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Patent News 2

This is the second series of abstracts of patents relating to the use of cyclodextrins, macrocyclics and other hosts. Patents relating to the use of zeolites will not be covered, since they are already available in the publication *Zeolites*. The previous abstracts can be found in Volume 7, pp. 657–660, 1989. The patents appearing below are reprinted by courtesy of *Cyclodextrin News*.

Furukawa, M., Hara, K. (1987): *Jpn. Kokai* JP 87,281,826 (*C.A.* **109**: 27602).

An anthelmintic composition has been prepared for domestic animals using methylated CDs. Methylated-β-CD containing 8 methyl groups/ring has been used to form a complex with C_2Cl_4. The solution contained 1.5% C_2Cl_4, and it was palatable for dogs. Dissolution was administered ad libitum, and no parasites were detected in feces after a 3-day administration.

Takahashi, M., Mochizuki, H. (1987): *Jpn. Kokai* JP 87,249,935 (*C.A.* **108**: 226850).

A gelatin-based coating composition for pharmaceuticals containing CD improves the shelf-life. The CD containing soft capsule showed a practically unchanged dissolution time even after 12 months storage, while without CD the dissolution time increased as a function of time, in 12 months it increased to about 2.5 fold.

Morioka, N. (1988): *Jpn. Kokai* JP 88, 42,665 (*C.A.* **109**: 21936).

Adding CD to prune extract inhibits foaming during the freeze drying, and the hygroscopicity of the product.

Ichioka, K., Niwa, H. (1988): *Jpn. Kokai* JP 88, 24,842 (*C.A.* **109**: 21939).

The emulsifying capacity of α-CD solutions is better than those of acyclic dextrins and some esters. α-CD and sodium caseinate can be used to prepare emulsified fats and oils for the manufacture of confectionery cream puff shells.

Moriyama, A., Hibi, H. (1988): *Jpn. Kokai* JP 88, 59,962 (*C.A.* **109**: 27007).

A deodorant for toilet air, or spoiled waste (e.g. mercaptan odor emitting from spoiled fish organs) can be prepared by dissolving β-CD in diluted ethanol, e.g. 1.8% β-CD in water–ethanol 4: 1.

Osada, H., Kuchiki, Y. (1988): *Jpn. Kokai* JP 88, 49,037 (*C.A.* **109**: 21929).

The penetrant fish odor can be reduced by using CDs. In addition to the usual preservative CD can be added to canned fish and shellfish before heat sterilization. After opening the cans, the following values were found (CD containing/control): pH = 6.45/6.25, H_2S μg % = 3.3/134.7, volatile basic nitrogen mg % = 3.7/4.6%.

Furukawa, M., Hara, K. (1987): *Jpn. Kokai* JP 87,289,501 (*C.A.* **109**: 50275).

Rodenticides can be complexed with methylated CDs to mask the unpleasant odor. Pellets were prepared containing the methylated-β-CD complex of warfarin and formulated as usual.

Enmanji, K., Eto, S. (1985): *Jpn. Kokai* JP 85,230,895 (*C.A.* **104**: 177837).

The preparation of thermal-transfer recording media is described, which contains CD. The media can be used for thermal-transfer recording in facsimiles and printers giving high sensitivity and stable images.

Shibauchi, I. (1986): *Jpn. Kokai* JP 86,195,194 (*C.A.* **106**: 21088).

Petroleum fuels can be gelled with CD or CD containing starch hydrolyzate then mixed with hydroxypropyl cellulose or similar polymers dissolved in ethanol, resulting in an alcohol-based gelled fuel.

Kunichika, K., Matsumoto, H. (1987): *Jpn. Kokai* JP 87,275,782 (*C.A.* **109**: 64379).

Lithographic plate surface protective solutions were prepared using CDs. Such solutions contain film-forming CDs and protect the hydrophilicity of the nonink-accepting areas. They are easily removable from the ink accepting areas by washing water or contacting with a wetting roller even after long-term storage.

Ito, M. (1987): *Jpn. Kokai* JP 87,275,183 (*C.A.* **109**: 66107).

Heavy metals or rare earth metal ions can be recovered from alkaline solutions—over pH = 12—with CDs or CD polymers. The metal ions are quantitatively bound to the CD polymers.

Chikahisa, N., Cho, S. (1988): *Jpn. Kokai* JP 88,23,939 (*C.A.* **109**: 56020).

By complexing plastic additives such as antistatic agents and UV adsorbers, with CDs and using these complexes in plastics, more durable products can be produced.

Hayashi, Y., Mitsuhida, N. (1986): *Jpn. Kokai* JP 86,177,999 (*C.A.* **106**: 29341).

A reagent has been prepared for the assay of β-*N*-acetyl-*O*-hexosaminidase enzyme activity which contains the reagent 2-chloro-4-nitrophenyl-*N*-acetyl-β-D-glucosaminide, α-CD and citrate buffer. The enzyme activity is calculated from the absorbance at 400 nm.

Ueda, Y., Asakura, S., Murakami, Y., Shimojo, F., Kado, K. (1987): *Eur. Pat. Appl.* EP 241,806 (*C.A.* **108**: 173559).

