

Germany and the Cyclodextrin Science and Technology

The 17th International Cyclodextrin Symposium will be held in May, in Germany, organized by Prof. Gerhard Wenz at Saarland University.

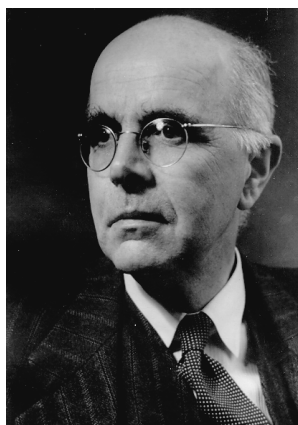
This Editorial is, therefore, intended to be an overview of the impact of German Science and German scientists on the cyclodextrin technology. This article is – at the same time– a **hommage à German Pioneers** and their followers, those who contributed remarkably to the scientific and technical advancements achieved in this field since the early 1930's to date.

It is interesting to realize that almost all major Universities across Germany have been involved in the cyclodextrin science to different extents. Almost all aspects of cyclodextrin chemistry and applications have been subject at German laboratories.

The very beginning: University of Heidelberg and Karl Freudenberg (1886–1983)

The great German pioneer, Karl Freudenberg (Photo 1) worked at the University of Heidelberg at the Chemistry Department. In 1935, he and his doctorant co-worker, Richard Jacobi, published an influential paper on the chemical structure of cyclodextrins convincingly stating their well-founded opinion, that these oligosaccharides are of cyclic structure. (*Justus Liebigs Annalen der Chemie* [Vol 518, Issue 1, pages 102–108](#), titled "About Schardinger dextrans from Starch".)

Freudenberg also reported – probably for the first time – that the two types of purified Schardinger-dextrans, the alpha- and beta-dextrans would show different aqueous solubility. Alpha is well soluble, while the beta is less soluble.

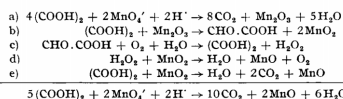


Karl Freudenberg 1951

Photo 1. Karl Freudenberg in 1951.

Five years later, in 1936, Freudenberg and Wilhelm Rapp reported on the laboratory scale simple process to prepare Schardinger dextrans from potato starch via controlled enzymatic hydrolysis. This paper also served for many years as a solid ground for making cyclodextrins from amylose and starch pre-hydrolysates under laboratory conditions, in particular on how the cyclic dextrin fractions can be efficiently separated from linear fragments (see cover page of that paper in Figure 1a). The kinetics of enzymatic hydrolysis of amylose was also studied and reported. Today, we certainly must appreciate the importance and technical significance of this work, since the current sophisticated cyclodextrin manufacturing technologies are similar to that what was described about 80 years ago by Freudenberg and co-workers. Also in the same year Freudenberg's group published on the acetolysis and hydrolysis of starch and Schardinger dextrans and set up well founded rules and the behavior of cyclodextrins during amyolytic degradation. They provided the very first hydrolysis kinetics data and rate constants of the hydrolysis of glycosidic linkages. (*Berichte der deutschen chemischen Gesellschaft A and B Series, Vol.69. pages 1258–1266, 10. 1936, Figure 1b*)

(1936) *Freudenberg, Rapp.* 2041



Hiermit übereinstimmend hat Schröder gefunden, daß bei rascher Titration und Durchleiten von Sauerstoff die Ergebnisse richtig bleiben¹⁾. Die Natur der „aktivierten Form“ der Oxalsäure und die bei der Wasserstoffsperoxyd-Bildung sich abspielenden Vorgänge dürften klargestellt und das bisher rätselhafte am Verhalten der Oxalsäure auf durchaus verständliche chemische Reaktionsweisen zurückgeführt sein.

374. Karl Freudenberg und Wilhelm Rapp: Zur Kenntnis der Stärke und der Schardinger-Dextrine.

[Aus d. Chem. Institut d. Universität Heidelberg.]
(Eingegangen am 3. August 1936.)

I) Stärke.

Bei den Versuchen über Stärke, die wir vor kurzem mitgeteilt haben¹⁾, wurden die beiden wichtigsten Anteile des Polysaccharids, die Amylose und das Amylopektin, getrennt untersucht. Die Kinetik der Hydrolyse war bei beiden Präparaten die gleiche. Hier soll zunächst berichtet werden, in welcher Weise die Stärke für die erwähnten und die hier zu schildernden Versuche in Anlehnung an die Vorschriften von M. Samec fraktioniert wurde.

Die verwendete Kartoffelstärke hatte nach Versicherung der Hersteller keinerlei chemische Behandlung (Bleiche usw.) durchgemacht, was besonders für die Bereitung der Schardinger-Dextrine zu beachten ist. Sie wird mit wenig Wasser angerieben und mit 50 Tln. einer 10-proz. wäßrigen Kaliumrhodanid-Lösung²⁾ 1/2 Stde. auf 55° erwärmt. Die opake, viscose Lösung wird nach dem Erkalten mit Essigsäure ganz schwach angesäuert und zuerst in einem gewöhnlichen Rührdialysator gegen destilliertes Wasser von Rhodanion befreit. Die letzten Elektrolyten werden in einem 5 l fassenden Elektrodialysator entfernt. An der Anode ballt sich das Amylopektin zusammen und sinkt zu Boden (85%), während die Amylose (12–15%) in Lösung bleibt. Nach Konzentration im Vakuum wird die Amylose durch Methanol gefällt. Das gallertige Amylopektin wird in so viel Wasser aufgeschlämmt, daß die Mischung in Bezug auf Trockensubstanz etwa 2-proz. ist. Hierzu wird Kaliumrhodanid gegeben (¹/₁₀ des Gewichts der Mischung). Nun wird durch Erwärmen gelöst, dialysiert und elektrodialysiert. Man unterbricht die

¹⁾ I. c.

