Statistics on Cyclodextrin-related Patents
(Review based on the paper of Deorsola et al. in World Patent Information)

Deorsola et al. have performed a thorough patent search on CD-related patents in various databases and evaluated their search results in a recent paper [1]. They used free databases (Espacenet, USPTO, PATENT SCOPE and INPI, a Brazilian database) and DERWENT Innovation Index (freely accessible for universities). The period they evaluated was 1981-2011. For this 30-year period the search for cyclodextrin as keyword resulted in the highest number of hits (14,572) in DERWENT II, therefore the refined search was made in this database.

The number of patents increased in three steps: the first period lasted till 1990 followed by a slight drop; then a much faster rise was observed in 2000-2005, stopped for 2 years, followed by the almost doubled number of patents in 2008-2011 (Figure 1).

![Figure 1. Number of cyclodextrin-related patents in the world based on Derwent II database (accessed on January 7, 2013) (with the courtesy of Prof. Deorsola)](image)

The patent applications filed in different patent offices were also evaluated. The statistics of the top 8 can be seen in Figure 2 showing the leading role of Asia, being Japan and China on the first and second positions, respectively. They are followed by the US and then by the European Patent office.
The leading companies concerning the number of their CD-related patent applications are Procter & Gamble Co. (>300), Kao Corp. (99), Schering AG (92), Ensuiko Sugar Refining Co. (83), and Ono Pharm. Co. (79).


The classification of the patents allows an evaluation according to the topic of the inventions. This analysis shows that the most often selected classification is a kind of medicinal preparation characterized by the presence of non-active ingredients (excipients).

![Figure 2.: Number of patent applications filed in patent offices of different countries based on Derwent II database (accessed on January 7, 2013) (with the courtesy of Prof. Deorsola)](image)

References


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1. CDs: Derivatives, Production, Enzymes, Toxicity

Ahn, H-J.; Li, C.; Cho, H-B.; Park, S.; Chang, P-S.; Kim, Y-W.

*Enzymatic synthesis of 3-O-α-maltosyl-L-ascorbate using an engineered cyclodextrin glucanotransferase*

L-Ascorbic acid, Cyclodextrin glucanotransferase, Acid/base mutant, 3-O-α-maltosyl-L-ascorbate, Transglycosylation, Mutant CGTase, Regioselective glycosylation

Food Chemistry, 2015, 169, 366-371; DOI:10.1016/j.foodchem.2014.07.110

2. CD complexes: Preparation, Properties in solution and in solid phase, Specific guest


*Influence of microheterogeneity on the solution phase photophysics of a newly synthesised, environment sensitive fluorophore 2-((7,8-dimethyl-1-oxo-2,3,4,9-tetrahydro-1H-carbazol-6-yl)oxy)acetic acid and its tagged derivative*

Stokes shift, 1-Keto-1,2,3,4-tetrahydrocarbazole, Sodium dodecyl sulfate, Cetyl trimethyl ammonium bromide, Triton X-100, β-cyclodextrin


Periasamy, R.; Kothainayaki, S.; Sivakumar, K.

*Investigation on intermolecular complexation between 4,4′-methylene-bis(N,N-dimethylaniline) and β-cyclodextrin: Preparation and characterisation in aqueous medium and solid state*

4,4′-Methylene-bis(N,N-dimethylaniline), β-Cyclodextrin, Inclusion complex, Atomic Force Microscope, Differential Scanning Calorimetry, Molecular docking study


Periasamy, R.; Kothainayaki, S.; Rajamohan, R.; Sivakumar, K.

*Spectral investigation and characterization of host-guest inclusion complex of 4,4′-methylene-bis(2-chloroaniline) with beta-cyclodextrin*

4,4′-Methylene-bis(2-chloroaniline), β-Cyclodextrin, Inclusion complex, Atomic Force Microscope, UV-fluorescence spectrum, Molecular docking

Carbohydrate Polymers, 2014, 114, 558-566; DOI:10.1016/j.carbpol.2014.08.006
Prabhu, A. A. M.; Kumar, G. S. S.; Fatiha, M.; Sorimuthu, S.; Raj, M. S.