2-Nitroxymethyl-6-chloropyridine (a vasodilator) containing sustained-release transdermal preparations have been prepared by complexing the drug with β-CD. The complex was granulated using 50% sucrose solution as a binder, then the granules were coated with Eudragit. These dry coated granules were mixed with agar, water and glycerol to give a sustained-release transdermal delivery pad. In rats this pad gave a blood level of the drug of 13–18 ng/mL for 24 h.

Furukawa, M., Hara, K. (1987): *Jpn. Kokai* JP 87,270,516 (*C.A.* **109**: 79501).

A shampoo composition has been prepared to control lice in hair. The shampoo contains surfactants like sodium laurylsulphate, pyrethroids and methylated CDs. The methylated CD treated pyrethroid is safe to human skin.

Yamagata, Y., Sato, M. (1987): *Jpn. Kokai* JP 87,267,220 (*C.A.* **109**: 79514).

Cationic surfactants and CDs act as synergistic deodorants for a prolonged period in hair preparation. An example for a scalp deodorant contains stearyltrimethylammonium chloride 0.5%, α-CD 0.5%, ethanol 30% in an aqueous solution.

Sato, M., Nagane, S., Kawasaki, T. (1987): *Jpn. Kokai* JP 87,49,065 (*C.A.* **109**: 27643).

The β-CD complex of *o*-methoxycinnamaldehyde has been incorporated in insoles to inhibit microbial growth and foul odours. Cotton fabric was immersed into the *o*-methoxycinnamaldehyde and β-CD containing ethanol–water solution to have 10 g active ingredient/m^2. This fabric was placed between two chlorovinylidene sheets. Patients with athlete's foot and symptoms such as rash, blisters and skin drying were effectively controlled.

Okazaki, M., Momoki, Y. (1987): *Jpn. Kokai* JP 87,215,261 (*C.A.* **108**: 229520).

A photographic spectral sensitizer, which is poorly soluble, can be dissolved in an aqueous medium in the presence of appropriate CD derivatives. The use of the highly soluble derivatives eliminate the need for any organic solvent, or strong acid solvent for the spectral sensitizer. The material overcomes the various problems caused by the solvents, such as coagulation of binder or coupler dispersion, reduced sensitivity, instability of the sensitizer solution or limitations on coating speed. Ag (Br, Cl) emulsion was spectrally sensitized by adding an aqueous solution containing $1-10^{-4}$ mol/L spectral sensitizer and 5% DIMEB, then a cyan coupler dispersion and other additives added, and coated on a paper substrate to give a red sensitive colour paper.

Matsui, K., Ishihara, K., Suzuki, K. (1987): *Jpn. Kokai* JP 87,258,702 (*C.A.* **109**: 23379).

Cross linked, CD containing membranes have been synthesized for optical resolution of amino acids. A mixture of acrylonitrile and *p*-nitrophenylacrylate copolymers were reacted with 6-[(aminoethyl)amino]-6-deoxy-β-CD, L-phenylalanine permeated through such a membrane with a selectivity of 1.39 over the D-isomer.

Korpela, T., Laakso, S., Makela, M. (1988): *Eur. Pat. Appl.* EP 268,997 (*C.A.* **109**: 131147).

The 1,8-naphthalenedicarboximide derivative of aminated Biogel P-6 is an appropriate matrix for the isolation and purification of CDs by clathration chromatography.

Imamura, T., Kamiya, H., Kurosaki, T. (1987): *Jpn. Kokai* JP 87,220,501 (*C.A.* **109**: 110838).

Methylated CDs with 8–11 methoxy groups per β-CD were prepared by methylating the β-CD in aqueous alkali with dimethylsulfate. The solubility of the methylated product in water is much better than that of the β-CD and forms soluble CD complexes.

Koizumi, K. (1987): *Jpn. Kokai* JP 87,281,855 (*C.A.* **109**: 116044).

The inclusion complexation of vitamins and hormones with maltosyl CDs has been studied. Incubating a solution of maltose, β-CD and isoamylase (obtained from Pseudomonas) in acetate buffer gave maltosyl β-CD. The maltosyl β-CD is more than ten times better as a solubilizer for vitamin D_3 than the unsubstituted β-CD.

Nakanishi, M. (1988): *Jpn. Kokai* JP 88, 33,340 (*C.A.* **109**: 176356).

Topical creams containing antiarrhythmics were prepared for the treatment of angina pectoralis. For example isosorbide nitrate 2 parts, egg lecithin 10 parts, benzyl alcohol 10 parts, cetanol 20 parts, rice oil 15 parts, glycerin 15 parts and H_2O 28 parts by weight were mixed, but such formulations may contain also collagen.

Elger, G. A., Leslie, S. T., Malkowska, S. T. A., Miller, R. B., Neale, P. J. (1988): *Eur. Pat. Appl.* EP 251,459 (*C.A.* **109**: 98849).

Controlled-release pharmaceutical matrices which contain polydextrose or CDs and fatty alcohols or polyalkylene glycols are reported. The formulation of theophylline, naproxen, salbutamol, and metoclopramide are described.

Motono, M. (1988): *Jpn. Kokai* JP 88,188,609 (*C.A.* **109**: 196920).

A β-CD containing cosmetic preparation is described, which inhibits the formation of melamin, i.e. the discoloration of the human skin upon exposure to light. This formulation contains kojic acid (or its derivatives) as the UV absorber, β-CD, and EDTA. This formulation is not irritating to the human skin.

