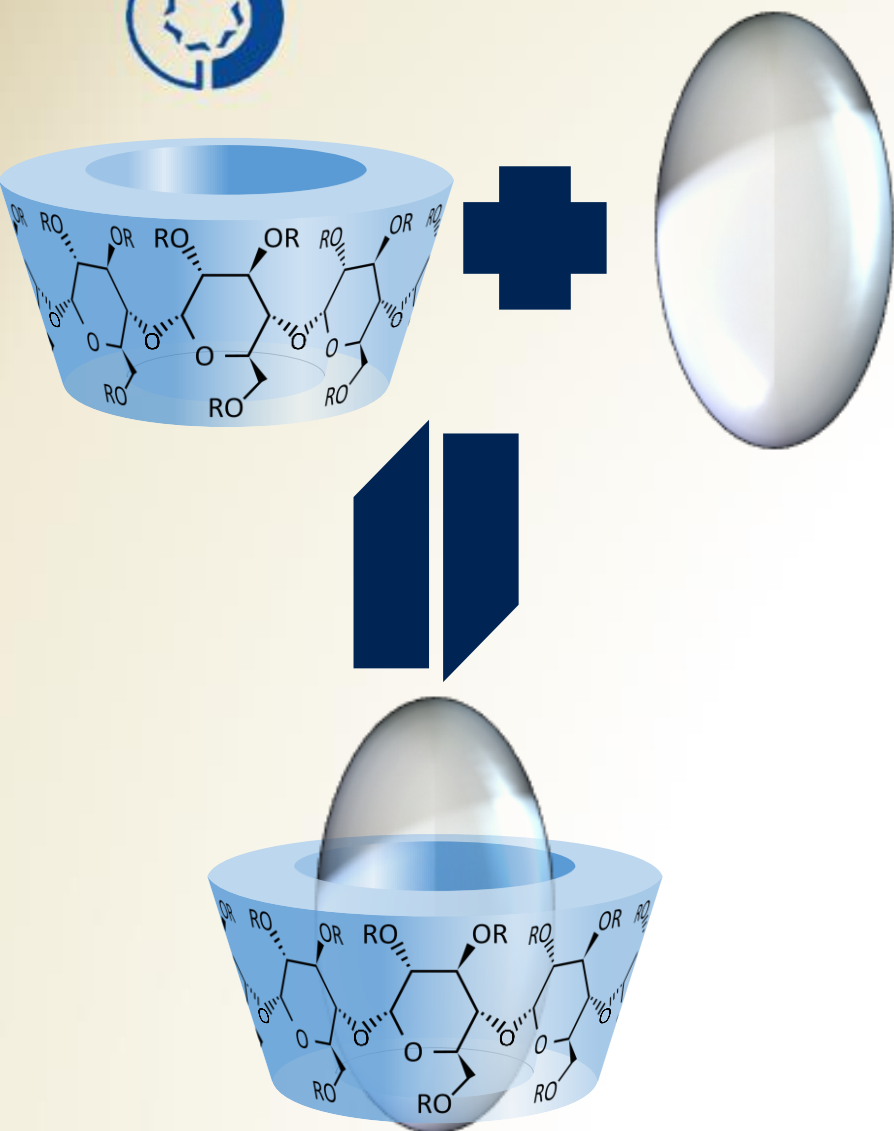


# Inclusion complexes





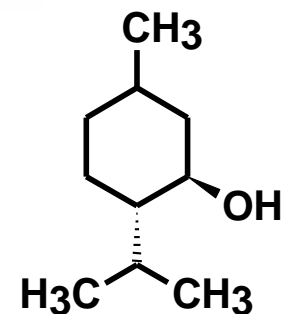
# Inclusion complexes



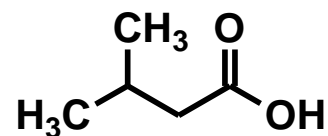


# Inclusion complexes

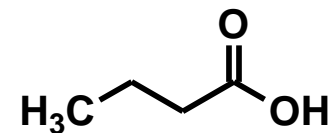
- Improvement of physical and chemical stability (volatile, oxygen-, light- and heat sensitive compounds)
- Reduction of undesirable tastes and odors
- Increased solubility in water
- Stable aqueous solutions of insoluble compounds can be prepared without the use of organic co-solvents or surfactants
- Enhanced rate of dissolution
- Improved wettability
- Liquids can be transformed into solid form
- Extended release of compounds
- Alleviation of local irritations (reduced side effects)
- Enhanced absorption
- Incompatible compounds can be mixed and used together in complexed form
- Stabilization of emulsions and suspensions



