

## APPROVED PHARMACEUTICAL PRODUCTS CONTAINING CYCLODEXTRINS

The list of the cyclodextrins-containing pharmaceutical products approved and marketed has been continuously increasing (Table 2 and 3)<sup>1,2,3</sup>.

Table 1 gives a summary of the number of active ingredients formulated with various CDs showing that most of them contain BCD or its derivative. Among the derivatives hydroxypropyl (HP), sulfobutyl ether (SBE) and random methyl (RM) cyclodextrins can be found in some formulations.

These tables do not show the two drugs where the active ingredient is a CD: Bridion (Sugammadex) and HPBCD, which are used for reversal of neuromuscular block in anesthesia and for the treatment of fatal genetic Niemann Pick Type C disease, a cholesterol metabolism disorder, respectively. The latter one has recently received an orphan drug designation.

The tables do not show either the FDA-approved cosmeceuticals, sunscreens, hydrating creams and lotions, antiage dermaceuticals etc, which contain also cyclodextrin among the ingredients.

Vitamins, various herbal compositions, phytosterols, carotenoids, unsaturated fatty acids, fish oil, etc. usually marketed as nutraceuticals have not been taken into account either although they are on the borderline between drugs and healthy foods. The nutrition supplements with steroids for body builders have not been included either.

Table 1 Number of active pharmaceutical ingredients formulated with various cyclodextrins

	<b>ACD</b>	<b>BCD</b>	<b>GCD</b>
<i>Parent</i>	1	31	1
<i>HP</i>		8	2
<i>SBE</i>		4	
<i>RM</i>		2	
<b>Total</b>	1	45	3

Table 2 Approved pharmaceutical products with parent cyclodextrins (partial list)

<b>Drug</b>	<b>CD</b>	<b>Trade Name</b>	<b>Dosage Form</b>	<b>Company</b>	<b>Country</b>
Aceclofenac	BCD	Aceclofenac-B-Cyclodextrin	Tablet	Taj Pharm.	India
Benexate	BCD	Ulgut/ Lonmiel	Capsule	Teikoku/ Shionogi	Japan
Betahistine	BCD	Betahist	Tablet	Geno Pharm.	India
Cefotiam	BCD	Pansporin-T	Tablet	Takeda	Japan
Cephalosporin (E1207)	BCD	Meiact	Tablet	Meiji	Japan
Cetirizine	BCD	Zyrtec	Chewing tablet	Losan Pharma/ UCB Pharma	Europe/ US
Cisapride	BCD	Propulsid	Suppository	Janssen	Europe
Chlordiazepoxide	BCD	Transillum	Tablet	Gabor	Austria
Dexamethasone	BCD	Glymesason	Oointment	Fujinaga	Japan
Dextromethorphan	BCD	Ryndthisol	Tablet	Synthelabo	Italy
Diphenhydramine	BCD	Stada-Travel	Chewing tablet	Stada	Germany
Ethinyl estradiol	BCD	Safyral/Beyaz/Lorina	drospirenone; ethinyl estradiol; levomefolate calcium tablet	Bayer Healthcare/ Sandoz	Europe
Flunarizine	BCD	Fluner	Tablet	Geno Pharm.	India
Garlic Extract	BCD		Various dragees	Various	USA/Europe
Histamine dihydrochloride	CD	Australian dream	Pain relieving antiarthritis cream	Nature's Health Connection	Australia
Iodine	BCD	Mena-Gargle	solution	Kyushin	Japan
Meloxicam	BCD	Mobitil	Tablet, suppository	Med. Union Pharm.	Egypt
Menthol/camphor	BCD	Pain relief gel	ointment	MMA Elite/ Doctor Hoy's	US
Metronidazole	BCD	Metrogel/ Flagyl/ Vandazol/ Nidagel	Vaginal gel	Curatek/Fougera /Tolmar	US/Canada
Minoxidil	GCD	Alopexy	Solution	Pierre Fabre	Europe
Naphasoline hydrochloride	CD	Clear eyes	Eye drop	Medtech	S. Africa



