



The Cyclodextrin Company



Industrial Application of Cyclodextrins in Food, Beverages and Personal Care Products

Lajos Szente, Mihály Bálint and István Puskás

CycloLab Ltd.
Budapest, Hungary



Prologue



I remember, József Szejtli said sometimes in early 1980:

*„In 2000, as I predict, people in civilised World will have an every day contact with products that **contain Cyclodextrins** or that **were made by using Cyclodextrins**”*

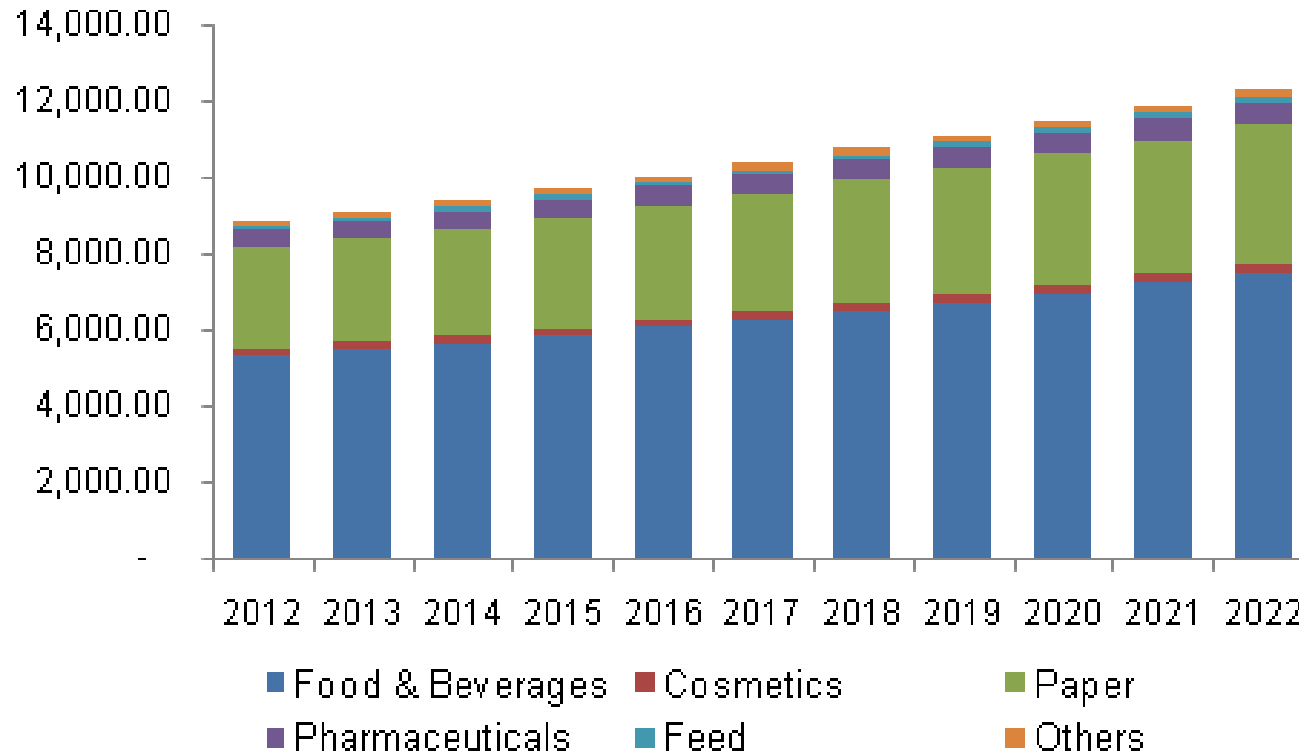
He also said:

*„We know a lot about Cyclodextrins, but this is **just the tip of the iceberg**”*



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United States starch derivative market volume by application, between 2012 - 2022 (Kilo tons)



Global starch derivative market size was 49,171 kilo tons in 2014

Starch Derivatives Market Analysis By Product (Cyclodextrin, Maltodextrin, Glucose Syrup, Hydrolysates, Modified Starch), By Application (Food & Beverage, Cosmetics, Paper, Pharmaceuticals, Feed) And Segment Forecasts To 2022, (Grand View Research March 2016, Report 978-1-68038-519-9)



Estimated amounts of different CDs utilized in Pharma, Food, Personal Care and Household fields

Estimated CD applications in 2015 *:

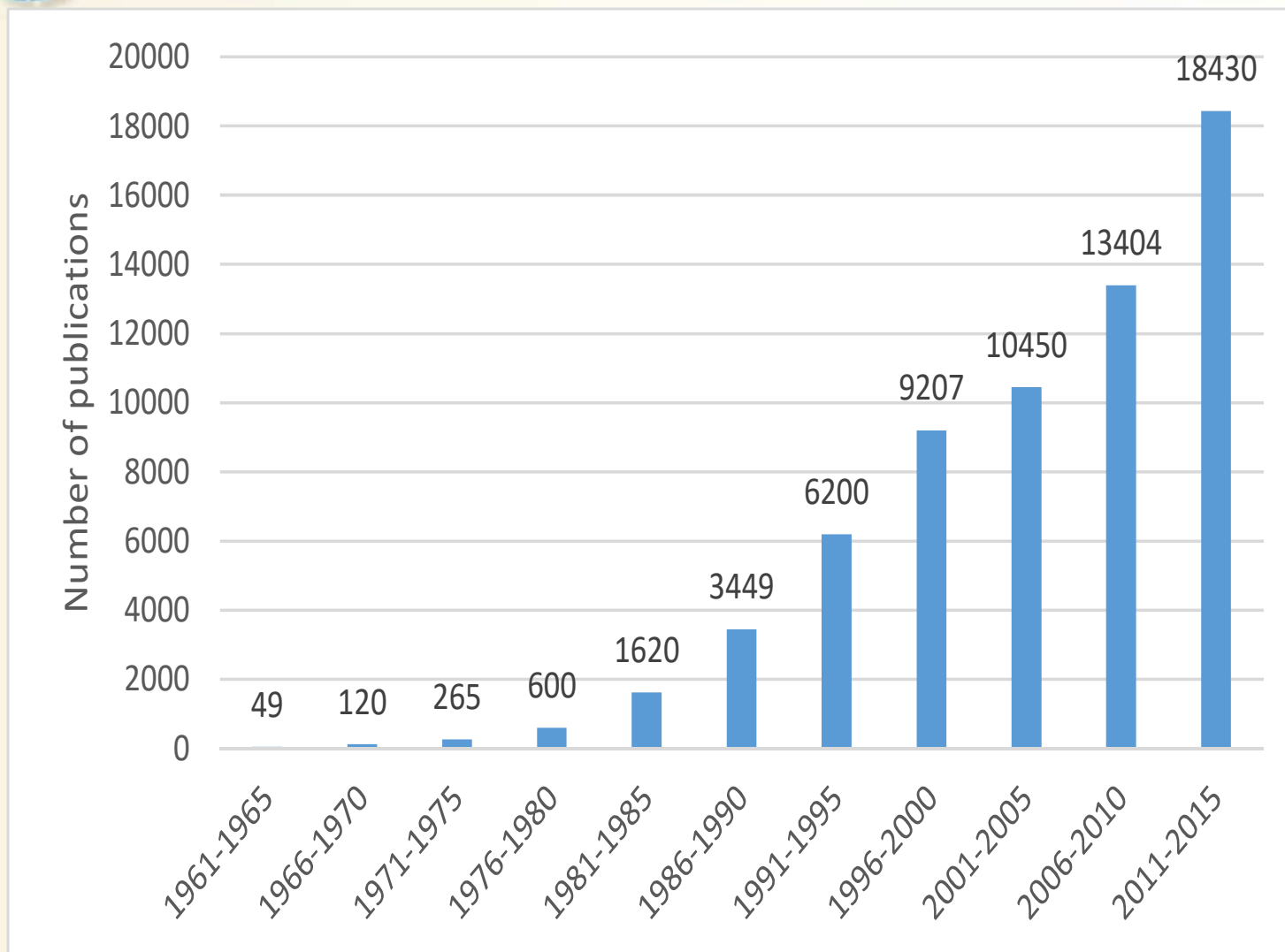
- | | |
|--|------------------|
| • beta-CD | 10.000 Mt |
| • alpha-CD | 700 Mt |
| • gamma-CD | 250 Mt |
| • HPBCD (technical grade) | 900 Mt |
| • HPBCD (pharma grade) | 600 Mt |
| • Sulfobutylether-BCD (? grade) | 100 Mt |

