Patent News

At the last Editorial Board meeting, it was suggested that a useful new feature in the Journal would be the publication 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 patents appearing below are reprinted by courtesy of *Cyclodextrin News*.

Szejtli, J., Szente, L., Fenichel, L., and Toke, L. (1987): *Hung. Teljes* HU 42,513 (*C.A.* **108**: 77532).

CDs can be methylated in a heterogeneous system. Crystalline CD suspended in non-dissolving organic solvents (e.g. tetrahydrofuran) can be methylated with powdered KOH and dimethyl-sulfate using an appropriate phase-transfer catalyst. The methylated product is dissolved in the organic phase and can be simply isolated by evaporating the organic solvent. The methylated product obtained is heterogeneous, but can be used for technical purposes at a much lower cost than the relatively pure nearly homogeneous dimethylated-β-CD.

Terawaki, F., Hasegawa, T., and Kamikama, K. (1987): *Jpn. Kokai* JP 87,148,423.

Mobenzoxamine has been stabilized by complexation with DIMEB. 4.0 g mobenzoxamine was dissolved in 50 mL methanol mixed with 32.6 g DIMEB, and then the solvent was removed. The residue was dissolved in water and freeze-dried to give an inclusion complex.

Yagi, Y., Tsuchiyama, Y., Sato, M., Fujii, K., and Ishikura, T. (1987): *Jpn. Kokai* JP 87,201,807 (*C.A.* **108**: 101114).

Methylated CDs and oils can be used in cosmetic preparations as substitutes for surfactants which frequently cause skin-irritation. E.g. 30 parts stearic acid, 6 parts lanolin, 16 parts paraffin wax, 50 g paraffin oil were mixed and 200 g water containing 7 g dissolved partially methylated CD was added, followed by a mixture of 15 g carbitol and some fragrance to give a cold cream.

Vernenghi, A., Kunesch, G., Ramianrasoa, F., Chuilon, S., and Ravise, A. (1987): *Fr. Demande*, FR 2,596,617 (*C.A.* **108**: 89484).

Fatty acid or fatty acid derivatives complexed by CD are pesticides for oil crops. Treatment of the pseudobulb with arachidonic acid-β-CD complex controlled fusariosis in oil palm.

Matolcsy, G., Gimesi A., Pelejtei K., and Sziaisz, J. (1986): *Faming Zhuanli Shenqing Gongkai Shuomingshu* CN 85,104,674 (*C.A.* **108**: 33632).

Benzene sulfonylurea derivatives form inclusion complexes with β-CD, which can be used as a herbicide or plant growing regulator. E.g. *N*-[4-methoxy-6-methyl-1,3,5-triazin-2-yl) carbamoyl]-(2-chlorophenyl) sulfamide converted into its β-CD complex, formulated to a wettable powder formulation and applied at the rate of 20 g/ha, totally controlled Sinapsis alba, within 3 months.

Shibani, I. (1988): *Eur. Pat. Appl.* EP 251,132 (*C.A.* **108**: 145468).

Fragrant paper or paper containing protective substances can be prepared using CD complexes of perfumes, insecticides, rust inhibitors, mould- and mildew-proofing agents, fungicides and bactericides. These complexes have to be mixed to the pulp and water before drying. The retention time of these active ingredients is greatly enhanced. E.g. fenitrothion β-CD complex sprayed on wet paper web and passed between drying rollers heated to 100° and wound to give an insecticide containing paper was shown to be effective for more than 6 months.

Quentin-Millet, M. J. B. J., Arminjon, F., and Donikian, R. R. (1987): *Eur. Pat. Appl.* EP 239,504 (*C.A.* **108**: 36339).

A medium which permits better growth of Bordetella and corresponding enhanced production of pertussis toxin and filamentous haemagglutinin comprises a modified, CD-containing Stainer-Scholte medium to which etherified glucose polymers have been added. B pertussis, in a 30-L laboratory or a 1000-L commercial fermentor, was cultured in a modified Stainer-Scholte medium containing DIMEB 1.67 and methylcellulose type A15 (molecular weight 9500) 0.1 g/L medium. At 40 h the industrial-scale culture was assayed for antigen: pertussis toxic 550 and haemagglutinin 2200 ELISA units/mL cell-free medium were present.

Szejtli, J., Hoklits, I., Keszler, B., Kovacs, G., and Fenyvesi, E. (1987): *Hung. Teljes* HU 41,824 (*C.A.* **108**: 77531.

Water-soluble CD polymer can be produced by cross-linking βCD with epichlorohydrin in the presence of an insoluble basic anion exchanger, because in this case only a small amount of NaOH is needed, and the NaCl formed can be removed by ion exchange. The salt content of the product is very low, and can be used e.g. in photographic emulsions.

Friedman, R. B. (1987): *Ger. Offen.* DE 3,712,246 (*C.A.* **108**: 9653).

