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PATENTS AND LITERATURE

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As part our continual effort to keep our readers fully up-to-date on recent developments in the field of biotechnology, we have with some regularity published this Patents and Literature section. In an effort to make our coverage still more useful, we have with this issue's presentation revised the format so that patent items—now restricted to one key field (in this issue, Enzymes)—are categorized into several topical subsections for each perusal.

The literature section remains compiled in alphabetical order on the first author's name, and we have attempted to provide a comprehensive listing of all 1982 journal articles on this issue's topic, Enzymes, that we judge to be especially significant and interesting. However, omissions seem inevitable because of the large number of possible citations, and to insure that no important papers remain unnoted, we urge authors to send a copy of any appropriate abstract or reprint/preprint to: Dr. S. L. Lee, Biosciences Research, Corning Glass Works, Sullivan Park FR6, Corning, New York 14831. We intend to make this section as complete and useful as possible, and promise careful attention to all material submitted.

Enzymes

I. Patents

Enzymes Acting on Carbohydrates

Debranching Enzyme Product, Preparation and Use Thereof; NIELSEN, G. C., DIERS, I. V., OUTTRUP, H., NORMAN, B. E.; EP 63909 (Nov. 3, 1982), Novo Industri.

Preparation of Debranching Enzyme from Rice for Producing a Low Calorie Beer; LINE, W. F., CHAUDHARY, V. K., CHICOYE, E, MIZERAK, R. J.; US 4355110 (Oct. 19, 1982), Miller Brewing.

Process for the Production of Branching Enzyme, Hayashibara Biochem. Lab. GB2095681 (Oct. 6, 1982).

Immobilization of Starch Degrading Enzyme; YONEYAMA, M.; US 4338398 (July 6, 1982), Kabushiki Kaisha Hayashibara Seibutsu Kagaku Kenkyujo.

Process for Isomerizing Glucose to Fructose; YOSHIOKA, T., TERAMOTO, K., SHIMAMURA, M.; US 4347316 (Aug. 31, 1982), Toray Industries, Inc. An enzyme bound to a monovinyl aromatic polymer having β-aminoprionamido group as a side chain is used in the isomerization of glucose to fructose.

Effective Production of Highly Active Immobilized Glucose Isomerase Sumitomo Chem. Co., Ltd., JP8236987 (Feb 27, 1982).

Glucose Isomerase Immobilized on Porous Phenolic Resin Support, and Method Employing; WALON, R. G. P., STOUFFS, R. H. M.; CA 1134765 (Nov. 2, 1982), CPC International Inc.

Isomerization of Glucose to Fructose Using Glucose Isomerase from Ampullariella; FOLEYS, S. E., ORIEL, P. J., EPSTEIN, C. C.; US 4308349 (Dec. 29, 1981), The Dow Chemical Co.

Process for the Production of Fructose Polymer and High Fructose Syrups; HEADY, R. E.; US 4317880 (Mar. 2, 1982), CPC International Inc. A sucrose-containing substrate is reacted with fructosyl transferase and glucose isomerase to form fructose polymers, glucose, and fructose.

Process for the Production of Fructose Transferase Enzyme; SMITH, J. A., LEUNSER, S. J.; US 4309505 (Jan 5, 1982), CPC International. Fructose transferase from *Aureobasidium pullulans* is used.

Fructose Production; LEISER, R. S.; US 4310628 (Jan. 12, 1982), A. E. Staley Manufacturing Co. By immobilized *Bacillus* glucose isomerase in the presence of Co^{2+} at temperature higher than 60°C, fructose is made.

Enhanced Immobilization of a Glucose Isomerase; TEAGUE, J. R., HEUBNER, A. L.; US 4337172 (Jan. 29, 1982), UOP Inc. Glucose isomerase is immobilized on magnesium impregnated support.

Method of Preparing a Plaque-Dispersing Enzyme; SIMONSON, L. G.; LAMBERTS, B. L., US 4328313 (May 4, 1982), US Secretary of the Navy. 1,3-Glucanase is produced from *Pseudomonas* NRRL B-12324, grown in an aqueous medium containing more than 90% alpha 1,3-glucan substrate.

Method of Dental Treatment; RABUSSAY, D. P.; US 4355022 (Oct. 19, 1982), Interon, Inc. Lysozyme is the primary active agent.