**QY Research Reports Global and China Cyclodextrin Industry*



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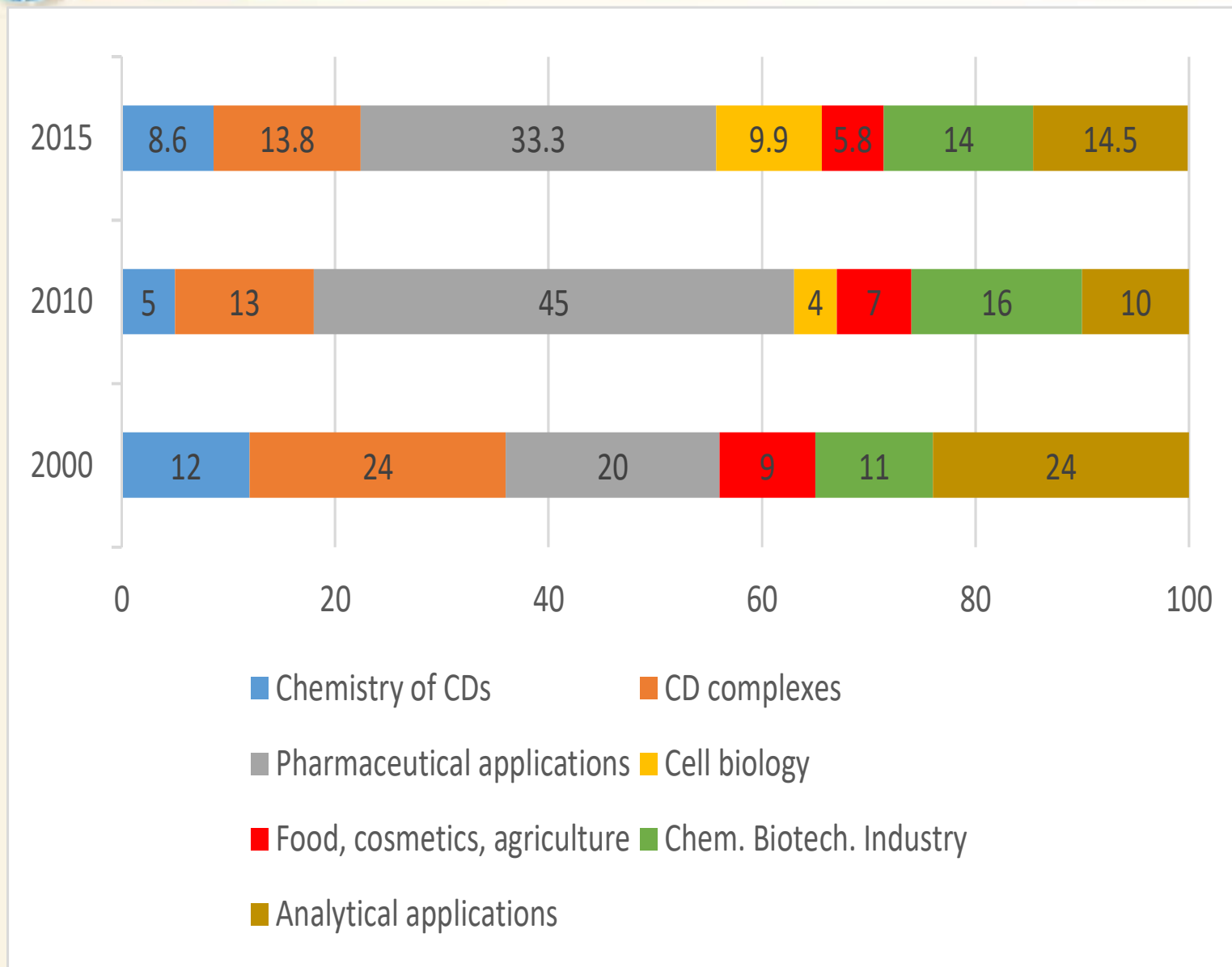
Trends in cyclodextrin-related publications in a four-year-period sections



(in 2017 the total number is around 66.000)



Distribution of Cyclodextrin research and application fields (2000-2015)





Cyclodextrins in Food and Nutrition



Utility of Cyclodextrins in Food

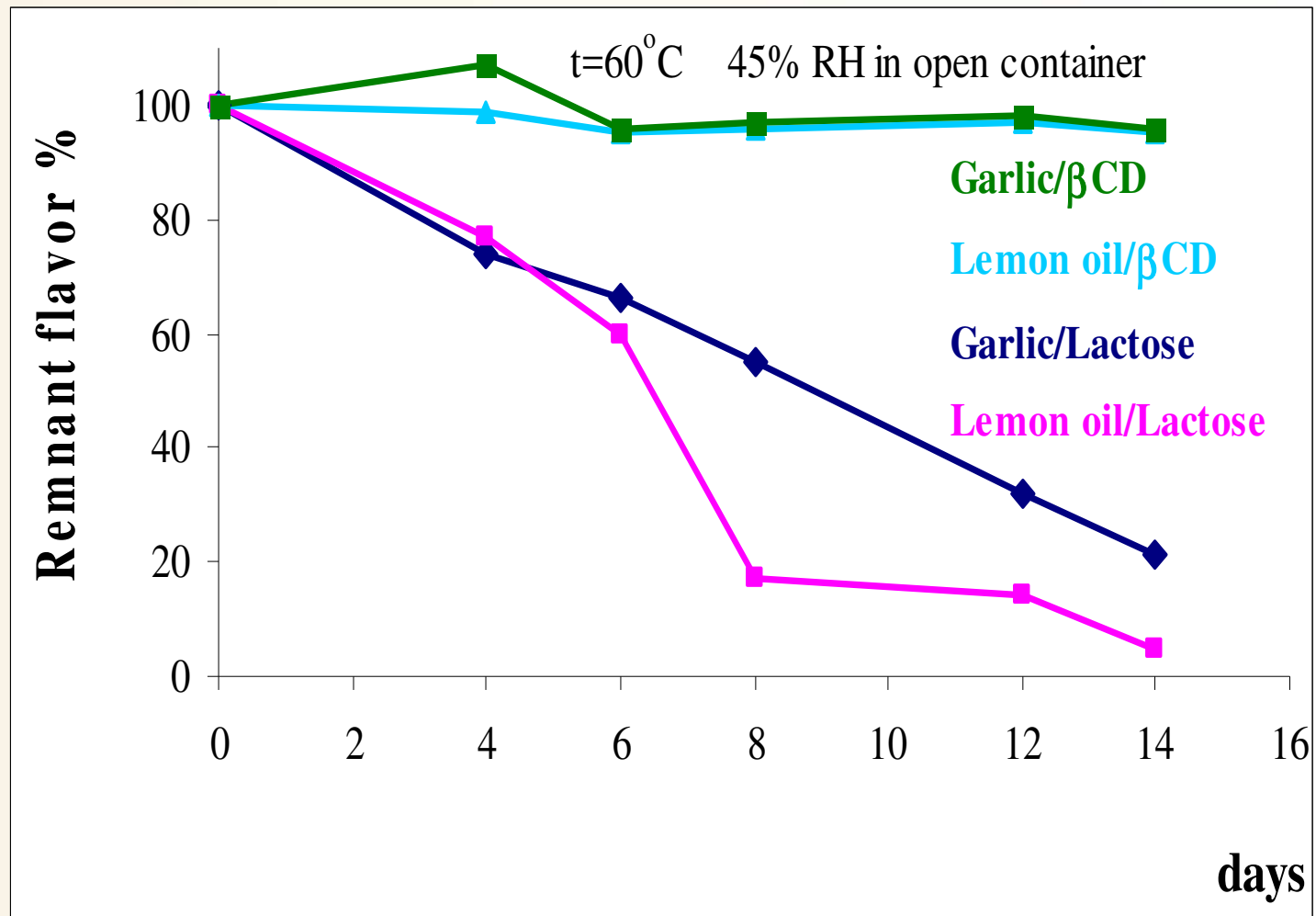
Between 1975-2000 CDs have been used as encapsulation agents (**complexed CDs**):

- for **stabilization** of flavours, colorants etc.
- for **solubilization** purposes (beverages)
- for **controlled-release** of food additives
- for improving food properties (against hygroscopicity, improving powder properties, etc.)