Hydroxylalkyl CD can be prepared by reacting CDs in anhydrous basic media with alkylene carbonates. For example reacting β-CD in the presence of K_2CO_3 with ethylene carbonate at 125° for 7.5 hours a hydroxyethyl-β-CD can be produced.

Skuballa, W., Vorbrueggen, H., Dahl, H., Stuerzebecher, C. S., and Thierauch, K. H. (1987): *Ger. Offen* DE 3,608,088 (*C.A.* **108**: 55762).

CD complexes of various carbocyclins (carboprostaglandin I_2) have been described.

Yamamoto, Y., Terayama, H., and Morita, Y. (1987): *Eur. Pat. Appl.* EU 233,615 (*C.A.* **108**: 44043).

The antiallergic hydroxydodecadiynyl-cyclohexa-dienedione has a very low aqueous solubility, which can be considerably enhanced by α-CD and DIMEB. The stability of the drug dissolved in polyoxyethylene sorbitan monooleate at pH 5 after two weeks was only 78.2%, while when dissolved in α-CD solution at pH 7 and stored at 60°C after two weeks 98.9% drug was retained. The preparation of a nose drop containing this drug and α-CD is described.

Nakanishi, M. (1987): *Jpn. Kokai* JP 62,149,626 (*C.A.* **107**: 242634).

An antitumour drug has been stabilized with CDs and/or collagens. This stabilized formulation was formulated as suppository capsules.

Shimizu, H., Oshina, M., and Terayama, H. (1987): *Eur. Pat. Appl.* EU 213,514 (*C.A.* **108**: 11238).

The antiinflammatory and antiallergic benzopyranopyridines can be used as eye or nose drops or for oral application especially when solubilized by appropriate solubilizers like CDs. Without polyvinyl-pyrrolidone the eye drops were more stable and less irritating.

Nakanishi, M. (1987): *Jpn. Kokai* JP 87,149,628 (*C.A.* **108**: 223306).

An antibiotic, Cephazolin Na was formulated with β-CD because in that form it showed an improved absorption and long-lasting activity. The β-CD formulated antibiotic was mixed with Witepsol and placed in a suppository capsule.

Kijima, T. (1987): *Jpn. Kokai* JP 87,105,908 (*C.A.* **108**: 58868).

Mono (6-β-aminoethylamino-6-dioxy)β-CD was dissolved in water and mixed with $Zr(HPO_4)_2$ powder and it resulted in an intercalation compound which can be used as a microcapsulating agent and packing material for chromatography.

Chikahisha, N., and Cho, S. (1987): *Jpn. Kokai* JP 87,169,844 (*C.A.* **108**: 113489).

Vinyl polymers have been prepared by polymerizing vinyl chloride and the vinyl β-CD complex. The obtained resin showed good chemical and physical stability.

Kijima, T., (1987): *Jpn. Kokai* JP 87,191,416 (*C.A.* **108**: 8333).

Montmorillonite with a lamellar structure was wetted with an aqueous solution of methylated-CD resulting in a montmorillonite-methylated CD intercalation compound which can be used as a microcapsulating agent of a packing material for gel chromatography.

Ishikura, K., and Hara, K. (1987): *Jpn. Kokai* JP 87,265,236 (*C.A.* **108**: 210221).

A pharmaceutical composition is suggested for the treatment of gastric disorders, which contains methylated CDs, menthol and at least one surfactant like polyoxyethylene sorbitan monolaurate.

Kamikama, K., Kurihara, M., and Urasaki, Y. (1987): *Jpn. Kokai* JP 87,120,344 (*C.A.* **107**: 223270).

The preparation of 4-biphenylacetic acid ester-β-CD complex tablet formulation is described.

Kamikama, K., Ueno, M., and Isane, T. (1987): *Jpn. Kokai* JP 87,198,675 (*C.A.* **108**: 210195).

Tocopherol nicotinate has been complexed with DIMEB, and the tablet, capsule and granule formulation of this composition is described.

Ishikawa, S., and Kadowaki, T. (1987): *Jpn. Kokai* JP 87,138,473 (*C.A.* **108**: 210193).

Hydroxypropyl-β-CD complexes of various carbostyril derivatives have been prepared for injectable solutions. The heptakis [6-*O*-(2-hydroxpropyl)]-β-CD was dissolved in water and this solution was dissolved in carbostryil derivatives and was filtered through a 0.2 μm membrane to eliminate microorganisms.

Murata, S., and Hara, K. (1987): *Jpn. Kokai* JP 87,263,143 (*C.A.* **108**: 220598).

The preparation of triglyceride (edible oil) β-CD complexes is described for food and pharmaceutical purposes. For example trioctanoylglycerol dissolved in ethanol was added to an aqueous CD solution (which can be a CD or a methylated CD) and the CD-triglyceride complex formed has been isolated. Storing the dry complex at 40°C for one month at 80% R. H., peroxide formation was less than 50% of the peroxide produced in the control which was not complexed with CD.

Hara, K. (1987): *Jpn. Kokai* JP 87,262,967 (*C.A.* **108**: 203566).