Encapsulation of phenylalanine and 3,4-dihydroxyphenylalanine into β-cyclodextrin: Spectral and molecular modeling studies

Phenylalanine, 3,4-Dihydroxyphenylalanine, β-Cyclodextrin, PM3 calculations, NBO
Journal of Molecular Structure, 20154, 1079, 370-382; DOI:10.1016/j.molstruc.2014.08.045

Quaranta, A.; Qu, H.; Vencel, T.; Zhang, Y.; Leibl, W.; Leach, S.; Bensasson, R. V.

Photophysical properties in aqueous solutions of C₆₀ embedded in 2:1 γ-cyclodextrin/[60] fullerene inclusion complexes

C₆₀ Triplet State, Photodestruction, Quantum Yields, γ-CD/C₆₀ Inclusion Complexes, 2:1 γ-CD Inclusion Complexes


Driving forces and electronic structure in β-cyclodextrin/3,3′-diaminodiphenylsulphone complex

β-CD, 3,3′-Diaminodiphenylsulphone, PM6, ONIOM2, NBO

Rajendiran, N.; Venkatesh, G.

Micrometer size rod formed by secondary self assembly of omeprazole with α- and β-cyclodextrins

Omeprazole, Cyclodextrin, Nanorod, Inclusion complex, Supramolecular architecture, Molecular modeling, Inter-nanotubular hydrogen bonding
Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 2015, 137, 832-840; DOI:10.1016/j.saa.2014.08.074

Rogeöz-Florent, T.; Azaroual, N.; Goossens, L.; Goossens, J-F.; Danel, C.

NMR investigation of the complexation and chiral discrimination of pyrazole sulfonamide derivatives with cyclodextrins

Cyclodextrin, Sulfonamide derivatives, Inclusion complex, NMR spectroscopy, Chiral discrimination, HP-β-CD, Me-β-CD, NH₂-β-CD
Carbohydrate Polymers, 2015, 115, 598-604; DOI:10.1016/j.carbpol.2014.09.046

Sengupta, C.; Sarangi, M. K.; Sau, A.; Mandal, D.; Basu, S.

A case study of photo induced electron transfer between riboflavin and aliphatic amine: Deciphering different mechanisms of ET operating from femtosecond to microsecond time domain

Riboflavin, Organized assemblies, Radical ions/pairs, Transient absorption, H-abstraction, β-Cyclodextrin
Shao, K.; Wang, H.; Peng, A.

**Inclusion of CdS quantum DoT into beta-cyclodextrin crystal by simple rapid crystallization**

Low dimensional structures, Nucleation, Growth from solution, Oxides

Journal of Crystal Growth, 2015, 409, 10-13; DOI:10.1016/j.jcrysgro.2014.09.022

Soleymanpour, A.; Ghasemian, M.

**Chemically modified carbon paste sensor for the potentiometric determination of carvedilol in pharmaceutical and biological media**

Carvedilol, Carbon paste electrode, Potentiometry, Pharmaceutical analysis, β-Blocker

Measurement, 2015, 59, 14-20; DOI:10.1016/j.measurement.2014.09.046


**Specific and nonspecific effects of biologically active inorganic salts on inclusion complex formation of cyclodextrins with aromatic carboxylic acids**

Cyclodextrin, m-Aminobenzoic Acid, Nicotinic acid, Complex formation, Salt effect, Thermodynamics, KCl, KBr, KH₂PO₄, K₂SO₄

Chemical Engineering Science, 2015, 122, 97-103; DOI:10.1016/j.ces.2014.09.025

Zhao, Y.; Yong, G.; Zhang, X.; Zhang, B.

**Reversibly photoswitchable dual-color (blue ↔ green) phosphorescence from β-cyclodextrin inclusion complex materials**

3-Formyl-2,3’-biimidazo[1,2-a]pyridin-2’-ones, Cyclodextrin inclusion complexes, Molecular assemblies, Supramolecular materials, Phosphorescence enhancement, Photoswitchable phosphorescent Colors, Excitation with Ultraviolet Light, Irradiation by Visible Light


### 3. CDs in Drug Formulation

Bulani, V.; Kothavade, P.; Nagmoti, D.; Juvekar, A.