Since 2000 more emphasis is put on use of „empty” **non-complexed CDs** as:

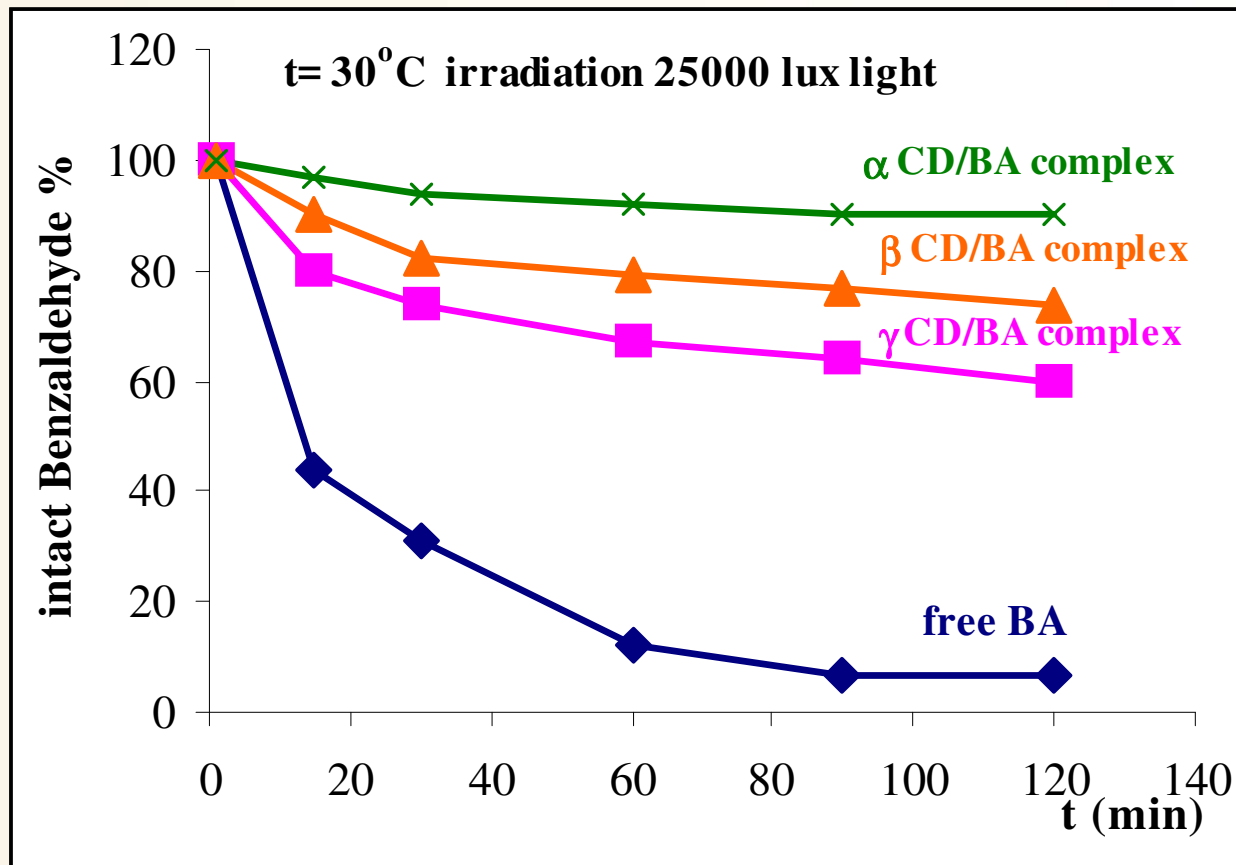
- tastes and odor masking agents
- dietary fibers, affecting human microflora,
- human lipid status altering agents
- glycemic response affecting agents

CD complexation protects volatile flavours from evaporation



Accelerated heat stability test of adsorbed and CD-encapsulated flavours

CD complexation protects against photodegradation: almond flavour (GC)



Cavity size matters! For small benzaldehyde flavour

the protection power of CDs: **alphaCD** > **betaCD** > **gammaCD**



CD-complexes are **controlled-release** systems



Driving force of the release of Cyclodextrin-encapsulated Flavours, Colorants:

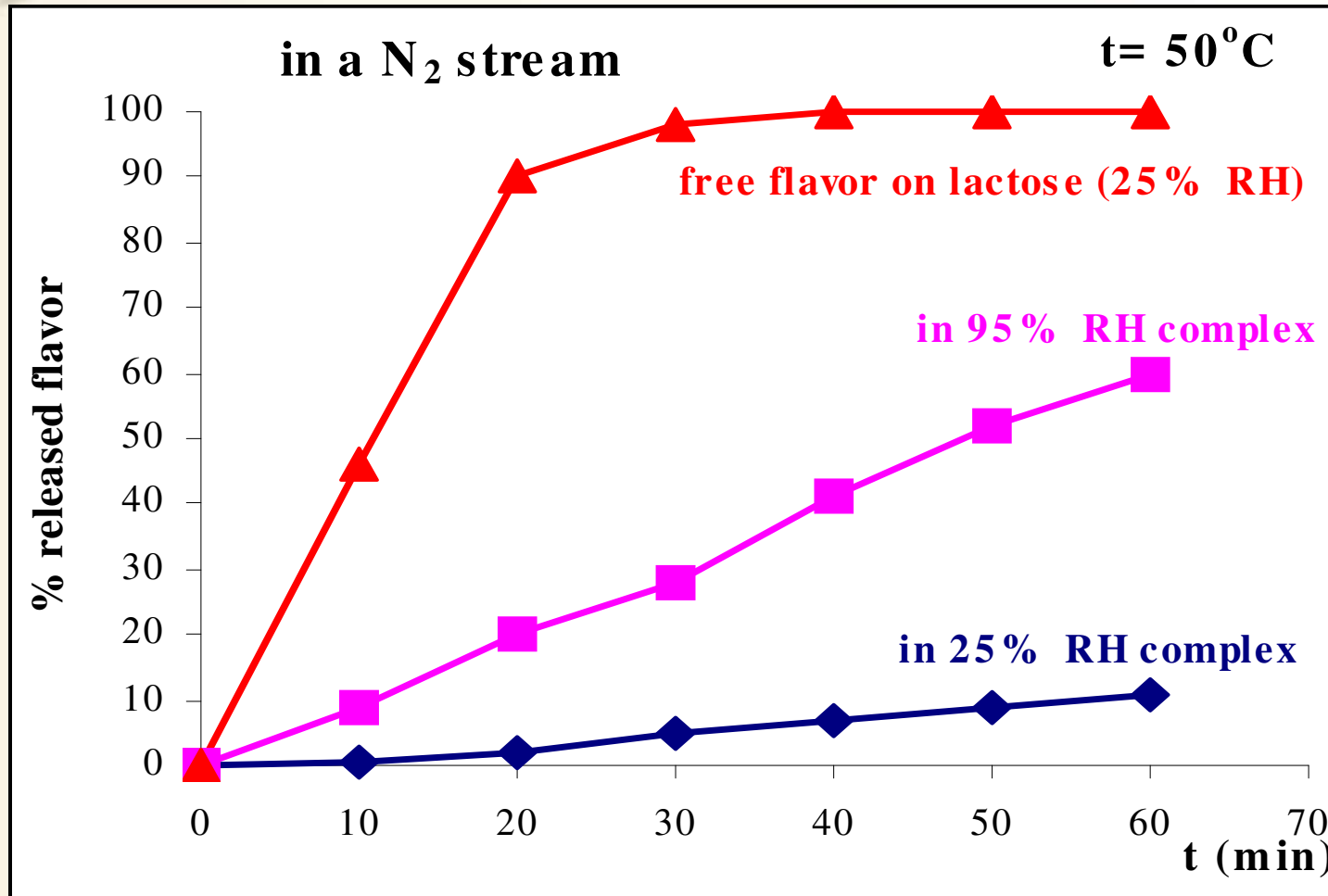
- Bulk water (dissolution/dilution on processing)
- Humidity + heat (shifting complexation equilibrium)
- competitive guests („third” component) + water

The CD-complexed flavors/fragrances are:

“water-activated” “controlled-release systems



Flavour CD complexes are „water-activated” formulations



Humidity driven release of a citrus flavor from lactose-adsorbate and β CD-complex (at 50°C in 25% and 95% R.H. air)



Solubilizing in Foods

CD-complexation improves solubility of lipophiles

Example: Prevention of precipitation, aggregation in canned juices,

Citrus beverages,

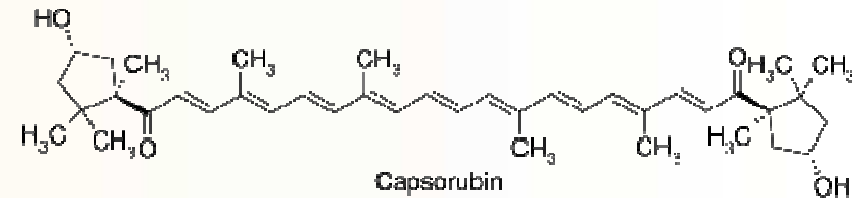
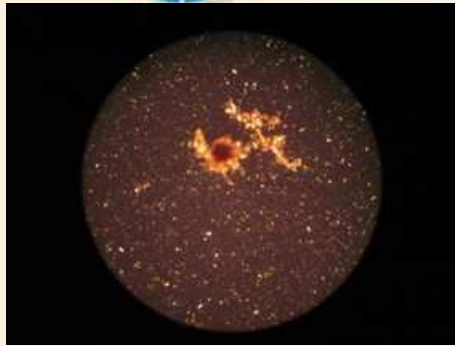
(hesperidin, naringin etc.)