²⁾ K. Freudenberg, G. Blomqvist, L. Ewald u. K. Soff, B. 69, 1258 [1936]; Zusammenfassung über Stärke: K. Freudenberg, Chem.-Ztg. 60 [1936], im Druck; Wiener Monatsh. Okt. 1936.

³⁾ E. Meusel, Die Quellkraft der Rhodanate, Gera 1886.

1258 *Freudenberg, Blomqvist, Ewald, Soff: Hydrolyse* [Jahrg. 69

231. Karl Freudenberg, Gunnar Blomqvist, Lisa Ewald und Karl Soff: Hydrolyse und Acetolyse der Stärke und der Schardinger-Dextrine.

[Aus d. Chem. Institut d. Universität Heidelberg.]
(Eingegangen am 15. April 1936.)

I) Stärke.

In der ersten Arbeit über die Hydrolyse von Cellulose und Stärke wurde festgestellt, daß beide Polysaccharide denselben Gesetzmäßigkeiten der Kinetik unterliegen¹⁾. Die Versuche wurden inzwischen an der Cellulose mit größerer Genauigkeit wiederholt²⁾. Dasselbe ist jetzt an der Stärke geschehen.

Hydrolyse.

Amylopectin und Amyloamylose aus selbst bereiteter Kartoffelstärke verhalten sich in 51-proz. Schwefelsäure völlig gleich. In den Tabellen wird daher kein Unterschied zwischen diesen Anteilen gemacht.

Aus dem nach t Min. gefundenen Spaltungsgrad α wurde nach $P = 1/t \ln 1/(1-\alpha)$ die zwischen den Zeiten 0 und t maßgebende mittlere Geschwindigkeitskonstante berechnet. P wurde gegen $1-\alpha$ aufgetragen und interpoliert. So ergeben sich die Spalten 2 und 3 in den Tabellen 1 und 2. Die zugeordneten Zeiten sind in Spalte 1 angeführt. Diese 3 ersten Spalten enthalten demnach das interpolierte Versuchsergebnis (siehe auch Figur 1, Kurve 1).

Unlängst wurde gezeigt³⁾, daß sich die Kinetik der Hydrolyse der Cellulose am besten erfassen läßt mit einer Formel 6a von W. Kuhn⁴⁾, die von der Annahme ausgeht, daß eine End-Bindung eines jeden Spaltstückes nach K_2 , der Konstanten der Hydrolyse des Disaccharids, gespalten wird, während die übrigen Bindungen eines jeden Spaltstückes der Anfangsgeschwindigkeit des intakten Polysaccharids folgen. Die Berechnung wurde ausgeführt mit der Geschwindigkeitskonstanten K_2 der Maltose und mit P_{50} , d. h. der gefundenen mittleren Geschwindigkeit zwischen $t = 0$ und der Zeit (6190 Min.), bei der 50-proz. Spaltung erreicht ist. Durch diese beiden Werte sind mit Hilfe der Formel 6a alle Kurvenpunkte bestimmt; für $P_0 = K_0$ (Anfangsgeschwindigkeit) ergibt sich 1.02×10^{-4} .

Die Spaltungsgeschwindigkeit der Maltose ist unter denselben Bedingungen $K_2 = 1.43 \times 10^{-4}$. α' ist der polarimetrisch ermittelte vermeintliche Spaltungsgrad. Wegen weiterer Einzelheiten wird auf die frühere Arbeit verwiesen⁵⁾ (siehe auch Figur 1, Kurve 2 und 4).

¹⁾ K. Freudenberg, W. Kuhn, W. Dürr, F. Bolz u. G. Steinbrunn, B. 68, 1510 [1930].

²⁾ K. Freudenberg u. G. Blomqvist, B. 68, 2070 [1935]. Eine Zusammenstellung sämtlicher verwendeter, von W. Kuhn sowie G. Blomqvist abgeleiteter Formeln findet sich in den Sitz.-Ber. d. Heidelberger Akad. d. Wiss. 1936; von G. Blomqvist.

³⁾ B. 68, 2070 [1935].

⁴⁾ Ztschr. physikal. Chem. (A) 159, 372 [1932].

⁵⁾ B. 68, 2074 [1935]. Die Formel für die Umrechnung von α in α' findet sich bei G. Blomqvist, Sitz.-Ber. d. Heidelberger Akad. d. Wiss. [1936].

Figure 1. a) The cover page of Freudenberg-Rapp paper and b) of Freudenberg paper on acetolysis both published in 1936.



After World War II: Friedrich Cramer (1923–2003), University of Göttingen (Max-Planck Institute of Experimental Medicine)

After the World War II, in early 1950s, two groups have taken up the dominating position in the cyclodextrin chemistry and applications: in the USA Dexter French at Iowa state University, while in Europe Friedrich Cramer's group at the Max-Planck Institute of Experimental Medicine, in Göttingen, Germany.

Interesting to note that Cramer wrote his PhD thesis under supervision of Karl Freudenberg in 1949, then made his habilitation in 1953 both on the Cyclodextrins subject.

Not many cyclodextrin chemists are aware of the really interesting fact, that Cramer has got a postdoctoral position at University of Cambridge in England to work with James Watson and Francis Crick in 1953. Watson and Crick involved Cramer in their double helix studies, as the German chemist had previous and solid knowledge on other type (glucose-based) helical structures (such as amylose/starch and their iodine complexes). In 1954 Cramer returned to Heidelberg University and delivered the very first lecture on new discoveries around DNA's helical structure and on the chemistry of heredity, in Germany.