**19: Ellagic acid hydroxypropyl-β-cyclodextrin inclusion complex alleviates adjuvant-induced arthritis: Attenuation of oxidative stress and inflammatory mediators**

Nitric oxide, Glutathione, Superoxide dismutase, IL-6, TNF-α


Uebelhack, R.; Busch, R.; Alt, F.; Beah, Z-M.; Chong, P-W.

**Effects of cactus fiber on the excretion of dietary fat in healthy subjects: A double blind, randomized, placebo-controlled, crossover clinical investigation**

Cactus Fiber, Litramine IQP-G-002AS, Acacia spp, Co-processed with cyclodextrin
Dandawate, P.; Vemuri, K.; Swamy, K. V.; Khan, E. K.; Sritharan, M.; Padhye, S.

**Synthesis, characterization, molecular docking and anti-tubercular activity of Plumbagin–Isoniazid Analog and its β-cyclodextrin conjugate**

*Plumbagin, Plumbagin-Isoniazid Analog, β-Cyclodextrin, Inclusion complex, Antitubercular activity, Molecular docking, Superior activity, Overcoming resistance*


Dsugi, N. F. A.; Elbashir, A. A.

**Supramolecular interaction of Moxifloxacin and β-cyclodextrin spectroscopic characterization and analytical application**

*Moxifloxacin, Inclusion Complex, β-CD, FTIR, NMR, Fluorescence spectroscopy*

Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 2015, 137, 804-809; DOI:10.1016/j.saa.2014.08.081

Gaurav, C.; Goutam, R.; Rohan, K. N.; Sweta, K. T.; Abhay, C. S.; Amit, G. K.

**(Copper-curcumin) β-cyclodextrin vaginal gel: Delivering a novel metal-herbal approach for the development of topical contraception prophylaxis**

*Copper-curcumin, β-Cyclodextrin, Nano-inclusion complex, Spermicidal gel, Spermicidal assay, Toxicity studies in rats and rabbits*


**β-Cyclodextrin-grafted on multiwalled carbon nanotubes as versatile nanoplatform for entrapment of guanine-based drugs**

*Click chemistry, Multiwalled Carbon nanotubes, β-Cyclodextrins, Guanine, Acyclovir, Sustained delivery*


Kim, J. Y.; Wood, R. I.

**Anabolic-androgenic steroids and appetitive sexual behavior in male rats**

*Anabolic agents, Androgen, Food reward, Operant behavior, Sexual behavior, animal*

Hormones and Behavior, 2014, 66, 585-590; DOI:10.1016/j.yhbeh.2014.08.009

Kono, H.; Teshirogi, T.

**Cyclodextrin-grafted chitosan hydrogels for controlled drug delivery**

*Carboxymethyl chitosan, Carboxymethyl cyclodextrin, Hydrogel, Acetylsalicylic acid, Controlled drug release*

International Journal of Biological Macromolecules, 2015, 72, 299-308; DOI:10.1016/j.ijbiomac.2014.08.030
Kumar, N.; Goindi, S.; Bansal, G.

**Physicochemical evaluation and in vitro release studies on itraconazolium sulfate salt**

*Itraconazole, Solubility, Dissolution, Cyclodextrins, BCS Class II, Antifungal, β-CD, HP-β-CD*


Li, X.; Yu, Y.; Ji, Q.; Qiu, L.

**Targeted delivery of anticancer drugs by aptamer AS1411 mediated Pluronic F127/cyclodextrin-linked polymer composite micelles**

*Aptamer, Composite micelles, Cyclodextrin, Pluronic F127, Doxorubicin, Targeted delivery of doxorubicin*

Nanomedicine: Nanotechnology, Biology and Medicine, 2014, In Press; DOI:10.1016/j.nano.2014.08.013

Luo, X.; Zhang, H.; Chen, M.; Wei, J.; Zhang, Y.; Li, X.