Food lipids: fats, sterols, carotenes,

Around 40 products marketed in Japan and Korea



Example: Cyclodextrins in solubilization of carotenoid colorants



Capsorubin solubility in 10% aqueous detergents cosolvents and RAMEB (Szente et al 2005)



Dietary Effects of Cyclodextrins



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Effect of dietary **alpha-CD** on human serum glucose and insulin levels

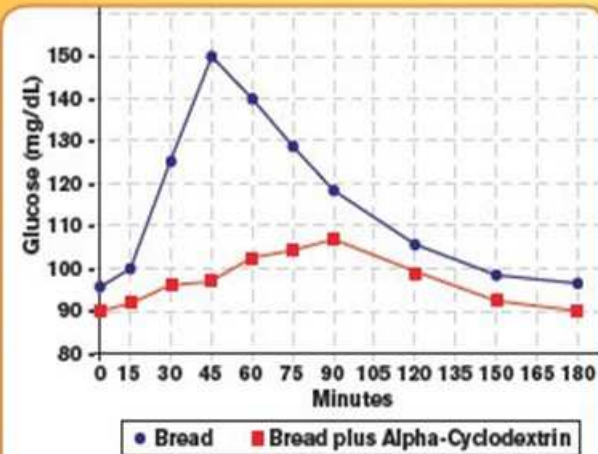


Figure 2. Blood sugar levels following "meal" of 100 grams of bread alone or with 10 grams of alpha-cyclodextrin in healthy volunteers. Note the peak rise of blood sugar to 150 mg/dL in control subjects, with gradual rise not reaching 110 mg/dL in supplemented group.

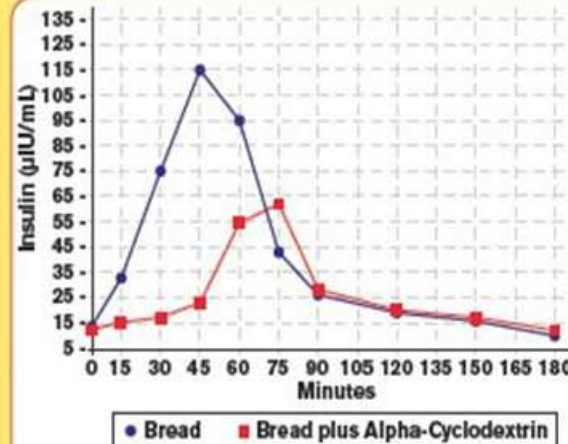


Figure 3. Blood insulin levels following "meal" of 100 grams of bread alone or with 10 grams of alpha-cyclodextrin in healthy volunteers. Note the sharp and early peak in insulin in control subjects, with much lower, later, and less-prolonged elevation in supplemented subjects.



Grunberger G, Jen KL, Artiss JD. The benefits of early intervention in obese diabetic patients with FBCx: a new dietary fibre. *Diabetes Metab Res Rev.* 2007 Jan;23(1):56-62.



Cyclodextrins to control body mass by affecting **fat absorption**



Supplement Facts	
Serving Size 2 Tablets	
Servings per container 90	
Amount Per Serving	
	% Daily Value
FBCx Alpha-cyclodextrin 2000 mg	**
**Daily Value Not Established.	
PRIMARY INGREDIENT:	
FBCx™ IS A NATURALLY SOURCED SOLUBLE DIETARY FIBER FROM CORN. EACH SERVING BINDS UP TO 18 GRAMS (162 CALORIES) OF DIETARY FAT.	

Calorease™ is a dietary supplement containing α CD/FBCx. FBCx is a patented, naturally sourced **dietary plant fiber with a fat-binding capacity**. It has the ability to bind up to 9 times its own weight of dietary fat, passing the fat out of the body.



Dietary α -CD product in Japan



Wacker's α -CD as
consumable product on the
grocery store shelf



A New-Zealand honey formulation prepared with alpha CD (Food Supplement product)



- Increased antimicrobial potency
- Sustained-release for enhanced delivery in the body
- **Lowers the Glycaemic Index**, suitable for pre-diabetics and people with reduced insulin sensitivity
- Has a **pre-biotic effect in the lower gut**



Plant Fats derived Milk powders Supplemented with CDs (Real Food Inc.)

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Ingredients:

Vegan Coconut Milk Powder, Organic Matcha Green Tea Powder (Ceremonial Grade), Organic Baobab Powder
Vegan Coconut Milk powder contains Coconut Milk, Maltodextrin (from Corn), Tapioca Syrup (<1%), **Cyclodextrin (dietary fibre <1%)**





CD-containing dietary supplement by Vitasome Labs, Inc. CA



Supplement Facts		
Serving size 1 sachet: 0.11 Oz. (3 g)		
Servings Per Container: 30		
	Amount Per Serving	% DV
Calories	5	-
Vitamin C (as L-Ascorbic- Acid)	250 mg	417%
L-Glutathione (Setria®)	250 mg	▲
Citrus Bioflavonoids	12.5 mg	▲
Phosphatidylcholine	125 mg	▲
Pterostilbene	50 mg	▲
Piperic Acid	1.5 mg	▲

▲ (Daily Value not established).
* (Percent Daily Values are based on a 2,000 calorie diet).

Other Ingredients: Sunflower lecithin, Citric Acid, Cyclodextrin, Acacia (Gum Arabic), Natural Flavors, Stevia.

Vitasome Labs, Inc.
Placentia, 92870
California, U.S.A
Support: 888-669-VITA (8482)

Setria® is a registered trademark of KYOWA HAKKO BIO CO., LTD.
Vitasome® is a registered trademark of Vitasome Labs, Inc.
Glutasome® is a registered trademark of Vitasome Labs, Inc.

Claims:

promotes **healthy skin**, helps diminish signs of aging, defends against environmental toxins



Effect of diets on mouse atherosclerosis (NIH study in 2017)

images of aorta stained plaques

(A) comparisons atherosclerotic lesions in aorta

LFD: low fat diet (5.2 % fat, w/w)

WD: Western diet (21.2 % fat)

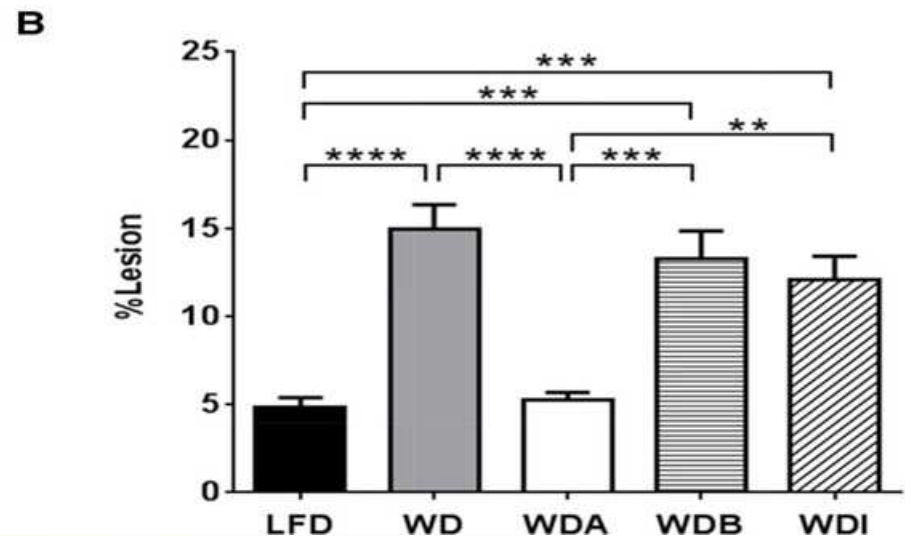
WDA: Western diet + 1.5% **Alpha-CD**

WDB: Western diet + 1.5 % **beta-CD**

WDI: Western Diet + 1.5% oligofructose
Inulin

(B). Percentage of atherosclerotic lesions: N=12

Sakurai et al, 2017 at NIH





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Official opinion

Alpha-cyclodextrin and glycaemic response

(*EFSA Journal* 2012;106 2713)