Cramer's group – benefiting from the availability of pure cyclodextrins in larger gram scales – worked on the preparation and characterization of cyclodextrin inclusion complexes. A number of even today useful complexation technologies were developed and communicated by the team. He and his group with Drs. Henglein, Dietsche, Kampe and others, convincingly published on the main physico-chemical properties of binary host-guest inclusion complexes. The diversity of guest substances studied by Cramer with the host (mainly alpha- and beta-) cyclodextrins in these studies was really remarkable. These studies included noble gases, halogens, aromatic organic substances, slim fatty acids, even the synthetic azo dyes and other types of colorants. Hundreds of different cyclodextrin complexes were isolated in crystalline form and the consequences of the inclusion phenomenon were described, in detail. Cramer and his co-workers set up rules for the basic terms of complex formation and they made suggestions on the putative step-wise mechanism of the complex formation and determined the main thermodynamic driving forces of the non-covalent interactions. In the early 1950s Cramer actually laid down the ground rules of inclusion complex chemistry. Interesting to mention that he made the first observation that the complexation with cyclodextrins may proceed in a stereochemically controlled manner. Also he suggested that cyclodextrins could have some utility in chiral recognitions via inclusion complex formation.

Friedrich Cramer and co-workers in Göttingen authored about 40 papers, and all of them are today valuable „scientific historical monuments“ for all of us.

In 1962 Cramer was appointed as the director of Max-Planck Institute of Experimental Medicine, in Göttingen and he acted in this position until 1991.



Freie University Berlin, Professors Wolfram Saenger (1939–) and Karl-Heinz Frömring (1923–2006)

The forerunner of Berlin Freie University, the Kaiser Wilhelm Institute was founded in 1911 for the promotion of natural sciences by the emperor, himself. (During the first few decades great scientists worked in these institutes such as Werner Heisenberg, Peter Debye, Albert Einstein, Fritz Haber, Otto Hahn, Walter Bothe, just to name a few eminent persons.)

After World War II, this neighborhood and the old buildings were reconstructed the university reorganized and the prestigious Freie Universität Berlin was established.

Freie University has played a decisive role in cyclodextrin science in particular regarding the structural aspects of cyclodextrin hydrates and the inclusion complexes. Wolfram Saenger – who had a privilege to work with F. Cramer in Göttingen – became one of the most influential scientist concerning the different hydrate forms of parent- and chemically modified cyclodextrins and the topology, crystal structure of host guest complexes.

Moreover from the early 1970 s Prof. Frömring at the pharmaceutical department started a decades-long project on the utilization of CDs in different pharmaceutical formulations.

Germany pioneers in separation science: Wilfried König (1939–2004) in Hamburg and Volker Schurig (1940–) in Tübingen

Professor Wilfried König at the Department of Organic Chemistry University of Hamburg has played a dominating role in the cyclodextrin-assisted chiral recognitions. He has been most active in the enantioseparations by gas chromatography. König invented a number of chemically modified cyclodextrins as stationary phases suitable as coatings in capillary gas chromatography. He and co-workers developed a number of chiral separation GC methods today routinely used for the analysis of natural substances, flavors, fragrances, essential oils, etc. using cyclodextrin-based capillary GC columns.

Another German separation scientist, Professor Volker Schurig, at the Institute for Organic Chemistry of University of Tuebingen has become one of the most influential person in cyclodextrin-based chiral separations both in capillary GC and electrochromatography. Schurig and his team published over 170 scientific technical papers and filed a number of patents concerning the use of alkylated CD-based chiral stationary phases.

Hans Bender (1907–1991) University of Freiburg im Breslau: The enzymology and biotransformation of polysaccharides including cyclodextrins, has been one of the major subjects of studies by Professor Hans Bender and his team at University of Freiburg. Both cyclodextrin forming and cleaving types of bacterial enzymes were involved in their studies. Bender and colleagues played a decisive role in locating and determining the active centers of



CTG-ase enzymes originated from different species. Such a pioneering work by Bender's group was the first detailed description of cyclodextrin glucanotransferase isolated from *Klebsiella pneumoniae* in 1977. (Arch. Microbiol., 111(3), 271-82, 1977)

Bender studied also the CD degrading enzymes from diverse microorganisms, for instance by developing partial purification processes and describing properties of the enzyme from a *Flavobacterium* species. Bender's contribution has been one of the most influential to the establishment of an industrially feasible enzymatic technology for manufacturing of cyclodextrins.

University of Darmstadt: Frieder W. Lichtenthaler (1932–) and Stefan Immel (1965–)

Professors Lichtenthaler and Immel played a fundamental role in the right and unanimous nomenclature of cyclodextrins in addition to constructing a molecular library with computer-aided illustrations of the most probable structures and geometries of cyclodextrins and other cyclic oligosaccharides. This library has been available for years as a reliable source of the computer-based generation of the three dimensional geometries and the contact surfaces for the cyclodextrins and cyclic oligosaccharides made up of galactose, mannose, altrose and fructose. The MOLCAD program's computation of the molecular lipophilicity patterns (MLPs), projected in color-coded form onto the respective contact surfaces, for the first time allowed a precise localization of hydrophobic and hydrophilic domains that determine complex formation of cyclic oligosaccharides.