Menthol



Isovaleric acid



Butyric acid



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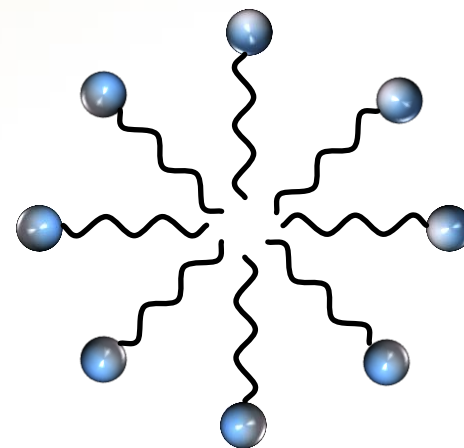
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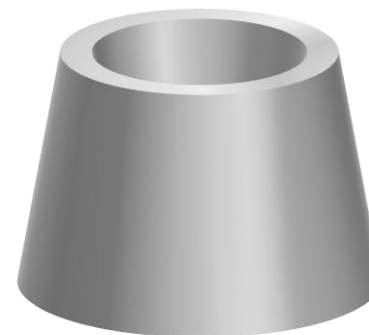
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vs





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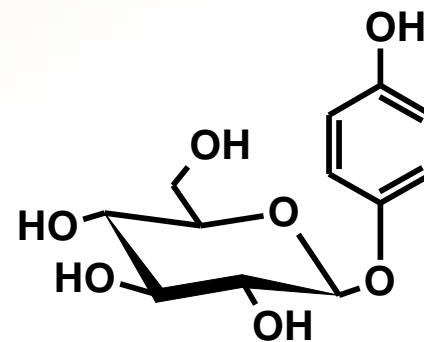
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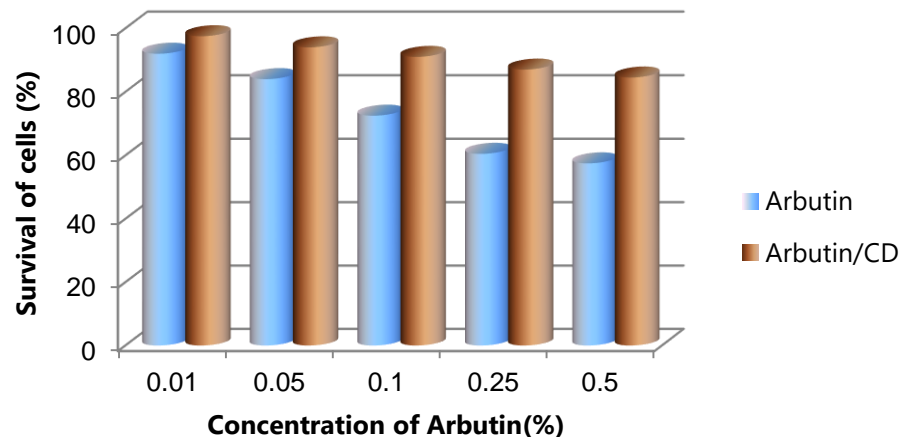
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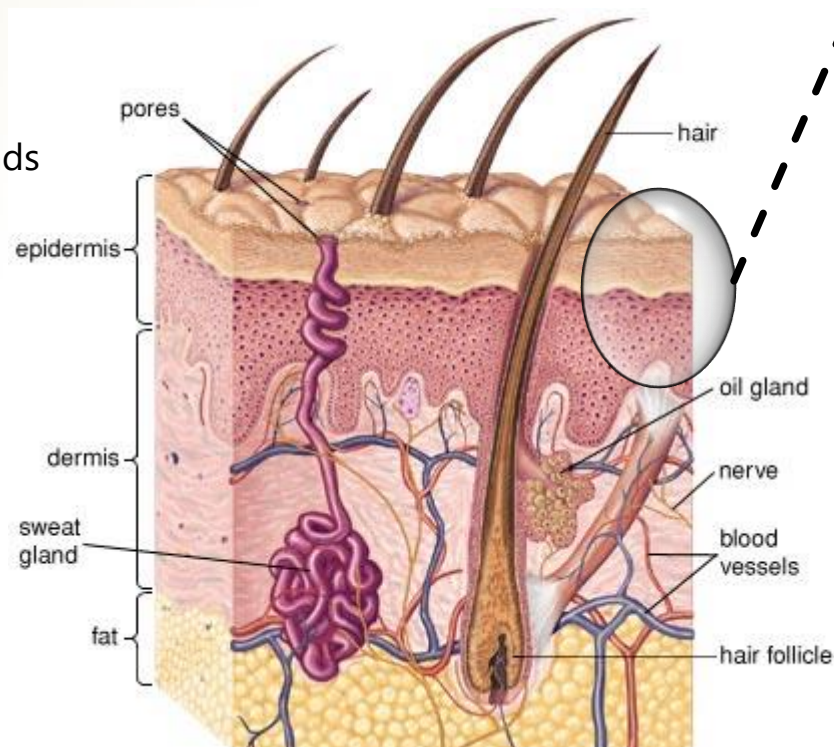