Furukawa, M., Hara, K. (1987): *Jpn. Kokai* JP 87,267,203 (*C.A.* **109**: 185484).

Pyrethroids (for example resmethrin) can be formulated against flies, mosquitoes, cockroaches by methylated β-CD. 25% Resmethrin and 75% methylated β-CD (substitution degree 9.4 methoxy groups per β-CD) were mixed and 5 g of this mixture was formulated with 95 g diatomaceous earth to give a dust preparation.

Furukawa, M., Hara, K. (1987): *Jpn. Kokai* JP 87,267,201 (*C.A.* **109**: 185483).

Insect repellent agents such as *N,N*-diethyltoluamide were formulated with methylated β-CD. 2 parts *N,N*-diethyltoluamide, 8 of methylated β-CD, 40 of ethanol, and 50 of water give an appropriate mosquito repellent formulation.

Yoshimura, M., Nakazawa, H., Kandori, H. (1988): *Jpn. Kokai* JP 88,165,498 (*C.A.* **109**: 192647).

Fabric softeners can be prepared which have long lasting deodorizing effects, using CDs in the formulation. The formulation contains quanternary ammonium-type cationic surfactants, ethylene glycol, perfume and CDs. Fabrics treated with such softeners provided sustained prevention of body and perspiration odor.

Haruta, M. (1988): *Jpn. Kokai* JP 88,104,887 (*C.A.* **109**: 180541).

An optical recording medium was prepared which contains CD complexes such as the α-CD–iodine complex. The medium shows discoloration on irradiation with long-wavelength light, and it is useful for optical recording.

Watanabe, N., Morioka, T. (1988): *Jpn. Kokai* JP 88, 68,520 (*C.A.* **109**: 155970).

An Oil–CD inclusion complex can be used in powder or solid cosmetic cleansers. The CD–squalane complex, di-sodium EDTA, TiO_2 and soap base containing cleanser produces more foam than conventional cleansers and conditions the skin.

Nishida, K., Takahashi, C., Kawaguchi, T. (1988): *Jpn. Kokai* JP 88,150,301 (*C.A.* **109**: 172467) and *Jpn. Kokai* JP 88,154,703 (*C.A.* **109**: 172464).

Passing a solution of branched CDs, non branched CDs and oligosaccharides through an octadecylsilyl-modified silica gel column, the oligosaccharides can be removed by eluting with water, then the CDs will be eluted with increasing ethanol concentration.

Hashimoto, H., Hara, K., Kogure, Y., Shiraishi, T., Sato, A., Sakai, S. (1988): *Jpn. Kokai* JP 88,112,601 (*C.A.* **109**: 172451).

Maltosyl-CDs can be separated from maltose on an Amberlite XT-1007 (Ba type strong acid cation exchanger) column, by eluting the adsorbed species with water.

Kobayashi, S., Monma, M., Takano, T. (1988): *Brit. UK Pat. Appl.* GB 2,193,963 (*C.A.* **109**: 168992).

Branched side chain containing branched CDs were prepared by reacting CDs with branched malto-oligosaccharides in the presence of a branching-splitting enzyme. For example panose as branched oligosaccharides, and pullulanase as the enzyme were used.

Sakai, S., Yoshida, S. (1988): *Jpn. Kokai* JP 88, 71,177 (*C.A.* **109**: 50881).

The hydrolysis of α-, β- and γ-CD has been studied by Taka amylase immobilized on a hydrophilic anion exchange resin. The immobilized enzyme could split the CDs even after continuous use for 40 days.

Nishida, K., Takahashi, C., Kawaguchi, T. (1988): *Jpn. Kokai* JP 88,154,702 (*C.A.* **109**: 172465) and *Jpn. Kokai* JP 88,154,701 (*C.A.* **109**: 172466).

CDs can be isolated from the enzymatic degradation mixture by adsorption on chemically modified silica, followed by a fractional elution of the adsorbed CDs by aqueous ethanol.

Nakanishi, M. (1988): *Jpn. Kokai* JP 88, 33,329 (*C.A.* **109**: 197203).

Antimicrobial ointments which contain quinolonecarboxylic acids, pyridonecarboxylic acids derivatives, nalidixic acid, etc., can be prepared using phospholipids and CDs or collagens.

Traue, J. K. H., Metzner, J., Shubert, E. (1987): *Ger. (East)* DD 249,186 (*C.A.* **108**: 226863).

A method is patented for enhancement of the solubility and bioavailability of glibenclamide through incorporation of the drug into hydrophilic water soluble matrices, such as polyvinylpyrrolidone, polyvinylalcohol or β-CD. Following oral administration the amorphous, spray dried substance resulted in lower sugar levels in rats. No example is given for the β-CD–glibenclamide complex, also mentioned in the patent.

Makino, T., Hirai, S., Kitamori, N. (1986): *Jpn. Kokai* JP 86,257,923 (*C.A.* **106**: 143996).

Vitamin B_1, salts or derivatives are formulated with vitamin C by coating the vitamin B_1, derivatives with CD thus preventing interactions between vitamin B_1 derivatives and vitamin C in the formulations. Thus, vitamin B_1 nitrate 10 parts, α-CD 10 parts, D-glucose 100 parts, and lactose 130 parts by weight were mixed and the mixture was made into granules. In this process, vitamin B_1 nitrate particles were coated with CD.