Nicotine	BCD	Nicorex/ Nicorette	Tablet	Pierre Fabre	Europe
Nimesulide	BCD	Nimedex	Tablet	Novartis, others	Europe
Nitroglycerin	BCD	Nitropen	Sublingual tablet	Nippon Kayaku	Japan
Norfloxacin and Tinidazole	BCD	Entronor –TZ/ Noroxin	Tablet		India
Omeprazol	BCD	Omebeta	Enteric caps.	Betafarm	Germany
PGE1	ACD	Prostavasin/	Intra-arterial inf.	Ono/Schwarz	Japan/Germany
PGE1	ACD	Viridal/ Alprostadil/ Edex/ Caverject	Intra- cavernous inj.	Schwarz	Germany
PGE1	ACD	Prostandin 500	Infusion	Ono	Japan
PGE1- OP-1206	GCD	Opalmon	Tablet	Ono	Japan
PGE2	BCD	Prostarmon E	Subl. tablets	Ono	Japan
Piroxicam	BCD	Cycladol/ Brexin/ Flamexin	Tablet	Chiesi	Europe
Piroxicam	BCD	Cycladol/ Pyrodex/ Medicam	Tablet	Ranbaxy/ Sun/ MMC	India
Piroxicam	BCD	Brexin	Suppositories	Chiesi	Europe
Piroxicam	BCD	Flogene	Pediatric liquid	Ache	UK
Refocoxib	BCD	Rofizgel	Tablet	Wockhardt	India
Salicylic acid	BCD	Own Breakout Control	Antiacne Lotion	Own products	US
Thiomersal	BCD	Vitaseptol	Eye drop	Europhta	Monaco
Tiaprofenic acid	BCD	Surgamyl	Tablet	Roussel- Maestrelli	Italy



Table 3 Approved pharmaceutical formulations with cyclodextrin derivatives  
(partial list)

<b>Drug</b>	<b>CD</b>	<b>Trade Name</b>	<b>Dosage form</b>	<b>Company</b>	<b>Country</b>
Cisapride	HPBCD	Prepulsid	Suppository	Janssen	Europe
Diclofenac	HPBCD	Dyolect	I.v. and i.m. Solution	Javelin Pharm.	Europe
Hydrocortisone	HPBCD	Dexacort	Mouth wash	Actavis	Europe
Indomethacin	HPBCD	Indocid/ Indocyllir	Eye drop	Chauvin/ Baush & Lomb	Europe
Itraconazole	HPBCD	Sporanox	Oral solution i.v. solution	Janssen	Europe/USA
Mitomycin	HPBCD	MitoExtra	I.v. infusion	Novartis	Europe
Televancin	HPBCD	Vibativ	I.v. solution	Astellas Pharma/ Therevance	Europe
Perindopril tert.butylamine	HPBCD	Perindopril Erbumine	Tablets	Sandoz	Europe
Voriconazole	HPBCD	Vorzu	Tablet	Rhambaxy	India
Diclofenac	HPGCD	Voltaren/ Voltarol	Eye drop	Novartis	Europe
Tc-99 Teoboroxime	HPGCD	CardioTec	I.v. solution	Bracco	USA
Amiodarone	SBECD	Nexteron	I.v. solution	Hikma	
Aripiprazole	SBECD	Abilify	I.m. solution	BMS/Otuska	USA/Europe
Maropitant	SBECD	Cerenia	Parenteral solution	Pfizer Animal Health	USA
Voriconazole	SBECD	Vfend	I.v. solution	Pfizer	USA/Europe
Ziprazidone	SBECD	Geodon, Zeldox	Capsule/ i.m. solution	Pfizer	USA/Europe
Chloramphenicol	RAMEB	Clorocil	Eye drop	Oftalder	Poland
Ostradiol	RAMEB	Aerodiol	Nasal spray	Servier	Europe

[1] [www.cyclolab.hu](http://www.cyclolab.hu)

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*GCD, carbohydrate utilization*

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*reversible gel-sol transforming process, irreversible sol-gel' transforming process based on heating, smart materials*