Arbutin

## Cytotoxicity of Arbutin



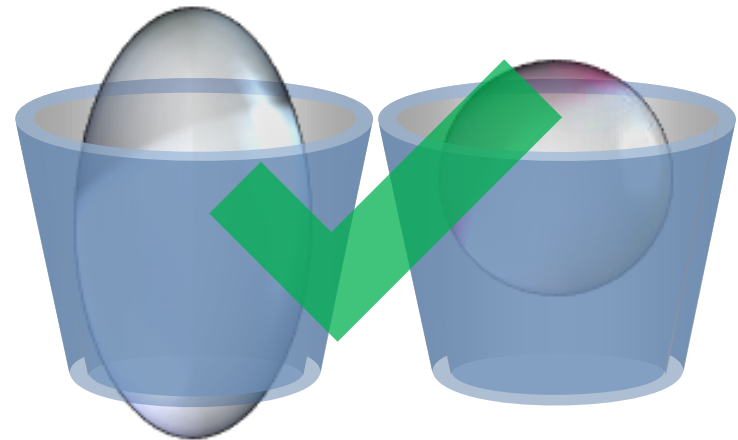
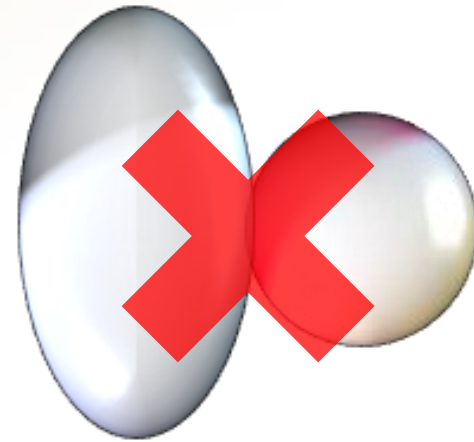
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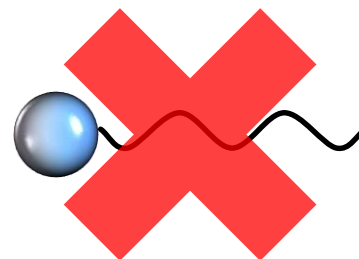






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# Inclusion complexes

## Methods of preparation of inclusion complexes:

**Coprecipitation**



**Coevaporation**

**Kneading**

**Mechanochemical  
activation**

**Sealed heating  
method**



# Inclusion complexes

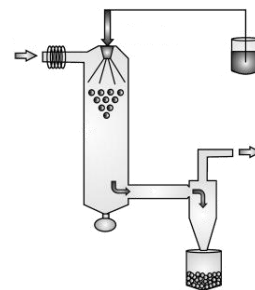
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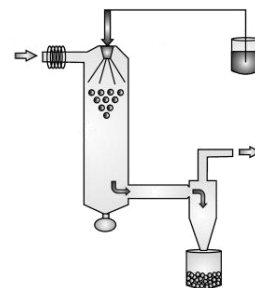
**Coprecipitation**



