

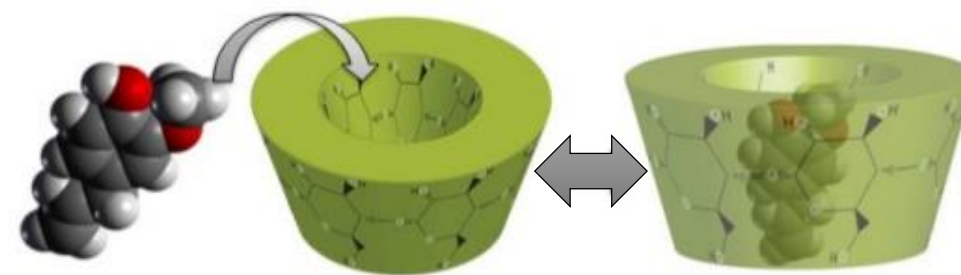
# GETTING THE BEST OUT OF CYCLODEXTRINS

Cyclodextrins in  
Agriculture



## What are cyclodextrins?

- 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



## Why use cyclodextrins?

- improvement of the physico-chemical characteristics of pesticides (lipophilicity, phase-transition, wettability, vapour pressure, solubility, reduced volatility etc.)
- improvement of shelf life (stabilization against light and biochemical degradation)
- minimizing the container/content interaction in packaged formulations
- prolonged or controlled release of active
- ensure homogeneity and content uniformity (molecular dispersity)
- enhancement of bioavailability and absorption
- reduction of the applied dose and thus the environmental pollution
- IP advantages (life-cycle management)

## CDs in agricultural use

16.3

### Application of Cyclodextrins in Agrochemistry

*Esmeralda Morillo*

The ability of cyclodextrins, CyDs, to form inclusion complexes with a wide variety of hydrophobic guest molecules has been used in agriculture. Their ability to alter the physical, chemical, and biological properties of guest molecules has been used for the preparation of new formulations of pesticides. CyDs form complexes with a wide variety of agricultural chemicals including herbicides, insecticides, fungicides, repellents, pheromones, and growth regulators [1, 2].

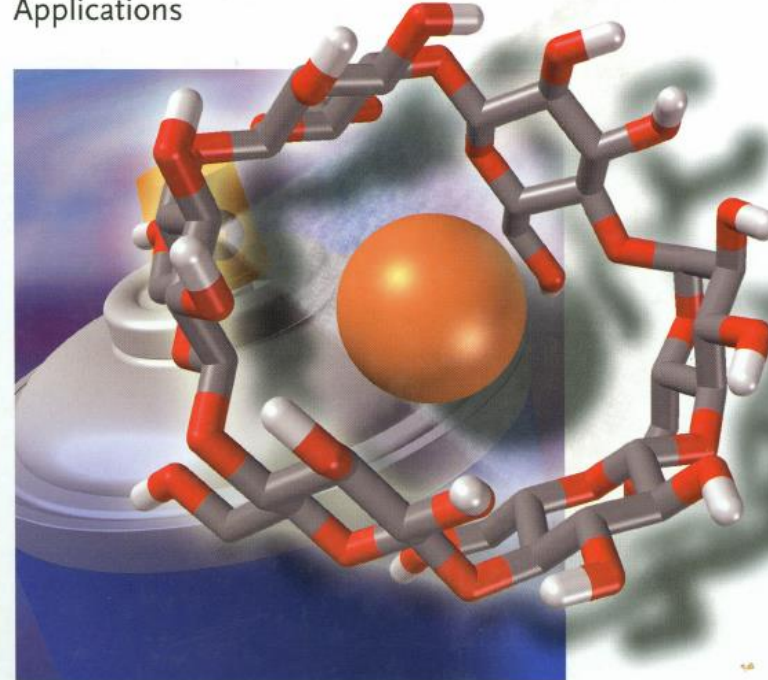
Each CyD has its own ability to form inclusion complexes with specific pesticides, depending on a proper fit of the pesticide molecule into the hydrophobic CyD cavity. The principal advantage is that the binding of pesticide molecules within the host molecule is not fixed or permanent but rather is a dynamic equilibrium. Dissociation of the inclusion complex is a relatively rapid process usually driven by a large increase in the number of water molecules in the surrounding environment [3].

Edited by Helena Dodziuk

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# Cyclodextrins and Their Complexes

Chemistry, Analytical Methods,  
Applications



## CDs in agricultural use

pesticide	type of cyclodextrin used	equilibrium water content in solid form (%) by weight	pesticide content in the formulation (g/100g)
Sumithrin	$\beta$ CD	6.0	11.6
MGR-264	$\beta$ CD	6.6	12.2
Malathion	$\alpha$ CD	7.0	10.8
Malathion	$\beta$ CD	7.5	19.0
DDVP	$\beta$ CD	5.9	16.0
DDVP	$\alpha$ CD	5.0	18.5
Dursban	$\beta$ CD	8.2	14.2
Sulprofos	$\beta$ CD	5.0	12.8
Sulprofos	$\alpha$ CD	4.3	13.7
Fenitrothion	$\beta$ CD	5.8	14.0
DEET	$\beta$ CD	6.0	10.7
DEET	$\alpha$ CD	4.6	12.2