Scientific Expert Opinion on the substantiation of health claims related to **alpha-cyclodextrin and reduction of post-prandial glycaemic responses** (ID 2926, further assessment) pursuant to Article 13(1) of Regulation (EC) No 1924/2006

- The Panel considers that the following wording reflects the scientific evidence: “ **Consumption of alpha-cyclodextrin contributes to the reduction of the blood glucose rise after starch-containing meals**”.
- The Panel considers that in order to obtain the claimed effect, at least **5 g of alpha-cyclodextrin per 50 g of starch** should be consumed.
- The target population is **adults** who wish to reduce their post-prandial glycaemic responses



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Scientific opinion on dietary value of alpha-Cyclodextrin



The key research findings include:

- Comerford (5) study demonstrated that supplementation of **6 g/day of α -CD**, without any diet or lifestyle changes, **induced weight loss, reduced cholesterol, and increased insulin sensitivity** in healthy overweight individuals.
- Jarosz (6) showed that α -CD significantly **lowered** acute postprandial **blood triglyceride** levels following the consumption of a fat-containing meal, when compared to placebo.
- Grunberger (7) showed that diabetic patients taking the fibre α -CD maintained their weight in comparison to the placebo group over 3 months, as well as showing a **reduction in their total cholesterol**.⁷

Comerford KB, et al. Obesity 2011;19:1200-1204.

Jarosz PA, et al. Metab. Clin. Expt. 2013;62(10):1443-1447.

Grunberger et al. Diabetes Metabolism Research and Reviews, 2007; 23:56-62.

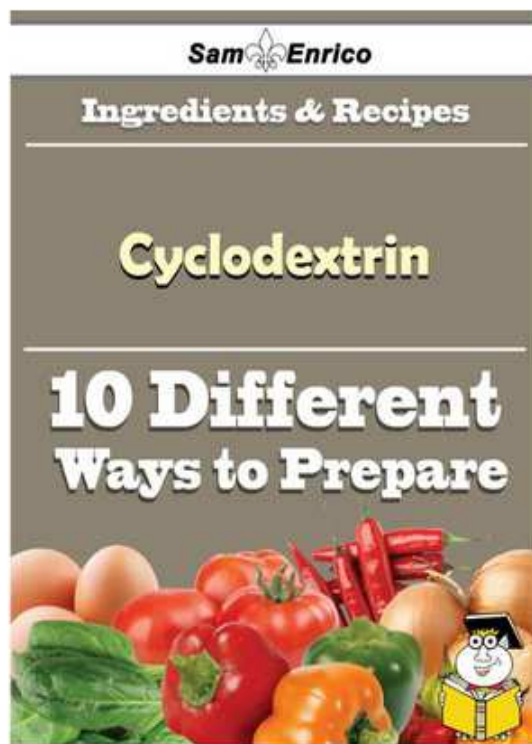


Believe it or not: there is a CD cook book!

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10 Ways to Use Cyclodextrin (Recipe Book) (eBook) by [Delcie Howerton, Sam Enrico](#) (Author)

★★★★★ [Read Customer Reviews](#)



This publication will teach you how to use Cyclodextrin in 10 different dishes. With step by step guides and instructions, you will not only learn how to prepare fantastic dishes, but enjoy wonderful meals using Cyclodextrin in 10 different dishes

Category: Cooking, Food & Wine Cooking, Food & Wine Cooking, Food & Wine

Released: January 8, 2015

[Free eBook Preview](#)

List Price: \$5.99

Our Price: **\$5.99**

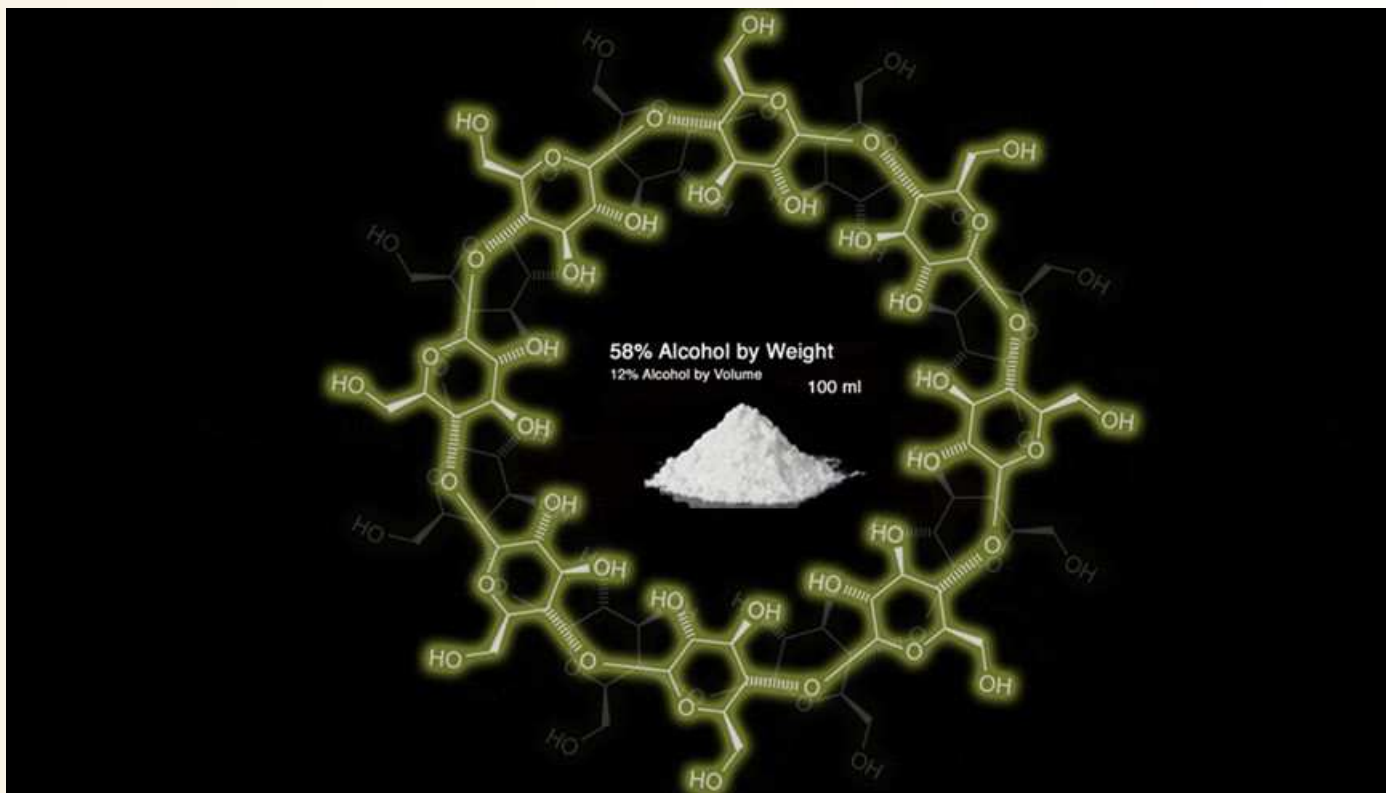
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A surprising CD-application



Cyclodextrin-entrapped ALCOHOL



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Re-discovery of CD-entrapped ALCOHOL

The History of Powdered Alcohol

1970s: Japanese company Sato Foods begins selling powdered alcohol as an additive to help preserve meat and fish.

1974: The first American application for a powdered alcohol patent is filed.

2005: German company Subyou introduces powdered alcohol for creating beverages.

2007: Students in the Netherlands invent Booz2Go, a powdered alcohol for creating beverages marketed at young people.

April, 2014: US Company Palcohol (owned by Lipsmark) seeks approval for distribution of powdered alcohol.

April 8, 2014: The Alcohol and Tobacco Trade and Tax Bureau in the US (ATTTB) approved Palcohol packaging labels.

April 18, 2014: ATTTB informs the associated press that approvals were issued in error.