Hasebe, K., Ando, Y., Chikamatsu, Y., Hayashi, K. (1987): *Jpn. Kokai* JP 87,267,261 (*C.A.* **109**: 110847).

The β-carotene which is used in drugs, foods and cosmetics is rather unstable. The preparation of its α-CD complex is reported.

Hara, K., Murata, S. (1987): *Jpn. Kokai* JP 87,270,545 (*C.A.* **109**: 197176).

The stability and solubility of shikonin and its derivatives were improved by complexation with methylated β-CD. The preparation of a shikonin and methylated β-CD containing suppository for hemorrhoid treatment is reported.

Terajima, Y., Tokuda, K., Nakamura, S. (1988): *Jpn. Kokai* JP 88, 35,517 (*C.A.* **109**: 115880).

CD complexed fragrant substances coated with oils can be used in cosmetics and hair preparations. For example 100 g β-CD in 100 mL water mixed with 25 g lemon oil gave 120 g of the lemon oil −β-CD complex. After drying and pulverizing it was mixed with 10 g liquid paraffin for coating. This substance can be used for example in soaps.

Kawakami, M., Sakamoto, M., Kumazawa, T. (1988): *Jpn. Kokai* JP 88,150,217 (*C.A.* **109**: 134972).

The iodine complex of maltosyl-CD can be used in mouthwashes. The aqueous solutions of 5–15 mg/mL iodine–maltosyl-CD act as a microbicide.

Katsuta, Y., Namite, Y. (1988): *Jpn. Kokai* JP 88,166,812 (*C.A.* **109**: 185495).

An insecticidal composition against cockroaches (*Blattella germanica*) contains boric acid and CD complexed organic phosphorus compounds, e.g. phenitrothion.

Kawabata, Y., Matsumoto, M., Tanaka, W. (1988): *Ger. Offen.* DE 3,710,569 (*C.A.* **109**: 131146).

Certain CD derivatives, like the heptakis(6-butylmercaptyl-6-deoxy)β-CD are shown to be excellent unimolecular film forming substances when the chloroform solution is evaporated to dryness. The patent application describes the preparation of appropriate CD derivatives.

Mizukami, F., Toba, M., Niwa, S., Imai, S. (1988): *Jpn. Kokai* JP 88,27,502 (*C.A.* **108**: 223369).

CD–silica composites and their preparation by alkoxysilane hydrolysis is reported. Such composites are useful as absorbents, catalyst supports, microencapsulants, and chromatographic packings with good thermal and chemical stability. The composites are practically a mixture of non-dissolved CD and the hydrolysis product precipitated when tetraethoxysilane has been contacted with water.

Okazaki, A., Yamanochi, J. (1988): *Jpn. Kokai* JP 88,73,241 (*C.A.* **109**: 139023).

CDs or CD derivatives are used in spectral sensitizers and fluorescent compounds and photographic materials, e.g. cyanine type dyes complexed with CDs or appropriate derivatives increases the photosensitivity of the photographic emulsion.

Soga, T., Oda, T. (1986): *Jpn. Kokai* JP 87,164,701 (*C.A.* **107**: 200797).

Treating dimaltosyl-α-CD with glucoamylase lead to the formation of diglucosyl-α-CD.

Hara, K., Murata, S. (1987): *Jpn. Kokai* JP 87,267,237 (*C.A.* **109**: 236987).

The biologically active components from oriental crude drugs can be extracted with methylated CD. For example the pulverized roots of *Atractylodes Lancea* was extracted with methylated β-CD and after filtering the extract and hydrolyzing the CD with appropriate enzymes the principal active components hinesol and β-eudesmol were recovered with considerably higher yields than without using methylated CD.

Sunami, M., Horiuchi, T., Tamada M., Ito, Y. (1987): *Jpn. Kokai* JP 87,53,662 (*C.A.* **107**: 102658).

A transdermal formulation contains a gel with good adhesive properties and analgesics, inflammation inhibitors, etc. PVA and β-CD were dissolved in water, then frozen at −20°C for 12 hours. After thawing for 10 h at room temperature a gel forming film was obtained, which could be used as a drug carrier.

Furukawa, M., Hara, K. (1988): *Jpn. Kokai* JP 88,101,317 (*C.A.* **109**: 237041).

A topical pharmaceutical formulation contains an oil base with CD or CD derivatives in which CO_2, H_2S and/or Rn as a pharmaceutical transport accelerator has been adsorbed. β-CD was treated with H_2S at 8 kg/cm^2 pressure. Under such conditions 100 g β-CD adsorbed 4.3 g H_2S. This H_2S complex mixed with methylsalicylate, menthol, liquid paraffin and white vaseline forms a topically applied drug.

Karl, C. L., Schynoll, W. G. (1988): *U.S.P.* US 4,751,095 (*C.A.* **109**: 229167).

Complexing aspartame with β-CD resulted in improved stability. Mixing 1 part aspartame with 3 parts β-CD in a Waring blender with water, and drying the product formed, the aspartame content was shown to be more stable than in the simple mixture of aspartame and β-CD.