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*ACD, BCD, methanol, dimethyl sulfoxide, acetone,*

Yoshikiyo, K Matsui, Y Yamamoto, T: (2012) Bull. Chem. Soc. Jpn. 2012, 85, 11, 1206-1209;

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*BCD, lithium chloride, N,N-dimethylformamide, ethylene diamine, heating-cooling process, SEM, XRD, FTIR, smart materials*

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*octakis-[6-deoxy-6-(2-sulfanyl ethanesulfonate)]-GCD, SEM, DSC, MTT, immunocytochem. tests*

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*BCD, folic acid, glutathione, magnetically guided delivery*

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*disulfide bonds, paclitaxel, NIH3T3 cells, cytotoxic effect*

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## 4. CDs in Cell Biology

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*methyl-BCD, HPBCD, pulmonary artery endothelial cell, morphology alterations, cellular proteins, membrane fatty acid composition*

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*PVP, GCD, mitochondria, UV irradiation, cytoprotective action, phototoxicity*

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*mediated removal of cholesterol, fast pool, superlattices*

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*N,N-dimethylaminoethyl (DMAE) group-modified ACD, poly(ethylene glycol), human cervical carcinoma, gene silencing*

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## 5. CDs in Food, Cosmetics and Agrochemicals

### **Method for producing anticariogenic composition containing cyclodextran.**

*inhibiting the formation of water-insol. glucans, cyclodextran synthase, dentifrices, sweetening agents, foods, beverages*

Miyagi, Sadao; Gibu, Shigehachi; Izena, Shinichiro; Funane, Kazumi.: (2012) WO2012172635A1, 2012/12/20/ PCT Int. Appl., 37pp.

### **Quantitative analysis of pheromone-binding protein specificity.**

*Drosophila odorant-binding protein, 11-cis vaccenyl acetate, fluorescence, BCD, silk moth pheromone bombykol*

Katti, S.; Lokhande, N.; Gonzalez, D.; Cassill, A.; Renthal, R.: (2013) Insect Molecular Biology 22(1), 31-40

### **Inclusion of the insecticide fenitrothion in dimethylated-beta-cyclodextrin: unusual guest disorder in the solid state and efficient retardation of the hydrolysis rate of the complexed guest in alkaline solution.**

*organophosphorus insecticide, DIMEB, XRD, kinetic studies*

Cruickshank, Dyanne L.; Rougier, Natalia M.; Vico, Raquel V.; Bourne, Susan A.; Bujan, Elba I.; Caira, Mino R.; de, Rossi, Rita H.: (2013) Beilstein Journal of Organic Chemistry 9, 106-117, No. 14

## 6. CDs for other Industrial Applications

### **Synthesis of graphene oxide decorated with magnetic cyclodextrin for fast chromium removal**

*wastewater, adsorption kinetic, Langmuir isotherm*

Fan, LL Luo, CN Sun, M Qiu, HM: (2012) J. Mater. Chem. 2012, 22, 47, 24783-24791;

### **Preparation and characterization of poly-carboxymethyl-beta- cyclodextrin superplasticizer**

*ring-opening polymerization of epoxy chloropropane and CM-beta-CD, FTIR, NMR, GPC, adsorption properties, zeta-potential, cement particles, concrete engineering*

Lv, SH Gao, RJ Cao, Q Li, D Duan, JP: (2012) Cem. Concr. Res. 2012, 42, 10, 1356-1361;



**Evaluation of 14 Organic Solvents and Carriers for Screening Applications in Zebrafish Embryos and Larvae**

*bioassays, DMSO, maximum tolerated concentration, HPBCD*

Maes, J Verlooy, L Buenafe, OE de Witte, PAM Esguerra, CV Crawford, AD: (2012) PLoS One 2012, 7, 10, e43850;

**Variation of the Viologen Electron Relay in Cyclodextrin-Based Self- Assembled Systems for Photoinduced Hydrogen Evolution from Water**

*CD-appended photosensitizer, CD-modified Pt nanoparticles as the catalyst, ethylenediaminetetraacetic acid (EDTA), cyclic voltammetry, electron transfer*