March, 2015: Several US states including: Alaska, Louisiana, South Carolina, Vermont and Virginia, prohibit the distribution of Palcohol.

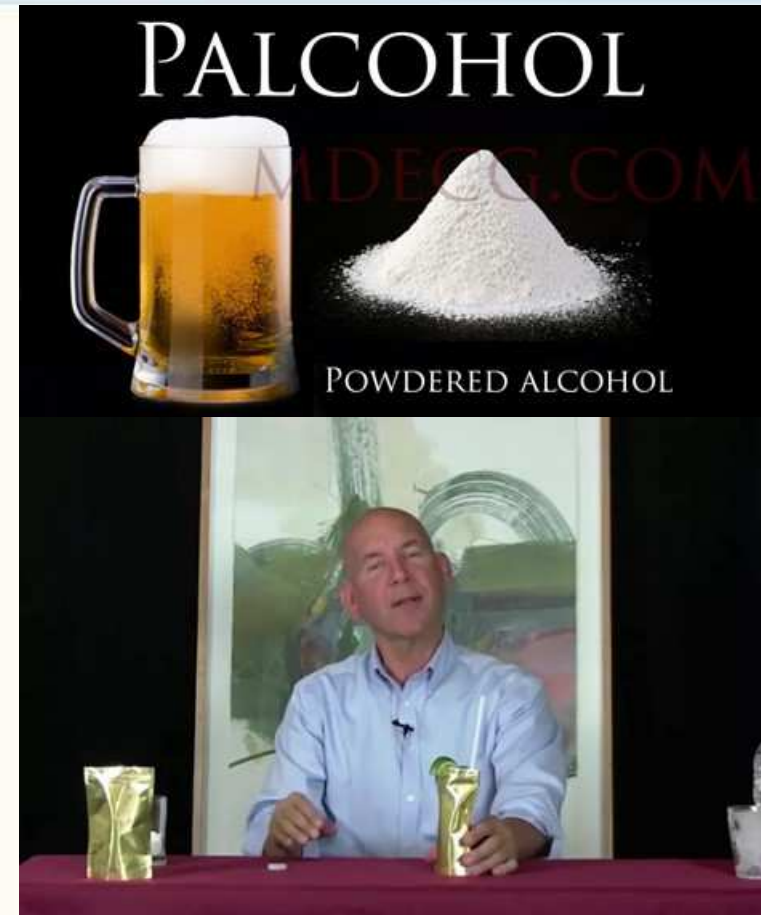
March 21, 2015: Palcohol confirms that the plan is to bring Palcohol to Australia in the next few months.





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Powdered Alcohol

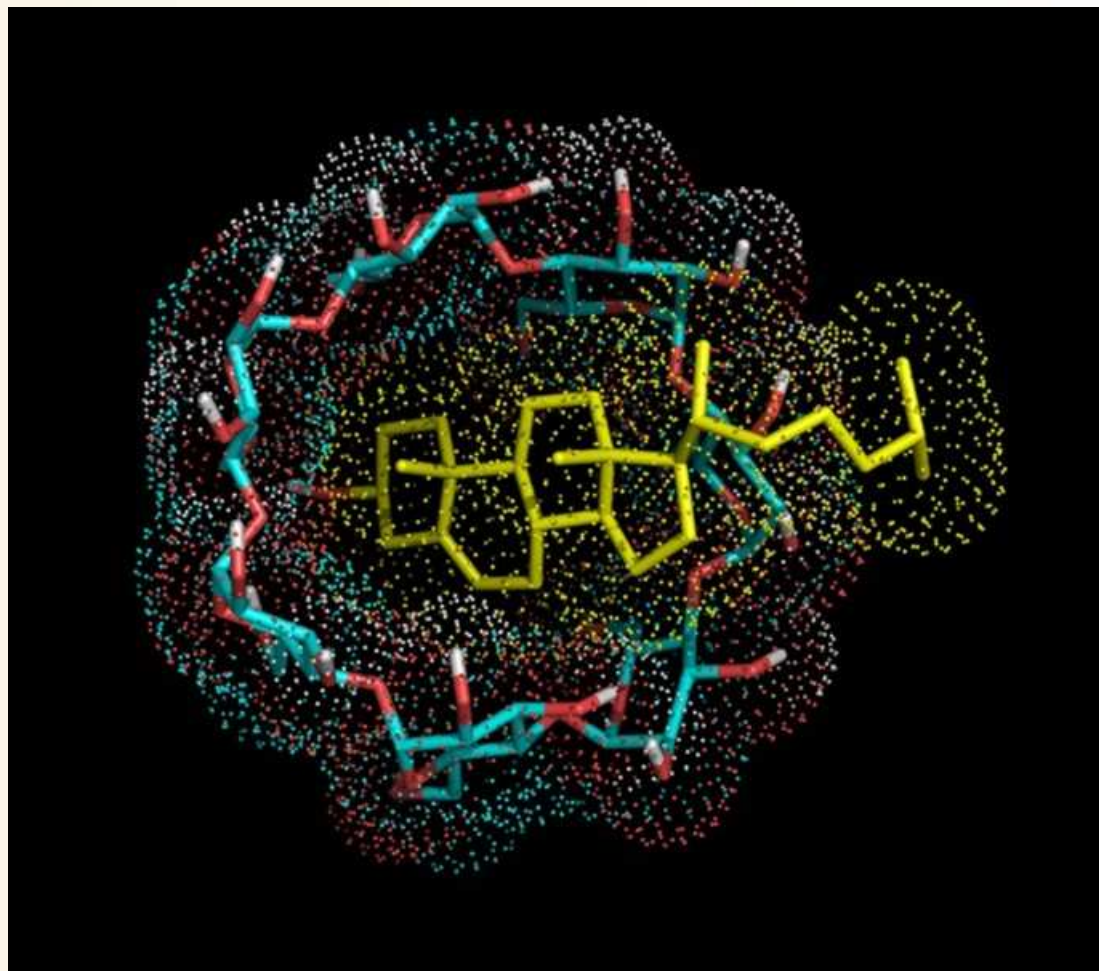


Powdered Alcohol Approved For Sale In The U.S. in March 2015
„Powdered alcohol lets you turn water into wine or vodka”

(Mark Phillips, CEO Palcohol)



Utility of Cholesterol-CD interaction in Food Industry





Low cholesterol egg

Solvent-free cholesterol-removal process:

- yolks and whites are separated,
- beta-CD is mixed with the yolks and then removed, along with the crystalline cholesterol-BCD complex by centrifugal force
- yolks and whites are rejoined,
- the mixture is Pasteurized and packed

Pioneers of egg cholesterol removal:

- Bayol et al: EP 326469 A1 2 Aug 1989
- Cully, J. et al EP 454099 A1 30 Oct 1991
- Sidhu-Oakenfull: 6th Intl. CD Symp. Chicago (1992)



Michael Foods / Simply eggs products



CD-assisted Cholesterol immobilization Award winning **Balade®** products by Corman Co.