Kuwabara, N., Takaku, H., Oku, S., Kogure, Y. (1988): *Jpn. Kokai* JP 88,164,878 (*C.A.* **109**: 189105).

Spray-drying ethanol with CDs, maltose and dextrins resulted in 55% retention of ethanol. Spray-drying ethanol with maltosyl CDs, 79% of the ethanol was retained. Such a CD stabilized ethanol complex can be used for example in brandy flavoured pound cakes.

Ogino, S., Kamya, H. (1988): *Jpn. Kokai* JP 88,192,706 (*C.A.* **109**: 236737).

Skin or hair lotion preparations are described, which contain methylated-β-CD without an irritating effect on the skin. Such a cosmetic preparation contains 0.1–10% methylated CD, which contains 8–11 methyl groups per CD unit and 0.01–2% aromatic volatile substances. Such a lotion has to contain lower amounts of ethanol and surfactant than the commercial ones, therefore it has no irritating effect on the skin. Volatilization of the aromatic substances are prevented by the presence of the CDs.

Chikahisa, N., Cho, S. (1988): *Jpn. Kokai* JP 88,79,801 (*C.A.* **109**: 224730).

An insecticide effective in controlling termites, cockroaches, etc., consists of the insecticide-CD inclusion complex, an adhesive and a fine powder of foam-producing plastic. The mixture may be sprayed on the tree trunk to prevent termite infestation.

Nakamura, E., Azuma, A., Fukada, M. (1988): *Jpn. Kokai* JP 88,79,802 (*C.A.* **109**: 224729).

The wettable powder formulation of *m*-tolylmethylcarbamate (MTMC) is described using β-CD. 25 parts MTMC, 5 parts β-CD, 2 parts NPE-100 detergent, 4 parts Ca ligninsulfonate, 25 parts water containing silicic acid, and 39 parts clay were mixed and pulverized in this formulation. The solubility of MTMC was increased by about 10%.

Friedman, R. B. (1988): *US Appl.* 1952/87 (858,067).

A process for removing polychlorinated biphenyl compounds from waste waters can be made by using insoluble CD polymers.

Takahashi, S., Harada, A., Ko, S. (1987): *Jpn. Kokai* JP 87,126,148 (*C.A.* **107**: 153924).

Ketones were prepared in high yield by oxidation of olefins in the presence of CD using Pd and Cu compounds as catalysts. Thus, 1-decene was oxidized in water in the presence of $PdCl_2$, $CuCl_2$ and α-CD under stirring at 75°C with oxygen for 10 hours, and the product was 2-decanone in a yield of 76%.

Nagata, H., Kaburagi, K., Saito, Y. (1988): *Jpn. Kokai* JP 88,143,926 (*C.A.* **109**: 236136).

Odorous gases (especially from treatment of industrial wastes, fecal sewage or slaughterhouse effluents) are treated by scrubbing with an atomized aqueous solution containing CDs. The aqueous solution is injected into a spray nozzle and atomized with compressed air to form a hydrophilic mist curtain. The waste gases are then passed through the hydrophilic mist curtain to absorb odorous components. The operation cost can be reduced by 1/10 as compared to that by a conventional method.

Tanno, K., Kawagoe, K. (1987): *Jpn. Kokai* JP 87,138,199 (*C.A.* **107**: 214163).

For determination of pancreatic or salivary α-amylase activity, a reagent is described which contains β-(4-nitrophenyl)maltopentaoside, α-glucosidase, β-glucosidase and α- or β-CD. The biological samples were added to the above reagent dissolved at pH 7 in the presence of $CaCl_2$ and NaCl at 37°C for 5 minutes, thereafter α- and β-glucosidase and α-CD was added. The amylase activity was determined by spectrophotometry.

Ozaki, A., (1988): *Jpn. Kokai* JP 88,133,998 (*C.A.* **110:** 37811).

A new method for production of mainly γ-CD is described. The culture fluid of a 2-day culture of an appropriate Bacillus was absorbed with potato starch, washed and dried to obtain starch-absorbed CGT enzyme. Using this enzyme and ethanol γ-CD is mainly formed beside the β-CD. The conversion is performed in 15% starch solution, on several mL scale.

Beesley, T. E. (1988): *Ger. Offen.* DE 3,741,340 (*C.A.* **110**: 25651).

Appropriate complex forming agents are immobilized on solid surfaces like silica, cellulose, polyacrylamide gels, etc. Passing a mixture of different CDs in aqueous or ethanolic-aqueous solutions through such a complex forming matrix, the CDs are retained by complex formation. Using appropriate eluants (for example, sodium benzoate) at elevated temperature, a sequential separation of the CDs can be performed.

Hattori, K. Takahashi, K. (1987): *Jpn. Kokai* JP 87,275,102 (*C.A.* **110**: 75975).

C-6-NH_2-β-CD and β-CD copolymer was prepared from β-CD polymer, as intermediate for the preparation of *N*-methyldihydronicotinamide-CD polymer, which is intended to be useful as an artificial enzyme. β-CD polymer was tosylated then reacted with NaN_3, and the azide was then reduced to amino groups. This amino-β-CD polymer has a neutralization equivalent point of pH 9.9, and contains 33% amino and 67% non-substituted CD.