Carballada, PC Mourtzis, N Felici, M Bonnet, S Nolte, RJM Williams, RM De Cola, L Feiters, MC: (2012) Eur. J. Org. Chem. 2012, 34, 6729-6736;

**An intelligent anticorrosion coating based on pH-responsive supramolecular nanocontainers**

*mesoporous silica nanoparticles, benzotriazole, hard-template method, cucurbit[6]uril, ACD/aniline, NMR, TG, SEM, TEM, alkaline- and acid-responsive nanocontainers, hybrid zirconia-silica sol-gel coating, electrochemical impedance spectroscopy*

Chen, T Fu, JJ: (2012) Nanotechnology 2012, 23, 50, 505705;

**Acetylated and methylated beta-cyclodextrins as viable soluble supports for the synthesis of short 2'-oligodeoxyribo- nucleotides in solution.**

*immobilizing a 5'-O-protected 3'-O-(hex-5-ynoyl) thymidine to peracetylated or permethylated 6-deoxy-6-azido-beta-CDs, cycloaddition, phosphoramidite strategy, pentameric oligonucleotide*

Molina, Alejandro Gimenez ; Kungurtsev, Vyacheslav ; Virta, Pasi ; Lonngberg, Harri.: (2012) Molecules 17, 12102-12120;

**Beta-cyclodextrin-mediated acetic acid catalyzed diastereoselective Mannich reaction in water.**

*chiral host, beta-aminoketones, Bronsted acid-chiral CD composite*

Sukumari, Subbiah ; Azath, Ismail Abulkalam ; Pitchumani, Kasi.: (2012) Synlett 23(16), 2328-2332;

**Fabrication of beta-cyclodextrin conjugated magnetic HNT/iron oxide composite for high-efficient decontamination of U(VI).**

*halloysite, removal efficiency of U(VI), sorption kinetic data, sorption irreversibility, wastewater*

Yang, Shitong; Zong, Pengfei; Hu, Jun; Sheng, Guodong; Wang, Qi; Wang, Xiangke.: (2013) Chemical Engineering Journal (Amsterdam, Netherlands) 214, 376-385

**Preparation and characterization of anti-fouling beta-cyclodextrin/polyester thin film nanofiltration composite membrane.**

*trimesoyl chloride, triethanolamine, sulfated BCD*

Wu, Huiqing; Tang, Beibei; Wu, Peiyi.: (2013) Journal of Membrane Science 428, 301-308



**Rust inhibitor, its ingredients and application for cold-rolled steel in cold rolling process.**

*monoethanolamine benzoate, triethanolamine, octadecylamine, BCD, 1,2,4-triazole, 1-hydroxy benzotriazole, morpholine benzoate, phytic acid*

Chen, Yiqing; Xu, Xiaolian; Xiao, Yu; Zhong, Bin; Ai, Fangfang; Li, Lin; Gao, Peng.: (2013) CN102899669A, 2013/01/30/ Faming Zhuanli Shenqing, 5pp.

**Biodegradable lubricant and preparation method thereof.**

*CD stearate, polyol, long-chain fatty acid, inorg. nanoparticles, aviation, metal processing, textile and leather fields*

Li, Dongshuang; Yang, Fada; Huang, Changshou; Fu, Dongju; Wu, Weiwei; Tan, Manlin; Yuan, Kaijie; Chen, Jianjun; Yue, Fengshu; Yang, Jian.: (2013) CN102911770A, 2013/02/06/ Faming Zhuanli Shenqing, 8pp.