Wacker Chemie, the German Cyclodextrin Manufacturer

Consortium für Elektrochemische Industrie, Dr. Frank Müller (1929–??) and Wacker Chemie Dr. Gerhard Schmid (1957–) and his team

In early 1980's Wacker Chemie was the first German company that opened toward biotechnology-related projects. Manufacturing of enzyme-modified starch, in particular the cyclodextrins were in the focus of these attempts. Dr. Frank Müller, the managing director of Consortium for Electrochemical industry „crossed the iron curtain“ and discussed the details of Hungarian cyclodextrin manufacturing technology with József Szejtli at the Chinoin factory. A dedicated young biotechnology engineer, Dr. Gerhard Schmid optimized the type and use of cyclodextrin glycosyl transferase enzymes and the reaction conditions of bioconversion leading to the optimization of CD-manufacturing technology at an industrial scale. Since that time Wacker Chemie became a world-wide recognized key manufacturer of the parent alpha- beta- and gamma cyclodextrins (Cavamax™ product line), as well as HPBCD, HPGCD and methyl-beta-cyclodextrins (Cavasol™ product line). Wacker has also played a significant role in providing cyclodextrins and CD complexes for nutraceutical, food and cosmetic purposes. Wacker has recognized the possibility of utilization of parent gamma- and alpha-CDs as



valuable dietary fibers.

There are various research teams working on cyclodextrins even at present increasing the contribution of the country to the cyclodextrin science and technology, no wonder that the organizing committee accepted the offer of Prof. Wenz to organize the symposium in 2014. This is the 2nd time that Germany is the host of the International Cyclodextrin Symposium. The 4th ICS was held in Munich, West Germany in 1988 organized by Wacker Chemie. The conference proceedings book (still available at Kluwer) was published with the introductory remarks by Prof. Cramer.

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Budapest, HUNGARY



BIBLIOGRAPHY & KEYWORDS

1. CDs: Derivatives, Production, Enzymes, Toxicity

Cho, E.; Kim, H.; Yang, J. E.; Jun, B-H.; Paik, S. R.; Jung, S.

Supramolecular self-assembled aggregates formed by pentacosa-10,12-diynyl amidomethyl- β -cyclodextrin

10,12-Pentacosadiynoic Acid, Self-Assembly, Supramolecular Structure, Worm-Like Nano-Aggregates of Columnar-Type, Reacting 6-Monodeoxy-6-Monoamino-B-Cyclodextrin With N-Hydroxysuccinimide Ester of 10,12-Pentacosadiynoic Acid

Carbohydrate Research, 2014, 391, 37-42; DOI:10.1016/j.carres.2014.03.022

Nakamura, Y.; Aihara, S.; Crofts, N.; Sawada, T.; Fujita, N.

In vitro studies of enzymatic properties of starch synthases and interactions between starch synthase I and starch branching enzymes from rice

Amylopectin, Endosperm, Oryza Sativa, Starch Branching Enzyme, Starch Synthase

Plant Science, 2014, 224, 1-8; DOI:10.1016/j.plantsci.2014.03.021

Nguyen, D. H. D.; Tran, P. L.; Li, D.; Han, J-A.; Hwang, J-Y.; Hong, W-S.; Lee, J-S.; Kim, Y-R.; Yoo, S-H.; Park, J-T.; Choi, Y-J.; Lee, S-Y.; Park, K-H.

Modification of rice grain starch for lump-free cooked rice using thermostable disproportionating enzymes

α -Glucanotransferase, Cyclodextrin Glucanotransferase, Disproportionating Enzyme, Lump-Free Cooked Rice And Rice Porridge, Rice Starch, Thermostable Enzyme

Food Research International, 2014, In press; DOI:10.1016/j.foodres.2014.04.007

Tanabe, K.; Nakamura, S.; Oku, T.

Inaccuracy of AOAC method 2009.01 with amyloglucosidase for measuring non-digestible oligosaccharides and proposal for an improvement of the method

Accuracy Quantitation Method, Amyloglucosidase, Non-Digestible Oligosaccharide, Porcine Intestinal Enzymes, Sucrose, Palatinose, Panose, Isomaltooligosaccharide

Food Chemistry, 2014, 151, 539-546; DOI:10.1016/j.foodchem.2013.11.121

Xu, Z.; Chen, X.; Liu, J.; Yan, D-Q.; Diao, C-H.; Guo, M-J.; Fan, Z.

Self-assembly behavior of tail-to-tail superstructure formed by mono-6-O-(4-carbamoylmethoxy-benzoyl)- β -cyclodextrin in solution and the solid state

Crystal Structure, Self-Assembly Behavior, Supramolecular Chemistry, β -Cyclodextrin

Carbohydrate Research, 2014, In press; DOI:10.1016/j.carres.2014.04.010



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

Ji, Y.; Kang, W.; Meng, L.; Hu, L.; Yang, H.

Study of the solution behavior of β -cyclodextrin amphiphilic polymer inclusion complex and the stability of its O/W emulsion

Cyclodextrin Polymer, Enhanced Oil Recovery, Inclusion Association, O/W Crude Oil Emulsion, Rheological Property, Thickening, Critical Aggregation Concentrations

Colloids and Surfaces A: Physicochemical and Engineering Aspects, 2014, 453, 117-124; DOI:10.1016/j.colsurfa.2014.04.016

Kuchlyan, J.; Banerjee, C.; Ghosh, S.; Kundu, N.; Banik, D.; Sarkar, N.

Effect of room temperature surface active ionic liquids on aggregated nanostructures of γ -cyclodextrins: a picosecond fluorescence spectroscopic study

1-Dodecyl-3-methyl Imidazolium Chloride

Chemical Physics Letters, 2014, 601, 174-180; DOI:10.1016/j.cplett.2014.03.066

Lv, S.; Song, Y.; Song, Y.; Zhao, Z.; Cheng, C.