Ueno, M., Isane, T. (1987): *Jpn. Kokai* JP 87,123,196 (*C.A.* **107**: 242622).

Oral and transdermal formulations which contain prednisolone-heptakis (2,6-di-*O*-methyl)-β-CD were prepared. 1.0 g prednisolone and 7.38 g DIMEB were mixed with water and this complex was mixed with white vaseline, stearyl alcohol, propylene glycol, Na lauryl sulfate and ethyl 4-hydroxybenzoate containing ointments.

Tokumura, C., Tsushima, I., Tateishi, K., Kashino, M., Machida, R., Nagai, T., Nanba, M. (1987): *Jpn. Kokai* JP 87,59,212 (*C.A.* **107**: 183563).

Because cinnarizine forms a very stable complex with β-CD its release and absorption rate is not satisfactory. An appropriate competitor has to be mixed to this complex. Leucine or isoleucine is used for such purposes. 3.69 g cinnarizine and 28.38 g β-CD were dissolved in diluted hydrochloric acid then neutralized and spray-dried. 4.65 g of this cinnarizine: β-CD (1:2) complex was mixed with 2000 g leucine and 35 g Avicel and filled into 500 mg capsules.

Nakanishi, M. (1987): *Jpn. Kokai* JP 87,138,437 (*C.A.* **107**: 223301).

Anti-inflammatory suppositories were prepared using steroids, fenbufen, acemetacin, sulindac, diclofenac, flurbiprofen, ketoprofen or piroxicam as active ingredient and CD and/or collagen. The CD and collagen are absorption promoters in these formulations. For example 50 g prednisolone, 100 g β-CD were mixed with 60 g Witepsol E75 and 45 g Witepsol H-15 and formed into suppositories.

Shibazaki, M., Sodeoka, M., Izeki, K., Shinoda, M., Ishiyama, C., Hayashi, Y., Oguri, T., Kanayama, T. (1987): *Jpn. Kokai* JP 87,67,046 (*C.A.* **107**: 134118).

New prostacyclin analogs and derivatives were prepared and stabilized by CDs. These drugs are useful as antiulcer agents or agents for improving blood circulation.

Sugiyama, M., Ezure, Y., Yoshikuni, Y., Ozaki, T., Ojima, N. (1987): *Ger. Offen.* DE 3,634,496 (*C.A.* **107**: 132630).

N-(2-Hydroxyethyl) moranoline in aqueous solution was shaken at pH 5.7 for 3 days with α-CD and with CGT enzyme. By transglucosylation, oligoglucosyl-*N*-(2-hydroxyethyl) moranoline derivatives were formed. On treating these products with glucoamylases for 24 hours at 50°C (poly)hydroxyalkyl moranoline derivatives are formed, which are effective antidiabetics. Oral administration to beagle dogs (10 mg/kg) reduced blood sugar level from 114 to 68 mg/dL in 1 hour following ingestion of 2 g/kg soluble starch.

Hashimoto, H., Shibata, T., Nagano, T., Hara, K., Kuwabara, N., Yashiki, I. (1986): *Jpn. Kokai* JP 86,265,063 (*C.A.* **106**: 83310).

Edible seeds (for example pumpkin seeds, sunflower seeds) can be powdered or granulated with CDs, preferably with a mixture of cyclic and acyclic dextrins. The stability of such products is improved by using CDs. For example when ground with CD in the presence of water and then spray dried roasted pumpkin seeds gave a stable powder.

Kotani, A., Ito, T. (1987): *Jpn. Kokai* JP 87,134,045 (*C.A.* **107**: 153207).

A granulated dry tea preparation is described. The tea extract was mixed with dextrin and CD to 18–58% solid content and with 0.8–2.8% $(NH_4)_2CO_3$ or NH_4HCO_3. This mixture is spray dried and instantly soluble tea granules of low hygroscopicity are obtained.

Suzuki, O., Yokochi, T., Nakane, T., Ninomiya, Y., Higuchi, T. (1987): *Jpn. Kokai* JP 87,81,310 (*C.A.* **107**: 46327).

The preparation of therapeutic beverages containing γ-linolenic acid or its ester is described. For example 9 g β-CD was dispersed in 100 mL 50% ethanol at 60°C, and 1 g γ-linolenic acid was added. The precipitate was isolated and washed with acetone and dried. The preparation of the use of this product in salt containing fruit juices is described.

Hatae, S., Nakajima, K. (1988): *Jpn. Kokai* JP 88,08,311 (*C.A.* **110**: 13386).

A cosmetic preparation for inhibition of melanin formation is described, which contains the kojic acid–β-CD complex, other appropriate agents and fragrance substances.

Shibauchi, I. (1987): *Jpn. Kokai* JP 87,61,912 (*C.A.* **107**: 46066).

A finger nail lacquer remover cosmetic preparation contains γ-nonalactone and γ-undecalactone combined with squalane and its CD complexes. The CD is needed to emulsify the squalane.

Ogino, S., Hirota, H. (1987): *Jpn. Kokai* JP 87,62,897 (*C.A.* **107**: 161386).

A methyl-CD containing shampoo formulation is described. For example 15 g polyoxyethylene lauryl sulfate Na, 3 g coconut fatty acid diethanolamide and 0.5 g methylated-β-CD was diluted by water to 100 g. The methylated CD in this case is an amphoteric surfactant.