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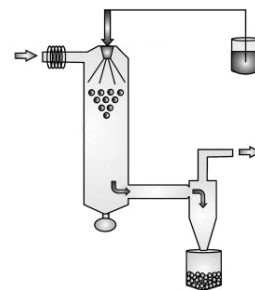
**Coprecipitation**



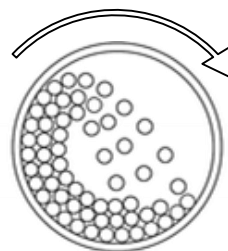
**Kneading**



**Sealed heating method**



**Coevaporation**



**Mechanochemical activation**

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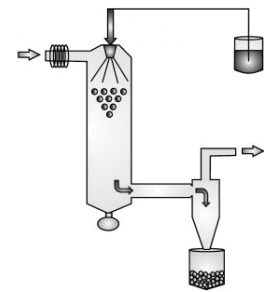
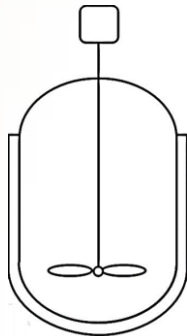
**Coprecipitation**



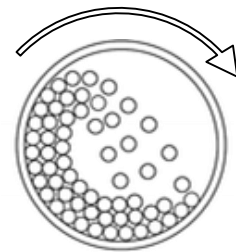
**Kneading**



**Sealed heating method**



**Coevaporation**



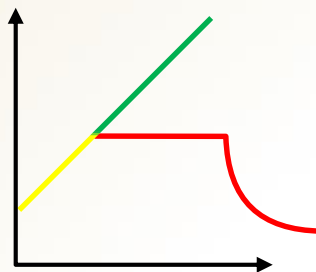
**Mechanochemical activation**



# Inclusion complexes

## Analysis of inclusion complexes:

Phase solubility study



HPLC

GC, head-space GC

CE

Thermoanalytical methods:  
TGA, DTG, DSC

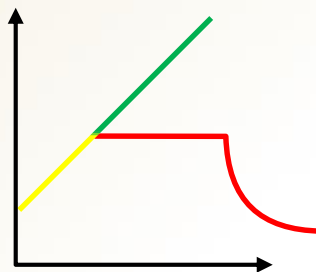
Spectroscopic methods: NMR,  
Raman, fluorescence, IR, UV



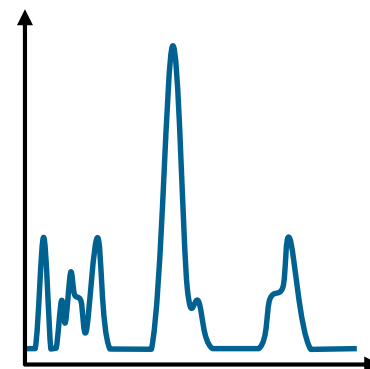
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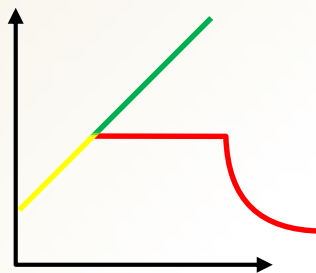