Beta-cyclodextrins conjugated magnetic Fe_3O_4 colloidal nanoclusters for the loading and release of hydrophobic molecule

(3-Glycidyloxypropyl) Trimethoxysilane, Functionalization, Hydrophobic Molecule, Inclusion Complex, Magnetic Colloidal Nanocrystal Clusters, β -Cyclodextrin, 8-Anilino-1-Naphthalenesulfonic Acid

Applied Surface Science, 2014, 305, 747-752; DOI:10.1016/j.apsusc.2014.03.191

Pandey, R. K.; Lakshminarayanan, V.

Cyclodextrin inclusion complexes with thiocholesterol and their self-assembly on gold: a combined electrochemical and lateral force microscopy analysis

Atomic Force Microscopy, Electrochemistry, Friction Force Microscopy, Inclusion Complex, Self-Assembled Monolayer

Thin Solid Films, 2014, In press; DOI:10.1016/j.tsf.2014.04.063

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

Spectral investigation and structural characterization of dibenzalacetone: β -cyclodextrin inclusion complex

1,4-Pentadien-3-one, 5-Diphenyl-1, Atomic Force Microscopy, Fourier Transform Infra Red, Inclusion Complex, Molecular Docking, Thermal Analysis, β -Cyclodextrin

J. Mol. Structure, 2014, 1068, 155-163; DOI:10.1016/j.molstruc.2014.04.004



Qin, L.; Duan, P-F; Liu, M-H.

Interfacial assembly and host-guest interaction of anthracene-conjugated l-glutamate dendron with cyclodextrin at the air/water interface

Dendron, Host-Guest Complex, Supramolecular Assembly, γ -Cyclodextrin, π - π Stacking, Langmuir Monolayer

Chinese Chemical Letters, 2014, 25, 487-490; DOI:10.1016/j.ccllet.2013.12.019

Sarkar, A.; Kedia, N.; Purkayastha, P.; Bagchi, S.

Spectroscopic study on encapsulation of two structurally similar donor-acceptor dyes in model cyclodextrin nanocavity

Donor-Acceptor Dyes, Encapsulation, Fluorescence, Guest-Host Complex, β -Cyclodextrin Nanocavity, Semi-empirical Calculations

J. Mol. Structure, 2014, 1068, 228-236; DOI:10.1016/j.molstruc.2014.04.027

Srinivasan, K.; Stalin, T.

Study of inclusion complex between 2,6-dinitrobenzoic acid and β -cyclodextrin by 1H NMR, 2D 1H NMR (ROESY), FT-IR, XRD, SEM and photophysical methods

2D 1H NMR (ROESY), 6-Dinitrobenzoic Acid, Inclusion Complex, β -Cyclodextrin, Molecular Docking, Cyclic Voltammetry

Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 2014, 130, 105-115; DOI:10.1016/j.saa.2014.03.106

Terekhova, I. V.; Chibunova, E. S.; Kumeev, R. S.; Alper, G. A.

Cyclodextrin-benzoic acid binding in salt solutions: effects of biologically relevant anions

Complex Formation, Salt Effects, Competing Interactions of Cyclodextrin-Anion, Ternary Complex Formation

Carbohydrate Polymers, 2014, 110, 472-479; DOI:10.1016/j.carbpol.2014.04.057

3. CDs in Drug Formulation

Almeida, H.; Amaral, M. H.; Lobão, P.; Lobo, J. M. S.

In situ gelling systems: a strategy to improve the bioavailability of ophthalmic pharmaceutical formulations

Biodegradable Polymers, (2-Hydroxy)propyl- β -Cyclodextrin, Methylated- β -Cyclodextrin, RAMEB

Drug Discovery Today, 2014, 19, 400-412; DOI:10.1016/j.drudis.2013.10.001

Cagno, M.; Nielsen, T. T.; Larsen, K. L.; Kuntsche, J.; Bauer-Brandl, A.

β -Cyclodextrin-dextran polymers for the solubilization of poorly soluble drugs

Calorimetry (ITC), Poorly Soluble Drugs, Solubilization, β CD-Dextran Polymers, Phase-Solubility Diagrams, Hydrocortisone

Int. J. Pharm., 2014, 468, 258-263; DOI:10.1016/j.ijpharm.2014.04.029



Celebioglu, A.; Umu, O. C. O.; Tekinay, T.; Uyar, T.

Antibacterial electrospun nanofibers from triclosan/cyclodextrin inclusion complexes

Antibacterial Activity, Electrospinning, Inclusion Complex, Nanofibers, Triclosan, HP β CD, HP γ CD, Gram-Negative (E. Coli) and Gram-Positive (S. Aureus) Bacteria

Colloids and Surfaces B: Biointerfaces, 2014, 116, 612-619; DOI:10.1016/j.colsurfb.2013.10.029

Constantin, M.; Bucatariu, S.; Harabagiu, V.; Ascenzi, P.; Fundueanu, G.

Do cyclodextrins bound to dextran microspheres act as sustained delivery systems of drugs?

Association Constant, Drug Release, Inclusion Complex, Liquid Chromatography, Indole, 3-Nitrophenol, p-Hydroxybenzoic Acid, Diclofenac, Sink Conditions

Int. J. Pharm., 2014, 469, 1-9; DOI:10.1016/j.ijpharm.2014.04.016

Duncan, M. J.; Franklin, K. M.; Peng, X.; Yun, C.; Legan, S. J.

Circadian rhythm disruption by a novel running wheel: roles of exercise and arousal in blockade of the luteinizing hormone surge

Circadian Rhythms, Hypocretin, Luteinizing Hormone, Orexin, Phase Shifts, ORX1 Antagonist, Vehicle, (2-Hydroxy)propyl-beta-Cyclodextrin in DMSO

Physiology & Behavior, 2014, 131, 7-16; DOI:10.1016/j.physbeh.2014.04.006

Hernandez-Montelongo, J.; Naveas, N.; Degoutin, S.; Tabary, N.; Chai, F.; Spampinato, V.; Ceccone, G.; Rossi, F.; Torres-Costa, V.; Manso-Silvan, M.; Martel, B.