**Synthesis of beta-cyclodextrin-calix[4]arene coupling product and its adsorption of basic fuchsin and methylene blue from water.**

*p-tert-butyl-25,27-dihydroxyl-26, 28-di(ethoxy carbonyl methoxyl) calix[4]arene, mono-6-ethylenediamino-6-deoxy-BCD, Freundlich adsorption isotherm*

Zhang, Xiaomei; Shi, Liang; Xu, Guocai; Chen, Chaoyue.: (2013) Journal of Inclusion Phenomena and Macrocyclic Chemistry 75(1-2), 147-153

## 7. CDs in Sensing and Analysis

**The use of methyl-beta-cyclodextrin to solubilize cholesterol prior to coating onto a C18 stationary phase**

*reversed-phase mobile phases, coating levels of cholesterol, selectivity*

Charlton, SA Coym, JW: (2012) J. Chromatogr. A 2012, 1266, 69-75;

**A novel enzyme-immobilized flow cell used as end-column chemiluminescent detection interface in open-tubular capillary electrochromatography**

*isolated BCD-modified gold nanoparticles-coated OTCEC column*

Xie, Haoyue ; Wang, Zuerong ; Kong, Weijun ; Wang, Lin ; Fu, Zhifeng: (2012) The Analyst (2013 Jan 22) 138(4), 1107-13.

**Beta-cyclodextrin decorated nanostructured SERS substrates facilitate selective detection of endocrine disruptor chemicals**

*monolayer of silica nanospheres, silver, gold, mono-6-deoxy-6-((2-mercaptoethyl)amino)-BCD, 3-amino-2-naphthoic acid, potassium hydrogen phthalate, beta-estradiol*

Fang, Cheng ; Bandaru, Narasimha Murthy ; Ellis, Amanda Vera ; Voelcker, Nicolas Hans: (2012) Biosensors & bioelectronics 42, 632-639





**The effects of diffusion on an exonuclease/nanopore-based DNA sequencing engine.**

*protein ion channel, computer simulations, lifetime*

Reiner, Joseph E. ; Balijepalli, Arvind ; Robertson, Joseph W. F. ; Drown, Bryon S. ; Burden, Daniel L. ; Kasianowicz, John J.: (2012) Journal of Chemical Physics 137(21), 214903/1-214903/7;

**Influence of Spacer Length between Actuator and Sensor on Their Mutual Communications in Poly(N-Isopropylacrylamide-co-beta- Cyclodextrin), an Autonomous Coordinative Shrinking/Swelling Polymer.**

*8-anilino-1-naphthalenesulfonic acid, pNIPAM main chain*

Ohashi, Hidenori ; Abe, Tomoaki ; Tamaki, Takanori ; Yamaguchi, Takeo.: (2012) Macromolecules (Washington, DC, United States) 45(24), 9742-9750;

**Determination of trace Cu, Co, Cr and Pb by X-ray fluorescence analysis with adsorption of beta-cyclodextrin polymer including PAN resin.**

*flake for XRF detn. wiyhout elution, filtration*

Tang, Hong-mei ; Qiu, Hai-ou ; Tian, Yu-he ; Zheng, Hong-tao ; Tang, Zhi-yong.: (2012) Fenxi Shiyanshi 31(10), 89-91

**Enantiomer separation with ice as a functional material-chiral ice chromatography.**

*ice particles, hydrogen bond formation between the polar groups in a solute mol. and the OH dangling bonds on the ice surfaces, chiral selector*

Okada, Tetsuo.: (2012) Kobunshi 61(10), 783-784

**A novel enzyme-immobilized flow cell used as end-column chemiluminescent detection interface in open-tubular capillary electrochromatography.**

*thiolated BCD-modified gold nanoparticles-coated OTCEC column*

Xie, Haoyue; Wang, Zuorong; Kong, Weijun; Wang, Lin; Fu, Zhifeng.: (2013) Analyst (Cambridge, United Kingdom) 138(4), 1107-1113

**Beta-cyclodextrin decorated nanostructured SERS substrates facilitate selective detection of endocrine disruptor chemicals.**

*river water, surface enhanced Raman scattering, silica nanospheres, mono-6-deoxy-6-((2-mercaptoethyl)amino)-BCD, 3-amino-2-naphthoic acid, phthalate, beta-estradiol*

Fang, Cheng; Bandaru, Narasimha Murthy; Ellis, Amanda Vera; Voelcker, Nicolas Hans.: (2013) Biosensors & Bioelectronics 42, 632-639



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