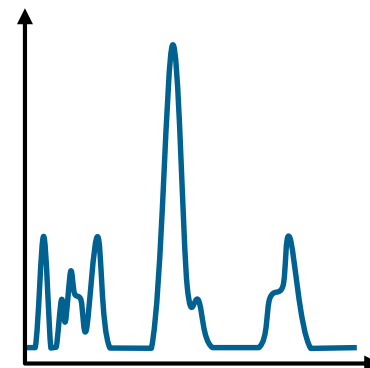
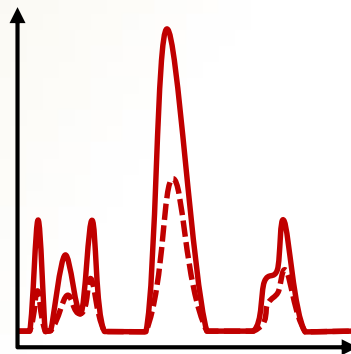
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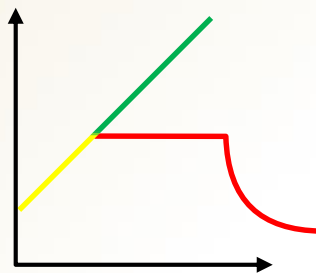
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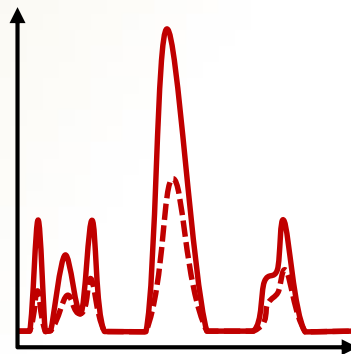
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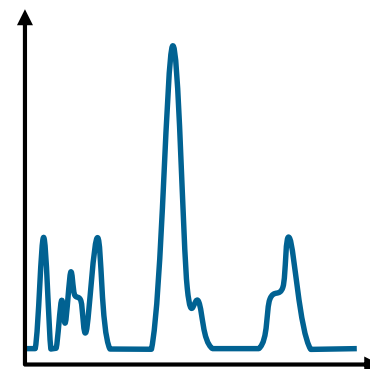
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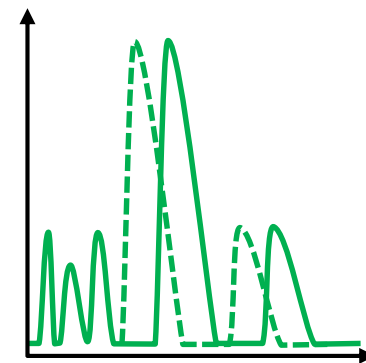
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HPLC