Porous silicon-cyclodextrin based polymer composites for drug delivery applications

Composites, Drug Delivery, β -Cyclodextrin-Citric Acid Polymer, In-Situ Polymerization, Ciprofloxacin, Prednisolone

Carbohydrate Polymers, 2014, 110, 238-252; DOI:10.1016/j.carbpol.2014.04.002

Hu, B-G.; Liu, L-P.; Chen, G. G.; Ye, C. G.; Leung, K. K. C.; Ho, R. L. K.; Lin, M. C.; Lai, P. B. S.

Therapeutic efficacy of improved α -fetoprotein promoter-mediated TBID delivered by folate-PEI600-cyclodextrin nanopolymer vector in hepatocellular carcinoma

AFP Promoter, Folate Grafted PEI600-CD, HCC, TBID, Nano-Particle Vector, Sorafenib

Experimental Cell Research, 2014, In press; DOI:10.1016/j.yexcr.2014.04.005

Ma, M.; Guan, Y.; Zhang, C.; Hao, J.; Xing, P.; Su, J.; Li, S.; Chu, X.; Hao, A.

Stimulus-responsive supramolecular vesicles with effective anticancer activity prepared by cyclodextrin and ftorafur

Ftorafur, Vesicle, Human Colon Carcinoma Cell Lines, Copper Ions

Colloids and Surfaces A: Physicochemical and Engineering Aspects, 2014, 454, 38-45; DOI:10.1016/j.colsurfa.2014.04.005



Mattioli-Belmonte, M.; Cometa, S.; Ferretti, C.; Iatta, R.; Trapani, A.; Ceci, E.; Falconi, M.; Giglio, E.

Characterization and cytocompatibility of an antibiotic/chitosan/cyclodextrins nanocoating on titanium implants

Chitosan Nanoparticles, Ciprofloxacin, Cytocompatibility, Gene Expression, Orthopaedic Infections, Orthopaedic Implant Surface, Sulfobutyl Ether-beta-Cyclodextrin and -gamma-Cyclodextrin

Carbohydrate Polymers, 2014, 110, 173-182; DOI:10.1016/j.carbpol.2014.03.097

Parsian, A. R.; Vatanara, A.; Rahmati, M. R.; Gilani, K.; Khosravi, K. M.; Najafabadi, A. R.

Inhalable budesonide porous microparticles tailored by spray freeze drying technique

Budesonide, L-Leucine, Porous Particles, Spray Freeze Drying, (2-Hydroxy)propyl-beta-Cyclodextrin, Mannitol-Based Dry Powder Formulation

Powder Technology, 2014, 260, 36-41; DOI:10.1016/j.powtec.2014.03.043

Simões, S. M. N.; Veiga, F.; Ribeiro, A. C. F.; Figueiras, A. R.; Taboada, P.; Concheiro, A.; Alvarez-Lorenzo, C.

Supramolecular gels of poly- α -cyclodextrin and PEO-based copolymers for controlled drug release

Controlled Drug Release, Cyclodextrin Polymer, Drug Delivery, Polypseudorotaxane, Syringeable Supramolecular Gel, Crosslinking with Epichlorohydrine, PEG, Pluronic® F127; Tetronic® 908, Cytocompatibility

European Journal of Pharmaceutics and Biopharmaceutics, 2014, In press; DOI:10.1016/j.ejpb.2014.04.006

Sun, Y.; Du, L.; Liu, Y.; Li, X.; Li, M.; Jin, Y.; Qian, X.

Transdermal delivery of the in situ hydrogels of curcumin and its inclusion complexes of hydroxypropyl- β -cyclodextrin for melanoma treatment

Erosion, In situ Hydrogels, Inclusion Complexes, Melanoma, Transdermal, (2-Hydroxy)propyl-beta-Cyclodextrin, Photochemical Stability, Apoptosis

Int. J. Pharm., 2014, 469, 31-39; DOI:10.1016/j.ijpharm.2014.04.039

Yao, Y.; Xie, Y.; Hong, C.; Li, G.; Shen, H.; Ji, G.

Development of a myricetin/hydroxypropyl- β -cyclodextrin inclusion complex: preparation, characterization, and evaluation

Characterization, (2-Hydroxy)propyl-beta-Cyclodextrin, In vitro Dissolution, Inclusion Complex, Myricetin, Pharmacokinetics, Bioavailability, Antioxidant Activity

Carbohydrate Polymers, 2014, 110, 329-337; DOI:10.1016/j.carbpol.2014.04.006

Zhao, M-X.; Zhao, M.; Zeng, E-Z.; Li, Y.; Li, J-M.; Cao, Q.; Tan, C-P; Ji, L-N.; Mao, Z-W.

Enhanced anti-cancer efficacy to cancer cells by doxorubicin loaded water-soluble amino acids-modified β -cyclodextrin platinum complexes

Combination System, Doxorubicin, Drug Delivery, Platinum Complexes, Delivery the Antitumor Drug Dox, Potential Antitumor Drug

J. Inorganic Biochemistry, 2014, 137, 31-39; DOI:10.1016/j.jinorgbio.2014.03.012



Gaur, S.; Wang, Y.; Kretzner, L.; Chen, L.; Yen, T.; Wu, X.; Yuan, Y.-C.; Davis, M.; Yen, Y.