**Pesticide load and water content of cyclodextrin complexed liquid pesticides converted into microcrystalline solids**

**10-20% active ingredient load with superior bioavailability can be achieved**

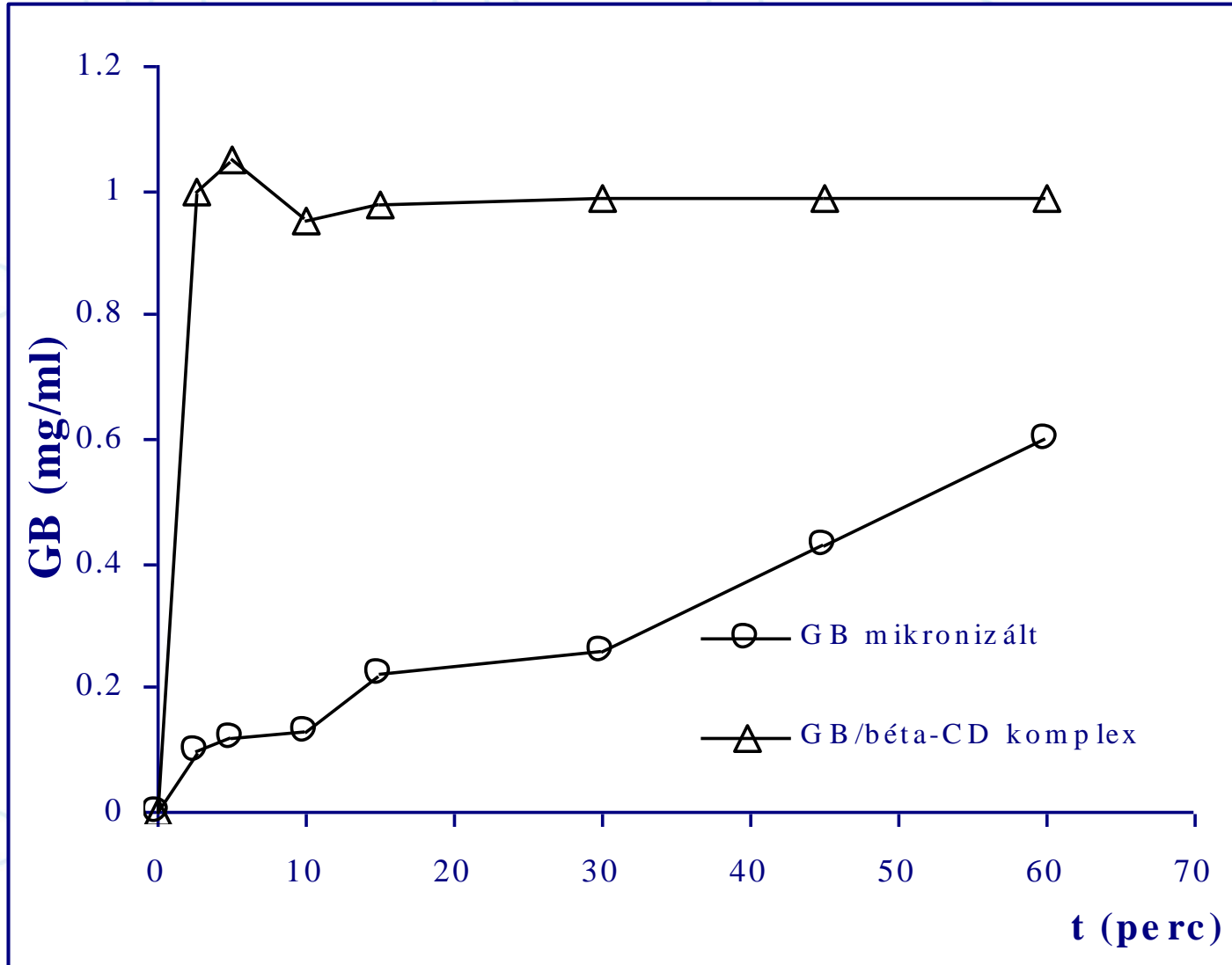
## CDs in agricultural use

### Thermal stability of insecticides (60°C)

formulation	remnant pesticide in percentage of the initial content				
	time zero	one week	two weeks	three weeks	four weeks
Fenithrothion /starch	100	82	70	58	52
Fenithrothion / $\alpha$ CD	100	90	84	68	64
Fenithrothion / $\beta$ CD	100	100	96	90	90
Malathion /starch	100	78	70	67	63
Malathion / $\beta$ CD	100	100	103	97	96
Malathion / $\alpha$ CD	100	100	100	101	98