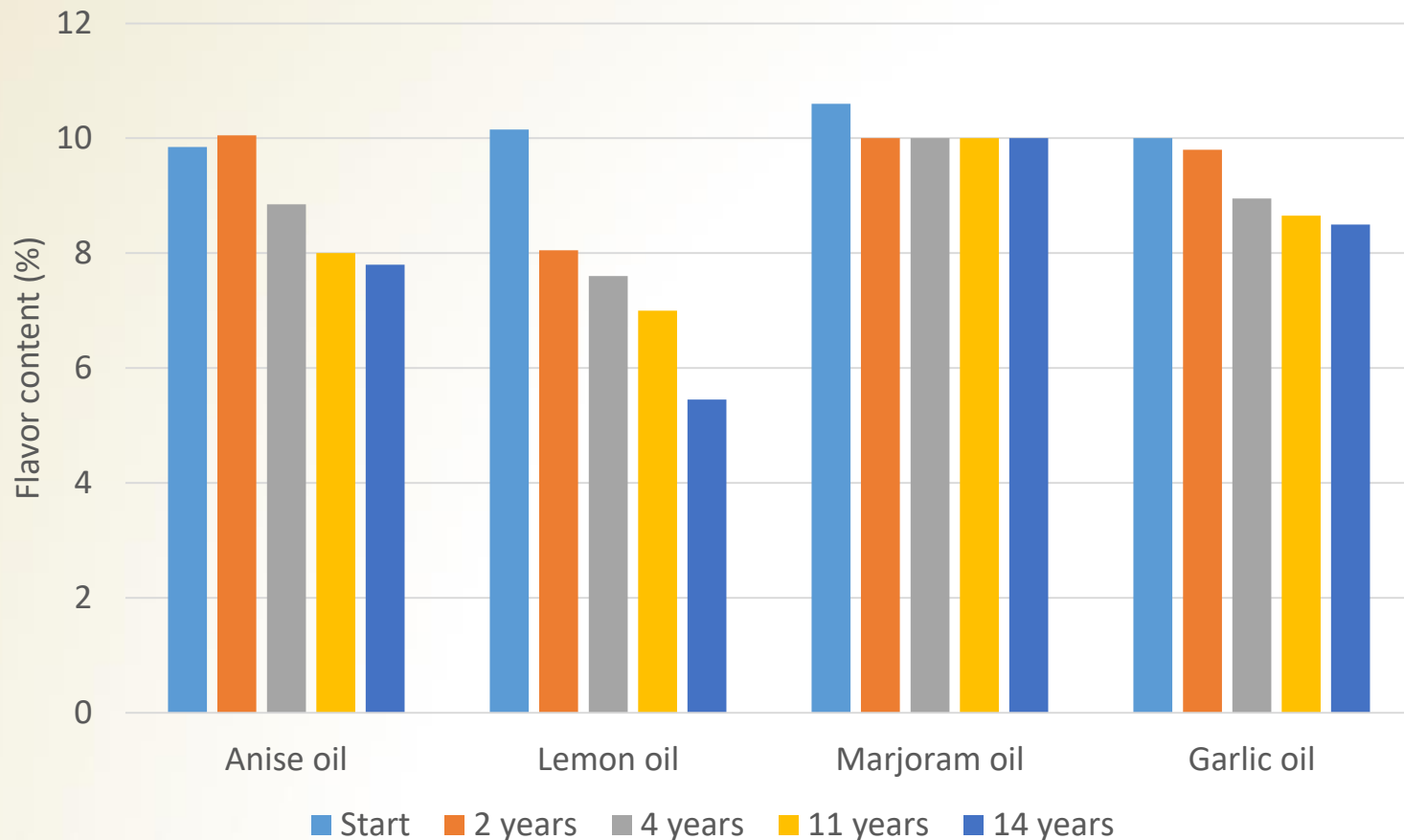


CE

Spectroscopic methods: NMR,  
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# Inclusion complexes





# Regulatory status in food

	<b>EU</b>	<b>USA</b>	<b>Japan</b>
<b><math>\alpha</math>CD</b>	<b>NOVEL FOOD INGREDIENT</b> (2008/413/EC Commission Decision)	<b>GRAS</b>	<b>NATURAL PRODUCT</b>
<b><math>\beta</math>CD</b>	<b>FOOD ADDITIVE</b> <ul style="list-style-type: none"> <li>• quantum satis, only foods in tablet and coated tablet form</li> <li>• max. 500 mg/l, only flavored powdered instant drinks</li> </ul>	<b>GRAS</b>	<b>NATURAL PRODUCT</b>
<b><math>\gamma</math>CD</b>	<b>NOVEL FOOD INGREDIENT</b> (2012/288/EU Commission Implementing Decision)	<b>GRAS</b>	<b>NATURAL PRODUCT</b>



Since 2007 nutrition and health claims made on foods within the EU are regulated by the 1924/2006/EC of the European Parliament and of the Council. In the EU Register on nutrition and health claims an approved claim can be found for  $\alpha$ CD:

**„Consumption of alpha-cyclodextrin as part of a starch-containing meal contributes to the reduction of the blood glucose rise after that meal“.**

The claim may be used for food which contains at least 5 g of alpha-cyclodextrin per 50 g of starch in a quantified portion as part of the meal.



# Regulatory status in pharmaceuticals

	<b>Monograph</b>	<b>Administration route of formulation</b>
<b><math>\alpha</math>CD</b>	USP, Ph.Eur., JP	Oral, ocular, parenteral
<b><math>\beta</math>CD</b>	USP, Ph.Eur., JP	Oral, nasal, rectal, dermal, ocular
<b><math>\gamma</math>CD</b>	USP, Ph.Eur., JP	Oral, dermal, parenteral
<b>HP<math>\beta</math>CD</b>	USP, Ph.Eur., JP	Oral, nasal, rectal, dermal, ocular, parenteral
<b>HP<math>\gamma</math>CD</b>	-	Ocular
<b>S<math>\beta</math>ECD</b>	USP, JP	Oral, nasal, rectal, dermal, ocular, parenteral
<b>RAME<math>\beta</math></b>	-	Nasal, ocular



# Regulatory status in cosmetics

EC Regulation (v.2)

## Search Results

Name or CAS/EC #  Version  Scope  Status

Go »