Pharmacodynamic and pharmacogenomic study of the nanoparticle conjugate of camptothecin CRLX101 for the treatment of cancer

Camptothecin, HIF-1 α , Immunohistochemistry, Nanoparticle, Polymer Conjugate, Solid Tumor, Topoisomerase 1, Cyclodextrin-Based Polymer, Tumor Growth Inhibition

Nanomedicine: Nanotechnology, Biology and Medicine, 2014, In press; DOI:10.1016/j.nano.2014.04.003

Roussenova, M.; Andrieux, J.-C.; Alam, M. A.; Ubbink, J.

Hydrogen bonding in maltooligomer–glycerol–water matrices: relation to physical state and molecular free volume

Anti-Plasticization, Hydrogen Bonding, Maltooligomers, Molecular Packing, Plasticization, Positron Annihilation

Carbohydrate Polymers, 2014, 102, 566-575; DOI:10.1016/j.carbpol.2013.12.003

4. CDs in Cell Biology

Suárez, D. F.; Consuegra, J.; Trajano, V. C.; Gontijo, S. M. L.; Guimarães, P. P. G.; Cortés, M. E.; Denadai, Â. L.; Sinisterra, R. D.

Structural and thermodynamic characterization of doxycycline/ β -cyclodextrin supramolecular complex and its bacterial membrane interactions

Antimicrobial, Cytotoxicity, Doxycycline, Membrane Interactions, Susceptibility, S. Aureus Cells, Adhesion of β CD to the Cell Membrane, Osteoblast Proliferation

Colloids and Surfaces B: Biointerfaces, 2014, 118, 194-201; DOI:10.1016/j.colsurfb.2014.01.028

Thomas, P. V.; Cheng, A. L.; Colby, C. C.; Liu, L.; Patel, C. K.; Josephs, L.; Duncan, R. K.

Localization and proteomic characterization of cholesterol-rich membrane microdomains in the inner ear

Caveolin, Cochlea, Hair Cell, Hearing, Lipid Raft, Microdomain, Calcium Signaling, Cholesterol-Modulator Beta-Cyclodextrin, Inducing Significant and Permanent Hearing Loss

Journal of Proteomics, 2014, 103, 178-193; DOI:10.1016/j.jprot.2014.03.037

5. CDs in Food, Cosmetics and Agrochemicals

Kayaci, F.; Sen, H. S.; Durgun, E.; Uyar, T.

Functional electrospun polymeric nanofibers incorporating geraniol–cyclodextrin inclusion complexes: high thermal stability and enhanced durability of geraniol

Electrospinning, Geraniol, Inclusion Complex, Nanofiber, Polyvinyl Alcohol (PVA), Ab initio Techniques, Electrospinning, Active Food Packaging, Functional Foods

Food Research International, 2014, 62, 424-431; DOI:10.1016/j.foodres.2014.03.033



Marroquin, M.; Vu, A.; Bruce, T.; Wickramasinghe, S. R.; Zhao, L.; Husson, S. M.

Evaluation of fouling mechanisms in asymmetric microfiltration membranes using advanced imaging

Aggregation, Beverage Clarification, Confocal Microscopy, Depth Filtration, Hermia Model, Pore Blocking, Microfiltration of Protein (Casein), Polyphenol (Tannic Acid), and Polysaccharide (β -cyclodextrin) Mixtures

Journal of Membrane Science, 2014, In press; DOI:10.1016/j.memsci.2014.03.077

Rosa, C. G.; Borges, Caroline D.; Zambiasi, R. C.; Rutz, J. K.; Luz, S. R.; Krumreich, F. D.; Benvenuto, E. V.; Nunes, M. R.

Encapsulation of the phenolic compounds of the blackberry (*rubus fruticosus*)

Chitosan, Hydrogel, Phenolic Compounds, Xanthan, β -Cyclodextrin, Gallic Acid, Epicatechin

LWT - Food Science and Technology, 2014, In press; DOI:10.1016/j.lwt.2014.03.042

Shao, P.; Zhang, J.; Fang, Z.; Sun, P.

Complexing of chlorogenic acid with β -cyclodextrins: inclusion effects, antioxidative properties and potential application in grape juice

Antioxidant Activity, Chlorogenic Acid, Copigmentation, Inclusion Complex, (2-Hydroxy)propyl-beta-Cyclodextrin, Preservation of Anthocyanin; Color Quality

Food Hydrocolloids, 2014, 41, 132-139; DOI:10.1016/j.foodhyd.2014.04.003

Zhang, M.; Zheng, J.; Ge, K.; Zhang, H.; Fang, B.; Jiang, L.; Guo, H.; Ding, Q.; Ren, F.

Glycation of α -lactalbumin with different size saccharides: effect on protein structure and antigenicity

glucose, maltose or maltooligosaccharides (up to maltopentaose) , glycation of Lys58

International Dairy Journal, 2014, 34, 220-228; DOI:10.1016/j.idairyj.2013.09.003

6. CDs for other Industrial Applications

Chen, M.; Meng, Y.; Zhou, J.; Diao, G.

Platinum nanoworms self-assemble on β -cyclodextrin polymer inclusion complexes functionalized reduced graphene oxide as enhanced catalyst for direct methanol fuel cells

Electrocatalysis, Inclusion Complex, Methanol Oxidation, Pt Nanoworms, Reduced Graphene Oxide, Self-Assemble, Self-Assembly, Thiol and Amino Groups

Journal of Power Sources, 2014, 265, 110-117; DOI:10.1016/j.jpowsour.2014.04.031

Jiang, Y.; Liang, Y.; Zhang, H.; Zhang, W.; Tu, S.

Preparation and biocompatibility of grafted functional β -cyclodextrin copolymers from the surface of PET films

Biocompatibility, Functional β -Cyclodextrin, Poly(Ethylene Terephthalate) Film, Surface-Initiated Atom Transfer Radical Polymerization (SI-ATRP)

Materials Science and Engineering: C, 2014, 41, 1-7; DOI:10.1016/j.msec.2014.04.031



Jung, J-W.; Nam, K.