Significantly increased physical and chemical stability can be achieved

# CDs in agricultural use

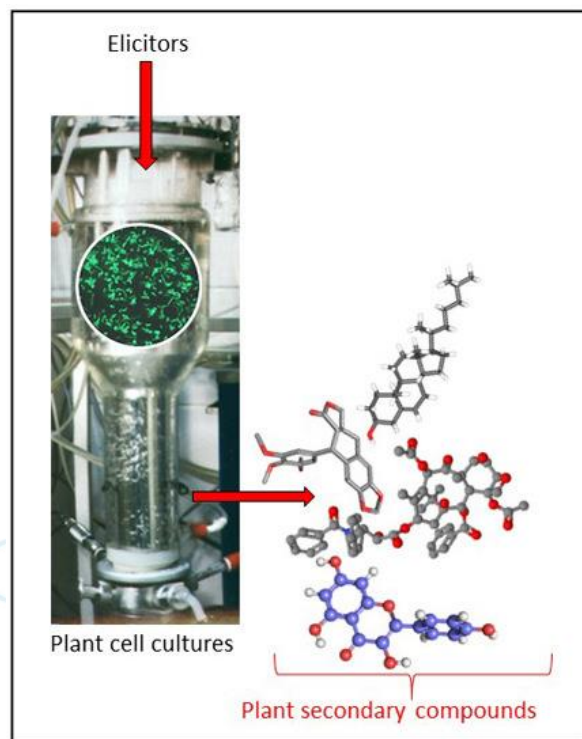


Comparison of micronized and CD-complexed formulations for Gibberellic acid (GB) release

Water-triggered release of the active ingredient

## Elicitation, an Effective Strategy for the Biotechnological Production of Bioactive High-Added Value Compounds in Plant Cell Factories

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**Table 2** Effect of cyclodextrins on secondary metabolite production in plant *in vitro* cultures.

Culture System	Plant Species	Secondary Metabolite (SM)	Type of SM	Reference
CS, HR	<i>Taxus globosa</i>	Taxanes	Diterpene alkaloid	[138]
	<i>Marinella citrifolia</i> and <i>Rubia tinctorum</i>	Anthraquinones	Phenolic compounds	[182]
	<i>Catharanthus roseus</i>	Vindoline, catharanthine and ajmalicine	Terpenoid indole alkaloids	[183]
	<i>Taxus media</i>	Taxanes	Diterpene alkaloid	[55]
	<i>Catharanthus roseus</i>	Ajmalicine	Monoterpenoid indole alkaloid	[184]
	<i>Vitis vinifera</i>	Trans-resveratrol	Stilbenes	[60,185–187]
	<i>Scutellaria lateriflora</i>	Verbascoside, the flavones: wogonin, baicalsin, scutellarein and their respective glucuronides	Phenolic compounds	[188]

CS: Cell suspensions; HR: Hairy root cultures.



## CD treatment of plant seeds

Delayed germination due to complexation of growth hormones

Enhanced growth and yield



## Protection and extension of bee lifespan by cyclodextrins

Methyl BCD and hydroxypropyl-BCD may provide good binding to organophosphates, pyrethroids and neonicotinoid pesticides. The treatment of healthy adult worker honey bees with CD acts to extend the lifespan of the bees and is absent of any measured negative effects.

A formulation containing CDs and one or more vitamins (vitamin A, D, E, etc.), minerals, nutrients, fat-soluble components increases the overall well-being of the bees.



## Cyclodextrin/carotenoid complex in fish feed

A complex between a carotenoid, e.g. astaxanthin, and cyclodextrin improves both the pigmentation in tissues of animals (especially fish with colored flesh: salmon and trout) and storage ability of the complex in relation to un-complexed carotenoid.

Suitable carotenoids in cyclodextrin complex are added to the feed given to farmed fish in order to achieve red/orange-colored flesh.



# Possibilities for cyclodextrin use in animal husbandry



## Vitamins and cyclodextrins

- $\beta$ -cyclodextrins improve pharmacokinetics of  $\alpha$ -tocopherol in heifers
- Cyclodextrin encapsulated vitamin K (K1, K2) can reduce osteochondral effects in animals

## Essential oils and cyclodextrins

Several patents are about essential oil formulations with cyclodextrins, e.g.:

- Camphor oil (-respiratory stimulant)
- Lemon oil (-flavor enhancer)
- Cinnamon oil (-flavor enhancer)
- Garlic oil (-antimicrobial)

## Cyclodextrins in feeds

Cyclodextrins were shown to have certain advantageous effects on feeds like inhibition of certain mycotoxins, and taste/odor masking for additives

## Effects of cyclodextrin complexes on methane production in heifers

The  $\beta$ -cyclodextrin complex with guest materials appears to be a promising solution to mitigate methane emissions without reducing energy intake

## Artificial fertilization

- Improvement of semen quality by cholesterol supplementation (cryopreservation)
- Enhancement of capacitation and fertility rate by pre-incubation of thawed sperms



Who are we at CycloLab?



The world's only all-round **CYCLODEXTRIN** company with over

**40-year experience of CD-technology**

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

### Experience

over 490 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



## 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

### IP services and consultation

30 years of experience in compilation of CD related patents (synthesis, application, etc.), patent claim analysis, consultancy in CD related projects

Over 62.000 CD related papers

### 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



### 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

## CDs in agricultural use

### COMPANY CONTACTS

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