**Antimetastasis and antitumor efficacy promoted by sequential release of vascular disrupting and chemotherapeutic agents from electrospun fibers**

*Electrospun fiber, Vascular disrupting agent, Release modulation, Antitumor efficacy, Tumor metastasis, Combretastatin, Inoculation of (2-hydroxy)propil-β-cyclodextrin in fiber matrices, Orthotopic breast tumor model, Sustained release*


Matloob, A. H.; Mourtas, S.; Klepetsanis, P.; Antimisiaris, S.

**Increasing the stability of curcumin in serum with liposomes or hybrid drug-in-cyclodextrin-in-liposome systems: A comparative study**

*Curcumin, Liposome, Cyclodextrin, Inclusion complex, Stability, Serum, HP-β-CD, HP-γ-CD*


**Effects of intracerebroventricular administration of 2-hydroxypropyl-β-cyclodextrin in a patient with Niemann-Pick Type C disease**

*Niemann-Pick Type C disease, Cyclodextrin, Cholesterol, Intrathecal administration, Intracerebroventricular administration, Pharmacokinetics, Blood-brain barrier, Intrathecal HP-β-CD*

Molecular Genetics and Metabolism Reports, 2014, 1, 391-400; DOI:10.1016/j.ymgmr.2014.08.004

Mura, P.; Bragagni, M.; Mennini, N.; Cirri, M.; Maestrelli, F.

**Development of liposomal and microemulsion formulations for transdermal delivery of clonazepam: Effect of randomly methylated β-cyclodextrin**
Clonazepam, Randomly methylated β-cyclodextrin, Microemulsions, Liposomes, Transdermal delivery, Permeation enhancers, Permeation through excised rabbit ear skin, Increased drug permeability


Sudha, N.; Chandrasekaran, S.; Sameena, Y.; Israel, V.M.V.E.

Mode of encapsulation of Linezolid by β-cyclodextrin and its role in bovine serum albumin binding

Linezolid, β-Cyclodextrin, 2D ROESY, Bovine serum albumin, Fluorescence, FRET, Fluorescence quenching, Förster resonance energy transfer

Carbohydrate Polymers, 2015, 115, 589-597; DOI:10.1016/j.carbpol.2014.09.022

Nguyen, D.N.; Van den Mooter, G.

The fate of ritonavir in the presence of darunavir

Ritonavir, Darunavir, Solid dispersion, Spray drying, Cyclodextrins, Solubility, (2-hydroxy)propyl-β-cyclodextrin


Étude in vitro de l’impact du Sugammadex (Sdx) sur les paramètres de Thrombélastométrie (TEM) chez un modèle porcin


Self-assembled biotransesterified cyclodextrins as potential Artemisinin nanocarriers. II: in vitro behavior toward the immune system and in vivo biodistribution assessment of unloaded nanoparticles

Bioesterified γ-cyclodextrins, Artemisinin, PEGylated amphiphiles, Con-nanoprecipitation, Surface-decorated nanoparticles, Hemolytic properties, Stealth properties, Biodistribution, γ-CD fatty esters

European Journal of Pharmaceutics and Biopharmaceutics, 2014, In Press; DOI:10.1016/j.ejpb.2014.08.012

Yum, M-S.; Lee, M.; Ko, T-S.; Velišek, L.

A potential effect of ganaxolone in an animal model of infantile spasms

Ganaxolone, Infantile spasms, Animal model, GABA, Neurosteroid

4. CDs in Cell Biology

Crichton, E. G.; Pukazhenthi, B.; Billah, M.; Skidmore, J. A.