Golden Archers award
Belgian Royal Retail
Committee

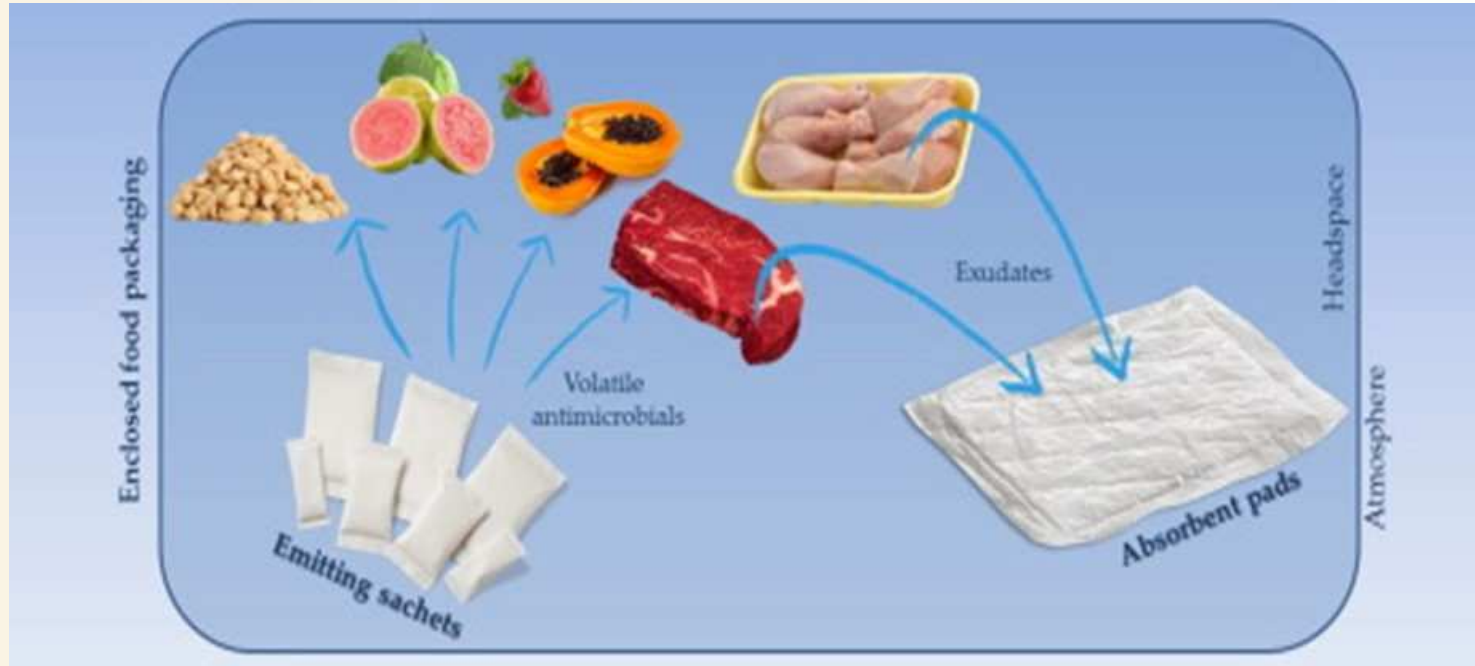
**Cholesterol selectively removed from dairy products by β CD:
(Patented by Roderbourg, et al Eur. Pat. 0 387 708, 1990 by Corman Co.)**



Cyclodextrins in packaging materials

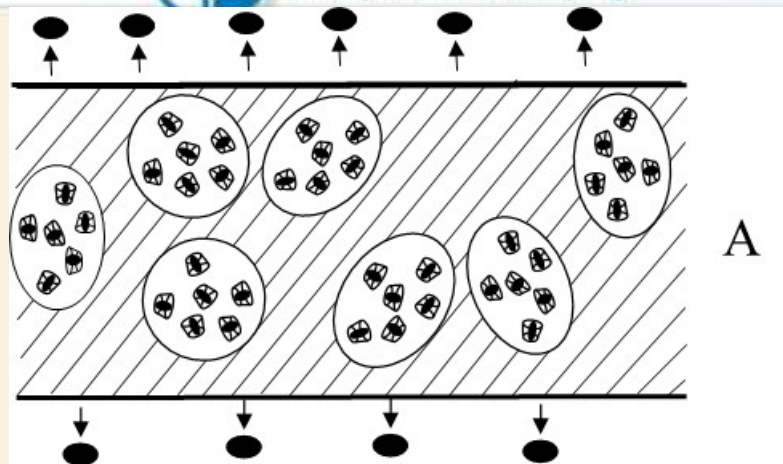


Cyclodextrin-enabled packaging materials: adsorber and emitter functions



- Empty CDs in **Adsorbent pads and bags** (collecting, fixing and immobilising odours and to prevent loss of volatiles)
- CD complexed volatiles: in **emitting sachets and bags** to provide released volatile antimicrobials, repellents etc. (moisture-activated!)

CD-enabled Food Packaging Polymer Films for preservation: humidity-driven release system (Fenyvesi et al, 2015)



Bananas stored unpacked (1), in control PVC film (2) and in film with **2.9 % imazalil/BCD complex** (3) after 12 days at 13°C



Cyclodextrins in odour safe trashbags

(by Procter and Gamble, in 1994)



- **Odor-neutralizing and liquid-absorbing trash bags**
WO 2000029311 A1 Toan Trinh P&G
- A container according to any of claims 1-4 wherein the odor-neutralizing composition is characterized by an ingredient selected from the group consisting of **cyclodextrin**, activated charcoal, baking soda, absorbent gelling materials, zeolite, silica and mixtures thereof.
- **Uncomplexed cyclodextrin solutions for odor control on inanimate surfaces**
US 5593670 A Toan Trinh P&G (filed in 1994)
- (a) **methylated-alpha-cyclodextrin** (b) **methylated-beta-cyclodextrin**; (c) **hydroxypropyl beta-cyclodextrin**; (d) **hydroxypropyl alpha-cyclodextrin**; and (e) **mixtures thereof.**



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Rodent repellent trash bags with CD-complexed mint oil (Mint-X Co.)



Patented CD-complex containing garbage bags: U.S. Patent No. 7,811,597

Problem



Solution



Results





Cyclodextrins in Cosmetics, Personal care and Household products



Facial cleansing and make up remover cloths

CD acts as lipid complexing agents

Concept was born in 1981 by J.Koch (Unilever) DE 2947742
alpha- and beta-Cyclodextrin as skin fat removing
antiacne agents



- Ingredients:** Petrolatum, PEG 100, Glycerin, **Methylcyclodextrin**, Cocamidopropyl Betaine, Sodium Lauroyl Sarcosinate, Decyl Glucoside, Lauryl Glucoside, Butylene Glycol, Fragrance, PEG 14M, Polyquaternium 10, Benzyl Alcohol, Panthenol, Salicylic Acid, Phenoxyethanol, Methylparaben, Propylparaben, Disodium EDTA, Sodium Ma/Diisobutylene Copolymer, Tocopheryl Acetate, Aloe Barbadensis Leaf Juice, Vitis Vinifera Seed Extract, Chamomilla Recutita Extract



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Gillette' products with CDs



- Ingredients
- **Active Ingredients:** Aluminum Chlorohydrate 24.1%
- **Inactive Ingredients:** Butane, Hydrofluorocarbon 152A, Dimethicone, Aluminum Starch Octenylsuccinate, **Cyclodextrin**, C12-15 Alkyl Benzoate, Fragrance, Distearidimonium Hectorite, Mineral Oil, Triethyl Citrate, Dimethiconol



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Estée Lauder Products with BCD and HPBCD



Moisturizing and anti-wrinkle effects in the focus CD + Hyaluronate combinations



CD containing L'Oreal products



MethylBCD-containing personal care products: Aqua di Roma® Brand by Laura Biagiotti



Long-lasting perfume products based on methyl-BCD entrapped perfume components:

challenging composition a finely tuned and balanced alcohol/water ratio! Equilibrium exists in bottle, too!

Developed by P&G in England





CoverGirl® Smoothers Aquasmooth Compact Foundation by Procter and Gamble

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- **Ingredients**

- Active Ingredients: Titanium Dioxide (9%). Purpose: Sunscreen. Inactive Ingredients: Cyclopentasiloxane, Water, Butylene Glycol, Silica, Niacinamide, Tridecyl Isononanoate, Sorbitan Isostearate, Talc, Euphorbia Cerifera (Candelilla) Wax, Ozokerite, Tocopheryl Acetate, Panthenol, Tocopherol, PEG/PPG-18/18 Dimethicone, Dimethicone, Phenoxyethanol, Methicone, Stearic Acid, Disodium EDTA, **Hydroxypropyl Cyclodextrin**, Iodopropynyl Butylcarbamate, Sodium Acetate, Aluminum Hydroxide, Mica, Titanium Dioxide, Iron Oxides.



Klorane Gentle Dry Shampoo products With Oat Milk

Contains: softening, protective oat extract,
cyclodextrins, and natural polysaccharides to
clean the hair without washing, as often as required.