Mobility and bioavailability reduction of soil TNT via sorption enhancement using monopotassium phosphate

Firing Range, Mobility Control, Monopotassium Phosphate, Sorption, Tnt, Hpcd-Extractable Fraction

Journal of Hazardous Materials, 2014, 275, 26–30; DOI:10.1016/j.jhazmat.2014.04.045

Nagy, Z. M.; Molnár, M.; Fekete-Kertész, I.; Molnár-Perl, I.; Fenyvesi, É.; Gruiz, K.

Removal of emerging micropollutants from water using cyclodextrin

Cyclodextrin-Based Sorbent, Drinking Water Purification, Ecotoxicology, Micropollutants, Waste Water Treatment, Bead Polymer, Ibuprofen, Naproxen, Ketoprofen, Bisphenol-A, Diclofenac, B-Estradiol, Ethinylestradiol, Estriol, Cholesterol

Sci. Total Environment, 2014, 485–486, 711–719; DOI:10.1016/j.scitotenv.2014.04.003

Noël, S.; Léger, B.; Ponchel, A.; Philippot, K.; Denicourt-Nowicki, A.; Roucoux, A.; Monflier, E.

Cyclodextrin-based systems for the stabilization of metallic(0) nanoparticles and their versatile applications in catalysis

Aqueous Phase, Hydrogenation, Metallic Nanoparticles, Zerovalent Metallic Nanoparticles, Hydrogenation Reactions

Catalysis Today, 2014, In press; DOI:10.1016/j.cattod.2014.03.030

Potier, J.; Menuel, S.; Rousseau, J.; Tumkevicius, S.; Hapiot, F.; Monflier, E.

Multifunctional cyclodextrin-based N,N-bidentate ligands for aqueous Heck arylation

Cyclodextrins–Palladium–Aqueous Reaction, Copper-Catalyzed Azide Alkyne 1,3-Cycloaddition, Catalysts for the Heck Reaction of Aryl Iodides

Applied Catalysis A: General, 2014, 479, 1–8; DOI:10.1016/j.apcata.2014.04.021

Yang, Z.; Ji, H.

Synergistic effect of hydrogen bonding mediated selective synthesis of benzaldehyde in water

Benzaldehyde, Cinnamaldehyde Oxidation, Hydrogen Bonding, Synergistic Effect, β -Cyclodextrin-Functionalized Cellulose

Chinese Journal of Catalysis, 2014, 35, 590-598; DOI:10.1016/S1872-2067(14)60056-5

7. CDs in Sensing and Analysis

Dai, Y.; Tang, W.; Wang, Y.; Ng, S-C.

Chromatographic Separations and Analysis: New Stationary Phases

Chiral Stationary Phase, Enantioseparation, HPLC

Comprehensive Chirality, Chapter 8.14, 286-310, Elsevier, 2012; DOI:10.1016/B978-0-08-095167-6.00828-4



Ahmed, M.; Ghanem, A.

Chiral β -cyclodextrin functionalized polymer monolith for the direct enantioselective reversed phase nano liquid chromatographic separation of racemic pharmaceuticals

Chiral Separation, Nano-LC, Polymer Monolith, Reversed Phase Chromatography, β -Cyclodextrin, Copolymerization of β CD Methacrylate and Ethylene Glycol Dimethacrylate, Propranolol, Ifosfamide, Alprenolol, Tertalol, 1-Indanol, Tebuconazole, O-Methoxymandelic Acid, Celiprolol, Cizolertine

Journal of Chromatography A, 2014, 1345, 115–127; DOI:10.1016/j.chroma.2014.04.023

Plotka, J. M.; Simeonov, V.; Morrison, C.; Biziuk, M.; Namieśnik, J.

Capillary gas chromatography using a γ -cyclodextrin for enantiomeric separation of methylamphetamine, its precursors and chloro intermediates after optimization of the derivatization reaction

Chemometric Analysis, Chiral Stationary Phase, Chromatography, Derivatization, Methylamphetamine

Journal of Chromatography A, 2014, In press; DOI:10.1016/j.chroma.2014.04.062

Zheng, H.; Liu, Q.; Jia, Q.

Preparation of poly(butyl methacrylate-co-ethyleneglyceldimethacrylate) monolithic column modified with β -cyclodextrin and nano-cuprous oxide and its application in polymer monolithic microextraction of polychlorinated biphenyls

Allylamine- β -Cyclodextrin, Gas Chromatography, Monolithic Column, Nanometer Cuprous Oxide, Polychlorinated Biphenyls

Journal of Chromatography A, 2014, 1343, 47–54; DOI:10.1016/j.chroma.2014.03.067

Zheng, J.; Chen, C.; Wang, X.; Zhang, F.; He, P.

A sequence-specific DNA sensor for hepatitis B virus diagnostics based on the host-guest recognition

DNA, Electrochemical, Hepatitis B Virus, Host-Guest Recognition, Sensor, Biotin, Labeled With 4-(4-Dimethyl Aminophenylazo) Benzoic Acid (DABCYL), Host-Guest Recognition Between B-CD and DABCYL

Sensors and Actuators B: Chemical, 2014, 199, 168-174; DOI:10.1016/j.snb.2014.03.110

Dai, Y.; Tang, W.; Wang, Y.; Ng, S-C.

Chromatographic Separations and Analysis: New Stationary Phases

Chiral Stationary Phase, Enantioseparation, HPLC

Comprehensive Chirality, Chapter 8.14, 286-310, Elsevier, 2012; DOI:10.1016/B978-0-08-095167-6.00828-4



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