The preparation of stable spice-CD complexes is described. The natural spice preparation is soaked in aliphatic triglycerides, containing oil and then the spice which is extracted into the oil is complexed by CD to give a stable spice preparation. For example the mixture of triglyceride, ethanol and powdered red pepper were mixed and filtered to remove the nonsoluble components of the red pepper powder. The ethanol was removed and the oil was mixed with a 3 fold amount of β-CD, and with the same amount of water for 3 hours, then ground and dried to give a powdered spice.

Yamada, K., and Tsunoda, H. (1987): *Jpn. Kokai* JP 87,263,047 (*C.A.* **108**: 203557).

A food packaging polyethylene film has been prepared in which the innermost layer – which is in contact with the food – contains a flavour CD complex. For example an orange juice packaging laminated container is made from a film, which is composed of three layers: a polyester film, an Al film, and a low density polyethylene film containing 10% β-CD limonene complex. The package was left at 3°C for 30 days. The residual d-limonene content was about 80%, compared with 35% in a similar control container which did not contain an inclusion compound.

Hibino, T., Nakao, K., Okada, T., and Sahashi, H. (1987): *Jpn. Kokai* JP 87,84,041 (*C.A.* **108**: 192767).

The stabilization of γ-linolenic acid with β-CD is described. For example 5 mL oil of the evening primrose, which contains 8.8% γ-linolenic acid, was homogenized at room temperature with β-CD and water (10 g in 10 mL) then the complex formed was isolated and dried. More than 75% γ-linolenic acid remained intact after the powder was stored at 40°C for 1 month.

Furukawa, M., and Hara, K. (1987): *Jpn. Kokai* JP 87,289,504 (*C.A.* **108**: 200242).

The methylated CD complexes of insect growth inhibitors – like methoprene – were described. 1 part methoprene, 5 parts methylated-β-CD and 94 parts water gave a transparent solution which had a residual activity of 92% after storing at room temperature for two weeks.

Toyama, T., Kunichika, K., and Matsumoto, H. (1987): *Jpn. Kokai* JP 87,242,946 (*C.A.* **108**: 213998).

The application of CDs in lithographic plate preparation is described. The CD is used as an aqueous solution for coating the developed photosensitive layers before heating to obtain the lithographic plate.

Kimura, S., and Kageyu, A. (1987): *Jpn. Kokai* JP 87,207,211 (*C.A.* **108**: 210186).

Dolichol (a long chain branched unsaturated fatty acid) can be complexed with α-CD resulting in a stable powder, which resulted in a significantly enhanced bioavailability in rats after oral administration.

Hara, K., and Murata, S. (1987): *Jpn. Kokai* JP 87,265,230 (*C.A.* **108**: 210222).

An antilipemic preparation has been prepared by mixing methylated-β-CD and menthol in a 10 : 1 ratio. Methylated CD administered to rats decreased the levels of triglycerides, cholesterol and phospholipids in blood.

Takahashi, M., Mochjizuki, H., and Satoie, K. (1987): *Jpn. Kokai*, 87,249,920 (*C.A.* **109**: 11734).

Tocopherol nicotinate is photosensitive. Using βCD it can be stablized against photodegradation, even in a gelatine capsule. Storing the gelatine capsules for 12 months under light at 40°C and 75% R. H. 55% of the tocopherol remained, but in presence of βCD 95% remained.

Kirsch, H. (1987): *Ger Offen.* DE 3,609,116 (*C.A.* **108**: 173544).

Spices, condiments or drugs of natural origin can be complexed by homogenizing the natural product with β-CD and water. For example garlic was deep frozen and treated with β-CD and water to produce a slurry which after dehydration resulted in a white, nearly odourless garlic powder.

Yorozu, H., Eguchi, Y., and Kamiya, H. (1987): *Jpn. Kokai* JP 87,265,216 (*C.A.* **108**: 173375).

A carbon dioxide complex of randomly methylated β-CD has been prepared, which upon contacting with water releases CO_2. This product can be used as a bath composition for hot-springlike bath water.

Matsumoto, S., and Adachi, S. (1987): *Jpn. Kokai* JP 87,265,302 (*C.A.* **108**: 187433).

The photopolymerization catalyst used in vinyl polymer production has been complexed with β-CD. For example the benzoin-isopropyl ether–β-CD complex can be used for such purposes. 100 ppm of such catalyst results in a polymerization of acrylamide–Na acrylate upon irradiation with light of 360 nm.

Matsumoto, S., Teraishi, S., Watanabe, J., Sato, M., and Shiratori, I. (1987): *Jpn. Kokai* JP 87,250,008 (*C.A.* **108**: 76130).

High molecular weight and highly cationic aminomethylated polyacrylamides were prepared, which can be used for solid waste treatment and as paper reinforcers, by mixing a high molecular weight and a low molecular weight polyacrylamide using 2–5% powdered oils (like palm oil) which have been previously complexed with β-CD.