**Cholesterol addition aids the cryopreservation of dromedary camel (Camelus dromedarius) spermatozoa**

*Camel, Sperm, CLC, Acrosomal integrity, Capacitation, Cholesterol-loaded cyclodextrin, Enhanced cryosurvival*


**Caveolae in ventricular myocytes are required for stretch-dependent conduction slowing**

*Cardiac mechanoelectric feedback, Caveolae, Capacitance, Membrane cholesterol depletion by methyl-β-cyclodextrin*

Journal of Molecular and Cellular Cardiology, 2014, 76, 265-274; DOI:10.1016/j.yjmcc.2014.09.014

5. CDs in Food, Cosmetics and Agrochemicals


**Incorporation of hydroxypropyl-β-cyclodextrins into chitosan films to tailor loading capacity for active aroma compound carvacrol**

*Chitosan, (2-Hydroxy)propyl-β-cyclodextrins, Carvacrol, Loading and release, Antimicrobial films, Glycerol, Plasticization of the film*

Food Hydrocolloids, 2015, 43, 603-611; DOI:10.1016/j.foodhyd.2014.07.017


**Effect of light, methyl jasmonate and cyclodextrin on production of phenolic compounds in hairy root cultures of Scutellaria lateriflora**

*Scutellaria, Lamiaceae, Hairy roots, Verbascoside, Wogonin, Baicalein, Scutellarein, Phenolics, Methyl jasmonate, Cyclodextrin, Elicitation, Methyl-β-cyclodextrin*

Phytochemistry, 2014, 107, 50-60; DOI:10.1016/j.phytochem.2014.08.020


**Interaction of ochratoxin A with quaternary ammonium beta-cyclodextrin**

*Ochratoxin A, Cyclodextrin, Molecular inclusion, Fluorescence spectroscopy, Detoxification, Decontamination of drinks*

Food Chemistry, 2015, 172, 143-149; DOI:10.1016/j.foodchem.2014.09.034
Santos, E. H.; Kamimura, J. A.; Hill, L. E.; Gomes, C. L.

**Characterization of carvacrol beta-cyclodextrin inclusion complexes as delivery systems for antibacterial and antioxidant applications**

Carvacrol, Natural antimicrobial, β-cyclodextrin inclusion complexes, Storage stability, Antimicrobial activity, Kneading, Freeze drying

LWT- Food Science and Technology, 2015, 60, 583-592; DOI:10.1016/j.lwt.2014.08.046

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**6. CDs for other Industrial Applications**

Liu, H.; Li, Y.; Wu, H.; Yang, W.; He, D.;

**Effects of Nd, Ce, and La modification on catalytic performance of Ni/SBA-15 catalyst in CO₂ reforming of CH₄**

Rare earth metal, Nd modification, Nickel, SBA-15 catalyst, Carbon dioxide reforming of methane, Carbon deposition, β-Cyclodextrin-modified impregnation method


Moulahcene, L.; Skiba, M.; Senhadji, O.; Milon, N.; Benamor, M.; Laiani-Skiba, M.

**Inclusion and removal of pharmaceutical residues from aqueous solution using water-insoluble cyclodextrin polymers**

Progesterone, Endocrine disruptor, Cyclodextrin polymer (PolyCyC®), Adsorption, Crosslinked with citric acid, Recycling column procedure

Chemical Engineering Research and Design, 2014, In Press; DOI:10.1016/j.cherd.2014.08.023

Spasojević, J. M.; Maletić, S. P.; Rončević, S. D.; Radnović, D. V.; Čučak, D. I.; Tričković, J. S.; Dalmacija, B. D.

**Using chemical desorption of PAHs from sediment to model biodegradation during bioavailability assessment**

PAH, XAD4, MCD, Biodegradation, Desorption, Methyl-β-cyclodextrin


**Cyclodextrin microencapsulated ammonium polyphosphate: Preparation and its performance on the thermal, flame retardancy and mechanical properties of ethylene vinyl acetate copolymer**

A. Polymer-matrix composites (PMCs), B. Physical properties, C. Thermal analysis, D. Mechanical testing, Microencapsulation, Toluene-2,4-diisocyanate, Ethylene vinyl acetate copolymer, Water durability

Composites Part B: Engineering, 2015, 69, 22-30; DOI:10.1016/j.compositesb.2014.09.015

Zhang, X.; Wang, Y.; Yang, S.

**Simultaneous removal of Co(II) and 1-naphthol by core-shell structured Fe₃O₄@cyclodextrin magnetic nanoparticles**
Zhang, F-B.; Jiang, J-X.; Ni, Y.