Shibauchi, I. (1987): *Jpn. Kokai* JP 87,114,909 (*C.A.* **107**: 140916).

A sustained release air freshener was prepared by dissolving polyvinylpyrrolidone in ethanol or methanol solution in the presence of hydroxypropyl cellulose and perfumes. The perfumes (lavender oil) may be complexed with β-CD to give a longer lasting air freshener effect for example in papers.

Yorozu, H., Eguchi, Y., Ohkawa, W., Matsumoto, Y. (1987): *Eur. Pat.* EP 229,616 (*C.A.* **107**: 223051).

Carbon dioxide and oily component (e.g. diisopropyl adipate, liquid paraffin) containing composition was prepared. As a source of carbon dioxide a CD-carbon dioxide complex can be used. The carbon dioxide in the bath water enhances the blood circulation and the skin is moisturised by the oils, resulted in a better feeling after finishing the bath.

Furukawa, M., Hara, K. (1988): *Jpn. Kokai* JP 88,83,003 (*C.A.* **110**: 71103).

Maleic acid and fumaric acid CD complexes are sustained-release fungicide compositions. The CDs are used in 0.5–2.0 time excess, based on the fungicides. For example 10 g dimethyl maleate, 86 g β-CD and 4 g water were mixed to give a dimethyl maleate–β-CD complex. This complex was then compressed to tablets with lactose and talc. Keeping these tablets in a closed container for 1, 3 and 6 months showed residual fungicide contents of 84, 59 and 11% while the control prepared without β-CD under identical conditions showed only 62, 19 and 3% content respectively.

Sakai, S., Yamamoto, I., Hashimoto, H., Hara, K. (1987): *Jpn. Kokai* JP 87,116,604 (*C.A.* **107**: 156853).

Glucosyl-CD can be separated from saccharide containing aqueous solutions by a strongly acidic cation ion exchanger. For example a 44.4% glucosyl-CD and 55.6% glucose mixture as aqueous solution when passed through an Amberlite XT 1007 (Ba containing cation exchanger) column at 60°C gives the glucosyl-CD in 95% yield.

Sakano, Y., Shiraishi, T., Niwa, H. (1987): *Jpn. Kokai* JP 87,106,901 (*C.A.* **107**: 156851).

Diglucosyl-β-CD can be prepared for pharmaceutical, food and cosmetics application by treating dimaltosyl-β-CD with glucoamylase. First maltose-β-CD and pullulanase are reacted to give the dimaltosyl-β-CD, which is then hydrolyzed by glucoamylase to diglucosyl-β-CD.

Sakano, Y., Shiraishi, T., Niwa, H. (1988): *Jpn. Kokai* JP 88,36,793 (*C.A.* **110**: 55990).

The preparation of dimaltosyl-γ-CD is described, which is characterized by a higher aqueous solubility than the γ-CD itself. Maltose and γ-CD were reacted in the presence of pullulanase enzyme. Dimaltosyl-γ-CD was produced in 23.6% yield.

Nishida, K., Takahashi, C., Kawaguchi, T., Sakai, S., Yoshida, S., Chiwa, M. (1988): *Jpn. Kokai* JP 88,254,103 (*C.A.* **110**: 93584).

The separation of glucosyl-CD and CDs is described by using chemically modified silica gel and eluting the components with hot water.

Friedman, R. B. (1988): *U.S.P.* US 4,774,329 (*C.A.* **110**: 44969).

A sustained-release cetylpyridinium chloride-CD complex is described, which can be used as a controlled-release source of cetylpyridinium chloride as an antiseptic or disinfectant agent.

Furukawa, M., Hara, K. (1988): *Jpn. Kokai* JP 88,83,021 (*C.A.* **110**: 101799).

An oral pharmaceutical contains fat-soluble vitamins and methylated CD. A mixture of methylated β-CD and vitamin A in water was stirred until complete dissolution occurred. The resulting compound was used in vitamin formulations. An oral liquid contained vitamin B_1 nitrate 5 mg, vitamin B_2 phosphate 5 mg, vitamin B_5 5 mg, nicotinamide 20 5 mg, inositol 50 mg, caffeine 50 mg, vitamin A-methylated-CD inclusion complex 1 mg, vitamin E-methylated-CD inclusion complex 10 mg, and vitamin D-methylated-CD inclusion complex 0.5 mg in 100 mL water.

Murata, S., Hara, K. (1987): *Jpn. Kokai* JP 87,281,819 (*C.A.* **110**: 13560).

Dried roots and stems of *Atractylodes Lancea* were pulverized and treated with a solution of methylated β-CD. Hinesol and β-eudesmol were extracted.

Iwayama, Y., Fujeda, S. (1987): *Jpn. Kokai* JP 87,185,011 (*C.A.* **108**: 101363).

Enteric formulations of antimicrobial phenol compounds were prepared using β-CD. 1 kg β-CD was mixed with 1.5 L H_2O or ethanol and then 100 g creosote was added, and the mixture kneaded for about 1 h until the odour of creosote disappeared. Formulating with the usual exicpients tablets were prepared, which contained 10 mg creosote. This drug can be used to combat enteric microbial infections.

Kuwabara, N., Oku, S. (1988): *Jpn. Kokai* JP 88,190,819 (*C.A.* **110**: 28923).