The great Japanese Player Shiseido

Shiseido's Eudermine Revitalizing Essence and Benefiance skin softener with **HPBCD**



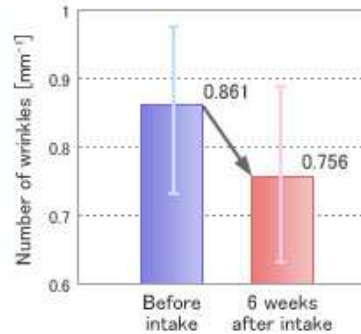


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Skin anti-aging products: CoQ10-gammaCD in eye wrinkle creams

Before intake

After 6 weeks



Special characteristics

Chemical Name	CoQ10 γ -CD inclusion complex
CAS-No.	γ -cyclodextrin: 17465-86-0 Coenzyme Q10: 303-98-0
Appearance	Free-flowing slightly yellow/orange colored powder
Bulk density	0.1-0.3 g/cm ³
Particle size	100 micron max
Dispersibility	Disperses easily in water (Picture→)

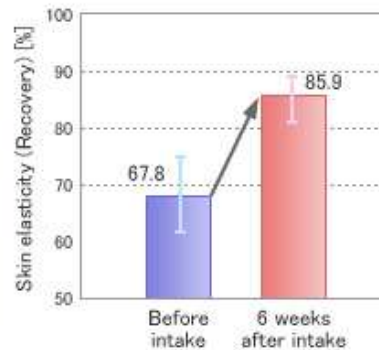
Water dispersibility



CoQ10 CoQ10- γ CD complex

Wrinkle

Male, 33 years old / Outer corner of the left eye



Skin texture (digital microscope)

Female, 32 years old / Cheek near the right eye

Number of wrinkles decreases
Skin elasticity increases

**Effect of CoQ10- γ CD complex supplemented eye wrinkle cream on human skin
(Terao, et al. 2006 CycloChem Bio)**



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Coenzyme Q10- γ CD -based Nivea Visage Brands



Soluble, absorbable Q10 by gammaCD complexation (Wacker Cawamax8/Q10)



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Cyclodextrins in Nivea lip stick/balsam products

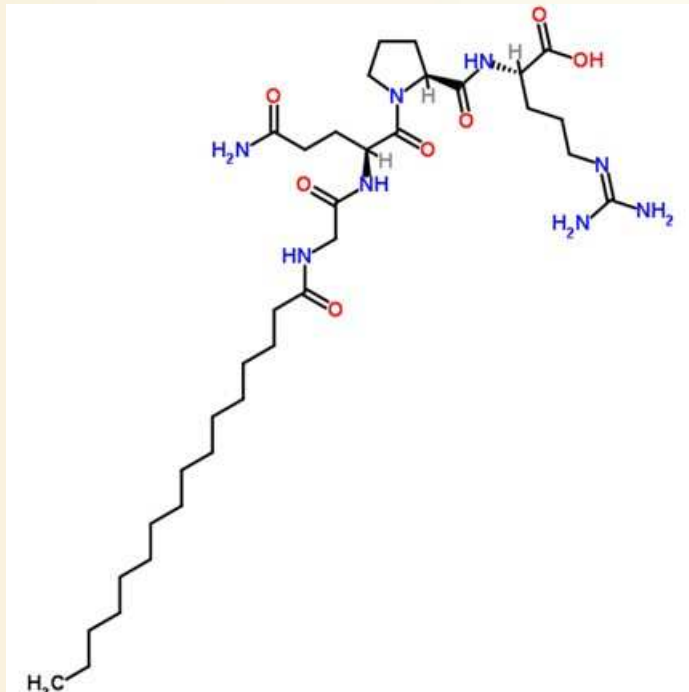


Olive Fruit Oil, Vaseline, Mineral Oil, Diisostearyl Malic Acid, Ceresin, Hydrogenated Kokoguriseriru, Hexa-hydroxy Stearic Acid Dipentaerythryl, Tri(Caprylic/Capric Acid) Glyceryl, Ethylhexyl Methoxycinnamate, **Cyclodextrin**, Polyethylene, Dimethicone, Squalane, Tocopherol Acetate, Isotridecyl Isononanoate, Microcrystalline Wax, Fragrance, Silica, t- Butylmethoxydibenzoylmethane, BHT, (+/-) 4 Yellow, Blue 1, Red 201



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HPBCD-BASED ANTIAGING PRODUCTS WITH PALMITOYL-PEPTIDE



Skin penetrating Palmitoyl-peptide

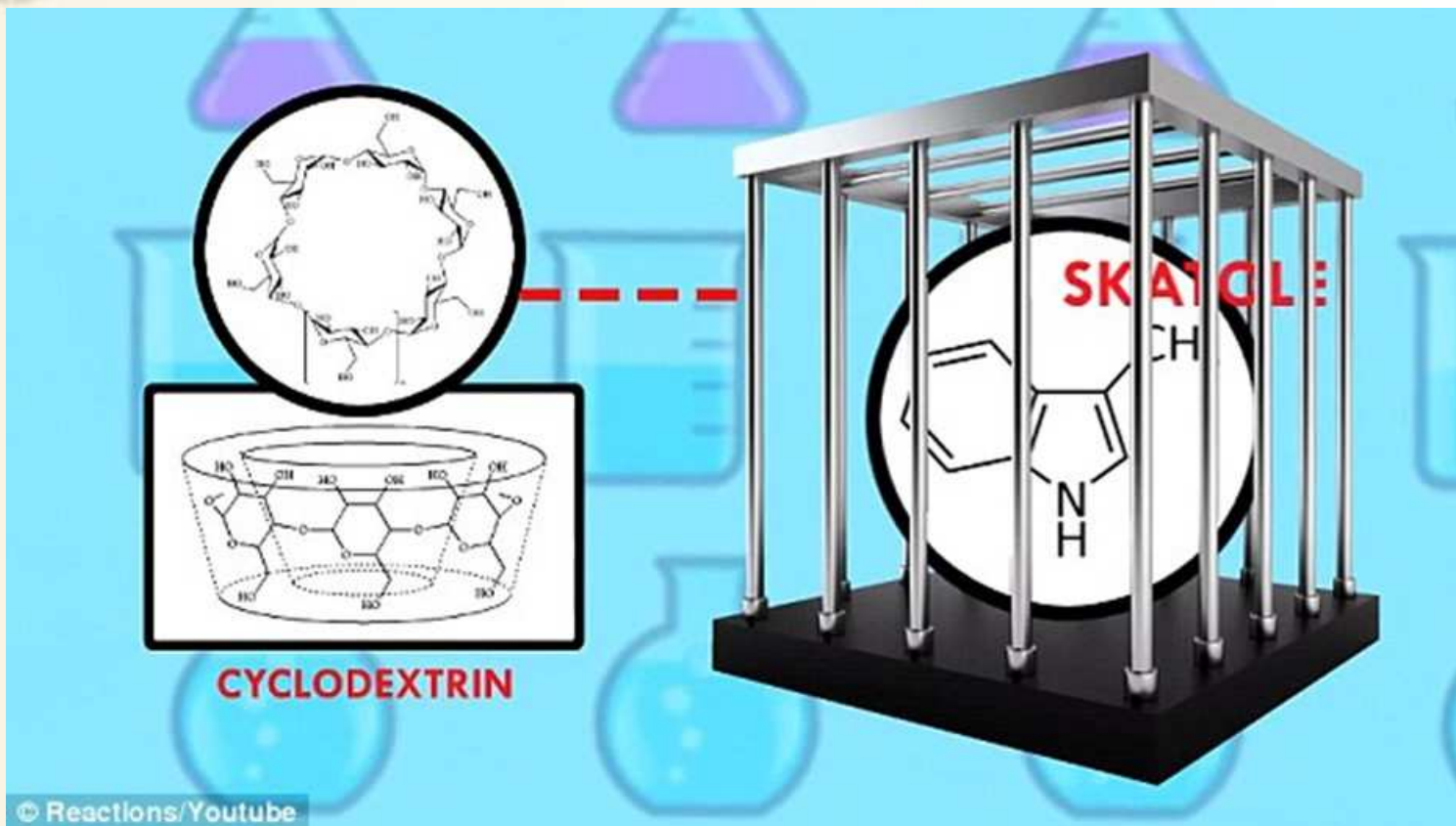


All above products contain: glycerin, Water, **HPBCD** and palmitoyl-peptide



Cyclodextrins in Household and Toiletry

Cyclodextrin-entrapped „bad odours”: route to **novel household deodorants**



A concept was born:

- Toan Trinh et al : EP 392607 A1 17 Oct 1990 (P&G)
- Toan Trinh et al : WO 9422999 A1 941013 (P&G)

Figure: curtesy of American Chemical Society



The **Bounce™** for laundry dryers with immobilised parent BCD by P&G (since 1994 on market)

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No wrinkles, no ironing!



Long action Bounce





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Febreze™ Laundry detergents and deodorants



The „Classic” Febreze™ Products from 1998



Follow up Febreze™ products



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Febreze™ for in-door odour „encapsulation”



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www.beaglesandbargains.com



Epiloque



József Szejtli said in early 1980's:

„In 2000, people in civilised World will have an every day contact with products that **contain Cyclodextrins** or that **were made by using Cyclodextrins**”

.....He was right!



Thank you!