**Synthesis of Pd/C composites from PdCl₂ and β-CD as a catalyst in methanol oxidation**

*Pd nanoparticles, β-CD, TEM, Electrode*

Materials Science and Engineering: B, 2014, 190, 90-95; DOI:10.1016/j.mseb.2014.09.012

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7. CDs in Sensing and Analysis

Bathinapatla, A.; Kanchi, S.; Singh, P.; Sabela, M. I.; Bisetty, K.

**Fabrication of copper nanoparticles decorated multiwalled carbon nanotubes as a high performance electrochemical sensor for the detection of neotame**

*Neotame, Electrochemical sensor, Cyclic voltammetry, Differential pulse voltammetry, β-Cyclodextrin/glassy carbon electrode*

Biosensors and Bioelectronics, 2014, *In Press*; DOI:10.1016/j.bios.2014.08.017

Ghanem, A.; Ahmed, M.; Ishii, H.; Ikekami, T.

**Immobilized β-cyclodextrin-based silica vs polymer monoliths for chiral nano liquid chromatographic separation of racemates**

*β-Cyclodextrin methacrylate, Silica monolith, Polymer monolith, Chiral separation, Nano-LC, Reversed phase chromatography, Baseline separation for alprenolol, bufuralol, carbuterol, cizolertine, propranolol, tebuconazole*

Talanta, 2015, 132, 301-314; DOI:10.1016/j.talanta.2014.09.006

Hamilton, A.; Breslin, C. B.

**The development of a novel urea sensor using polypyrrole**

*Polypyrrole, Urea sensor, Urease, Cyclodextrin, Ascorbic acid, Polypyrrole-urease-sulfonated-β-cyclodextrin*


Lenik, J.

**A new potentiometric electrode incorporating functionalized β-cyclodextrins for diclofenac determination**

*Potentiometric electrode, Diclofenac, Pharmaceutical analysis, Diclofenac-selective membrane electrodes, (2-Hydroxy)propyl-β-cyclodextrin, Heptakis(2,3,6-tri-O-methyl)-β-cyclodextrin, Heptakis(2,3,6-tri-O-benzoyl)-β-cyclodextrin*


Detection and classification of host-guest interactions using β-cyclodextrin-decorated carbon nanotube-based chemiresistors

- Carbon nanotubes, Chemiresistor, Cyclodextrin, Sensing, Correlation, 9-Anthracenecarboxylic acid, Diclofenac sodium, Curcumin, Perylene tetracarboxylic acid

Current Applied Physics, 2014, 14, 1649-1658; DOI:10.1016/j.cap.2014.09.017

Wahl, O.; Holzgrabe, u.;

Evaluation of enantiomeric purity of magnesium-L-aspartate dihydrate

- Pharmaceutical analysis, Capillary electrophoresis, Magnesium aspartate, Chiral separation, Racemization, (2-Hydroxy)propyl-β-cyclodextrin coupled to laser induced fluorescence detection

Journal of Pharmaceutical and Biomedical Analysis, 2015, 102, 100-109; DOI:10.1016/j.jpba.2014.08.013

Yang, L.; Zhao, H.; Li, C-P.; Fan, S.; Li, B.

Dual β-cyclodextrin functionalized Au@SiC nanohybrids for the electrochemical determination of tadalafil in the presence of acetonitrile

- Host-guest, β-Cyclodextrin functionalized Au@SiC, Molecular recognition, Tadalafil, Electrochemical sensing, SH-β-CD, Differential pulse voltametry

Biosensors and Bioelectronics, 2015, 64, 126-130; DOI:10.1016/j.bios.2014.08.068

Zhang, J.; Pan, M.; Gan, N.; Cao, Y.; Wu, D.

Employment of a novel magnetically multifunctional purifying material for determination of toxic highly chlorinated polychlorinated biphenyls at trace levels in soil samples

- Clean-up, Carboxymethyl-β-cyclodextrin, Organochlorine pesticide, Highly chlorinated polychlorinated biphenyls, Gas chromatography-mass spectrometry

Journal of Chromatography A, 2014, 1364, 36-44; DOI:10.1016/j.chroma.2014.08.076