A bath preparation which contains the CD-squalane inclusion complex as an active ingredient is reported. The squalane is released slowly from the inclusion complex and uniformly distributed because the CD acts as an emulsifier in the bath, thus giving better moisturizing effects on the skin, than squalane alone. The composition of a bath preparation is also reported.

Yamada, K., Mita, K. (1988): *Jpn. Kokai* JP 88,212,548 (*C.A.* **110**: 25128).

CD containing polyolefin laminates were prepared by coextrusion for use in the packaging of foods. Using for example the orange oil–β-CD complex in such a film, orange juice containers can be prepared.

Krysl, S. (1988): *Czech.* CS 247,765 (*C.A.* **110**: 15652).

CDs crystallized from polar solvent on granulated inert carrier surfaces can be saturated with volatile compounds, which can be used as a slow release medium in the medicinal, food and chemical industry. For example β-CD was dissolved in dimethyl formamide and diatomaceous earth was added to this solution, then dried at 110°C in vacuum.

Chikahisa, N. (1988): *Jpn. Kokai* JP 88,237,932 (*C.A.* **110**: 77113).

Antifogging vinyl films for houses are prepared by moulding a CD containing synthetic resin.

Chikahisa, N., Cho, S. (1988): *Jpn. Kokai* JP 88,218,063 (*C.A.* **110**: 77080).

CD containing permselective packaging film, useful for the packaging of food, rubber products, etc. are prepared from polyethylene containing up to 20% CD. The films have controlled permeability to substances which might impair the appearance of packages (e.g., aromatic amine antioxidants in tires can discolor the conventional polyethylene packaging film), release unpleasant odour (in vegetable and fruit packaging), while retaining the necessary respiratory properties of packages.

Ekusa, T., Naito, K. (1988): *Jpn. Kokai* JP 88,130,164 (*C.A.* **110**: 25039).

Films with stable electrical and optical properties contain inclusion complexes for example of CDs. A chloroform solution of β-CD-stearate and naphthalene was added dropwise to water at 15°C and deposited on a quartz plate to give a thin film absorbing at 225 and 280 nm.

Yagi, T., Hisada, T., Ogata, M., Shibata, H., Shimamoto, K., Osawa, T. (1988): *Jpn. Kokai* JP 88,243,101 (*C.A.* **110**: 77964).

Basic CD derivatives can be used to enhance the color development of nitrophenol in enzyme assays and clinical diagnostics. The 2-(*N*,*N*-diethylaminoethyl)-α-CD complex is useful for this purpose, for example in determining the enzymic cleavage of 4-nitrophenyl-*N*-acetyl-β-D-glucosaminide by *N*-acetyl-β-D-glucosaminidase, and the cleavage product can be monitored by determining the absorption at 410 nm.

Khanna, P., Pearlman, F. (1989): *U.S.P.* US 4,798,804 (*C.A.* **110**: 108173).

β-CD can be used for serum pretreatment in digoxin immunoassay. A sample suspected of containing digoxin is pretreated with excess of β-CD or β-CD polymer. It is removed from the solution by filtration and the bound digoxin then released by an appropriate competitor guest molecule such as cyclohexanol. The patient serum samples were mixed with β-CD and the mixtures were centrifuged at 4000 rpm for 1 hour and the ultrafiltrates were treated with cyclohexanol to release the digoxin from the β-CD then finally the digoxin was determined using a ^{125}I-RIA kit.

Nakakuki, T., Yoshida, M., Okada, M. (1988): *Jpn. Kokai* JP 88,196,290 (*C.A.* **110**: 131368).

CGT enzyme was immobilized on porous chitosan beads for continuous use. The Chitopearl was mixed in with phosphate-buffer dissolved CGT enzyme then crosslinked with glutaraldehyde. 70% of its initial activity was retained after 30 days continuous operation in manufacturing CD from starch hydrolyzate.

Koizumi, K., Okada, Y., Kubota, Y., Utamura, T. (1988): *Jpn. Kokai* JP 88,27,440 (*C.A.* **110**: 121385).

The preparation of glucosylated, branched CDs is described, the branched CDs have higher water-solubility than the parent CDs. The solubility of estriol from an estriol–α-CD containing tablet was 32 μg/mL, while the solubility of estriol from a freeze dried estriol and diglucosyl-β-CD complex containing tablet was 2606 μg estriol/mL.

Tokuda, K., Morii, S., Yamanishi, K. (1988): *Jpn. Kokai* JP 88,122,701 (*C.A.* **110**: 121422).

Various CD hydroxyalkyl ethers were synthesized as pharmaceutical solubilizers and stabilizers. The CDs were treated in the presence of alkali with 2-methyl-1,2-propylene oxide or with 3-chloro-1-propanol, resulting in 3-hydroxypropyl-β-CD.

Otsu, K., Takeno, S., Owaya, K. (1988): *Jpn. Kokai* JP 88,209,550 (*C.A.* **110**: 133999).

Wheat gluten is deodorized by the addition of CD. 400 g wheat gluten and 4 g β-CD were kneaded for 30 minutes, frozen at −200°C, stored for 2 days and thawed at 40°C. The gluten had a good texture and no bad odor and the drip amount was 2.3%.