#	INCI Name/Substance Name	CAS No.	EC No.	Restriction/Annex/Ref #
1.	<a href="#">ACETYL CYCLODEXTRIN</a>	-	-	
2.	<a href="#">BRASSICA SPROUT EXTRACT</a>			
3.	<a href="#">CYCLODEXTRIN</a>	7585-39-9 / 12619-70-4	231-493-2	
4.	<a href="#">CYCLODEXTRIN CROSSPOLYMER</a>	-	-	
5.	<a href="#">CYCLODEXTRIN HYDROXYPROPYLTRIMONIUM CHLORIDE</a>	-	-	
6.	<a href="#">CYCLODEXTRIN LAURATE</a>			
7.	<a href="#">DIMALTOSYL CYCLODEXTRIN</a>	-	-	
8.	<a href="#">HYDROXYETHYL CYCLODEXTRIN</a>	-	-	
9.	<a href="#">HYDROXYPROPYL CYCLODEXTRIN</a>	128446-33-3 / 128446-35-5	- / -	
10.	<a href="#">MALTOSYL CYCLODEXTRIN</a>	104723-60-6	-	
11.	<a href="#">METHYL CYCLODEXTRIN</a>	128446-36-6	*603-270-3	
12.	<a href="#">SODIUM CYCLODEXTRIN SULFATE</a>	37191-69-8		
13.	<a href="#">SODIUM HYDROXYPROPYL CYCLODEXTRIN OCTENYLSUCCINATE</a>			

Total: 13

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# Regulatory status in cosmetics

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6.	<a href="#">CYCLODEXTRIN LAURATE</a>	-	-	-
7.	<a href="#">DIMALTOSYL CYCLODEXTRIN</a>	-	-	-
8.	<a href="#">HYDROXYETHYL CYCLODEXTRIN</a>	-	-	-
9.	<a href="#">HYDROXYPROPYL CYCLODEXTRIN</a>	128446-33-3 / 128446-35-5	- / -	-
10.	<a href="#">MALTOSYL CYCLODEXTRIN</a>	104723-60-6	-	-
11.	<a href="#">METHYL CYCLODEXTRIN</a>	128446-36-6	*603-270-3	-
12.	<a href="#">SODIUM CYCLODEXTRIN SULFATE</a>	37191-69-8	-	-
13.	<a href="#">SODIUM HYDROXYPROPYL CYCLODEXTRIN OCTENYLSUCCINATE</a>	-	-	-

EC Regulation (v

Total:

Total:





## CycloLab's product

**Lemon essential oil /  $\beta$ -cyclodextrin complex diluted with fructose**



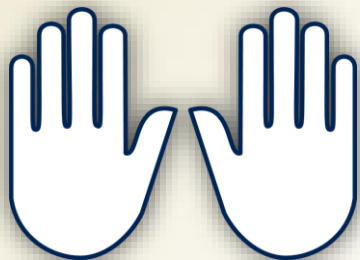
**Japanese market**

**Garlic essential oil /  $\beta$ -cyclodextrin complex  
in a spice mixture**

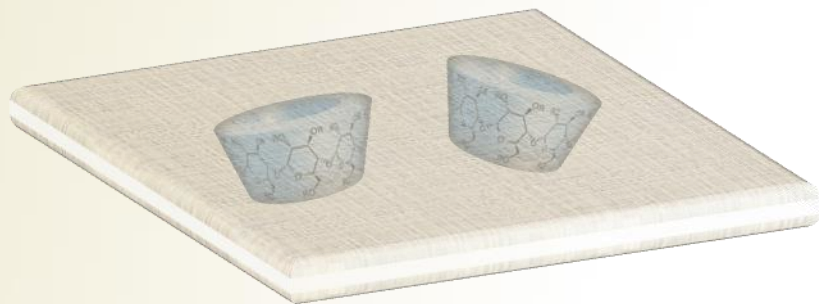


**Essential oils obtained as CD complexes in solid state (selection):**

**Garlic, tarragon, caraway, pepper, cinnamon, orange, bergamot, lemon, coriander, eucalyptus, clove, fennel, juniper, lavender, marjoram, basil, turpentine, sage, thyme and small-leaved mint essential oil**

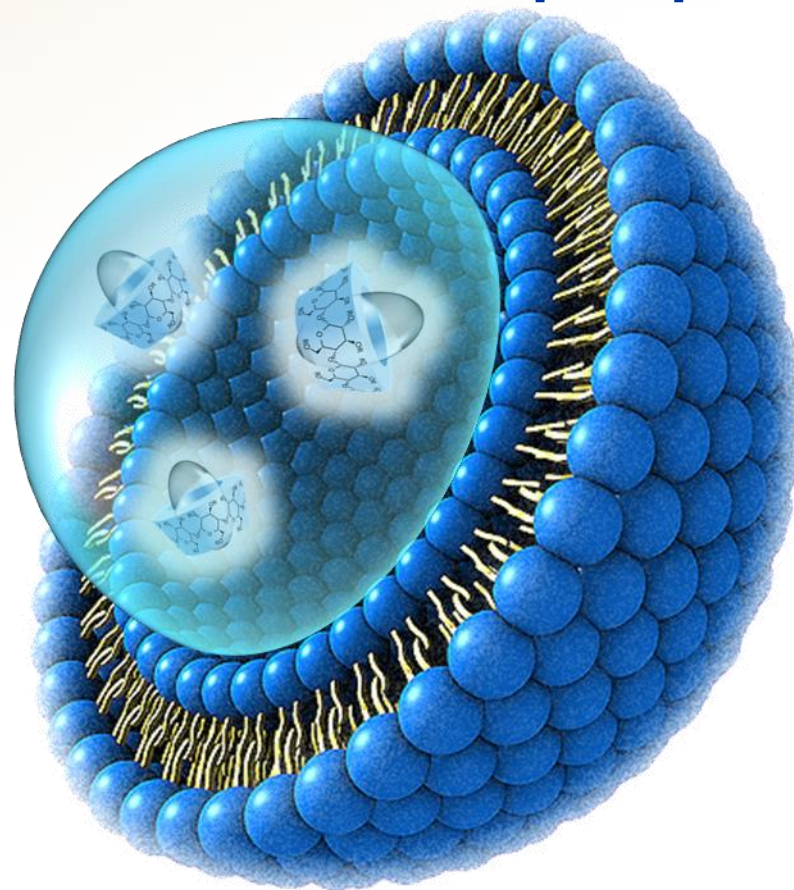


Krupcik, J.; Gorovenko, R.; Spanik, I.; Armstrong, D. W.; Sandra, P. **Enantioselective comprehensive two-dimensional gas chromatography of lavender essential oil** Journal of Separation Science, 2016, DOI:10.1002/jssc.201600986



Saini, S.; Quinot, D.; Lavoine, N.; Belgacem, M. N.; Bras, J.  **$\beta$ -Cyclodextrin-grafted TEMPO-oxidized cellulose nanofibers for sustained release of essential oil** Journal of Materials Science, 2017, 52, 3849-3861

## Future prospects



Sebaaly, C.; Charcosset, C.; Stainmesse, S.; Fessi, H.; Greige-Gerges, H. **Clove essential oil-in-cyclodextrin-in-liposomes in the aqueous and lyophilized states: From laboratory to large scale using a membrane contactor** Carbohydrate Polymers, 2016, 138, 75-85

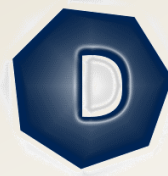


**Cyclodextrin-enabled  
Product Development**



**GMP Synthesis and  
Production**

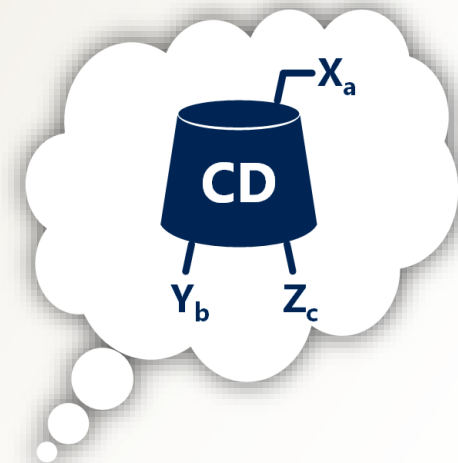
# CYCLOLAB



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**Analytical Services**



**Custom Cyclodextrin  
Synthesis**