Mutanase; GUGGENHEIM, B; MUHLEMANN, H. R.; US 4353891 (Oct. 12, 1982). Mutanase from *Trichoderma, Penicillium,* or *Streptococcus* hydrolyses alpha 1,3-glucosidic bond in dental plaque.

Immobilized Pectinase; MUJZNIECE, Z; ARENS, A; DAIJA, D.; CUDARS, V. A. SU 926008 (May 7, 1982). Pectinase immobilized on aminoepoxy silica gel is used.

Process for Producing Cyclodextrins; YAGI, Y.; KUONO, K.; INUI, T. US 4317881 (May 2, 1982), Sanraku-Ocean Co., Ltd. Cyclodextrins are produced from starch by a cyclodextrin glycosyltransferase from a *Micrococcus* species.

Process for Producing Maltase; COONEY, C. L., SCHAEFER, E. J.; US 4332899 (Jun. 1, 1982), Massachusetts Institute of Technology. Maltase from *Saccharaomyces italicus* is used.

Hydrolysis of Milk Sugar; PLAINER, H., SPROESSLER, B.; DE3112336 (Oct. 7, 1982), Roehm GmbH.

Thermal Stable beta-Galactosidase; GRIFfiths, M. W., Muir, D. D., Phillips, J. D.; US 4332895 (Jun. 1, 1982). National Research Development Corp. Lactase from *Bacillus stearothermophilus* suitable at 65°C.

Thermally Stable Lactase Derived from Bacillus; LONG, M. E., LEE, C. K.; US 4323651 (Apr. 6, 1982), R. J. Reynolds Tobacco Co. Lactase from *Bacillus coagulans* NRRL B-8100 is used.

Manufacture of Lactose Hydrolyzates with Immobilized Lactase; Sumimoto Chem. Co., Ltd.; Nippon Steel Chemical Co., Ltd.; JP 8274092 (May 10, 1982). Lactase from *Aspergillus oryzae* was bound on a macroporous amphoteric phenol–formaldehyde ion exchange resin.

Conversion of Guar Gum to Gel-Forming Polysaccharides by the Action of alpha-Galactosidase; WHISTLER, R. L.; US 4332894 (Jun. 1, 1982), Purdue Research Foundation.

Process for the Preparation of Galactose Oxidase; TERADA, O., AISAKA, K.; US 4335213 (Jun. 15, 1982), Kyowa Hakko Kogyo Co., Ltd., Enzyme from *Gibberella fujukuroi* or *Gibberella zeae* was used.

Substrate-Specific Galactose Oxidase Enzyme Electrodes; JOHNSON, J. M.; US 4356074, (Oct. 26, 1982), The Yellow Springs Instrument Co., Ltd.

Immobilized Glucose Oxidase-Catalase Mixtures; FILIPIAK, M., KRAUZE, J., KIRSTEIN, D., MOHR, P.; DD 152808 (Dec. 9, 1982), Akademie der Wissenschaften der DDR, Zentralinstitut fur Molekularbiologie. Crosslinked gelatin as carrier.

Process for the Manufacture of Aldonic Acids by an Enzymatic Method; COPPENS, G., US 4345031 (Aug. 17, 1982), Solvay & Cie. Glucose is oxidized by glucose oxidase to gluconic acid in water and oxygen (partial pressure between 1 and 100 bar). Yields are between 40 and 10,000 mg/L.

Carbohydrate Process; MASELLI, J. A., HORWATH, R. O.; US 4321323 (Mar. 23, 1982), Standard Brands Inc. Glucose is oxidized enzymatically by glucose-2-oxidase into glucosone and hydrogen peroxide. The products are separated by a semipermeable membrane permeable to molecules of less than 100 daltons.

Proteases

Acylation of Mucor pusillus Microbial Rennet Enzyme; CORNELIUS, D. A., ASMUS, C. V., STERNBERG, M. M.; US 4362818 (Dec. 7, 1982), Miles Laboratories. Acylation of *Mucor pusillus* rennet by a selected anhydride (maleic, citraconic, phthalic, *cis*-1,2-cyclohexanedicarboxylic, 1,2,4-benzenetricarboxylic, homophthalic, 3-nitrophthalic, bromomaleic, or dichloromaleic) increases the milk coagulating activity of the enzyme by over 100%. Acylation of *Mucor miehei* rennet with maleic anhydride decreases the coagulating activ ity.

Thermal Destabilization of Microbial Rennet; BRANNER-JORGENSEN, S., SCHNEIDER, P., EIGTVED, P.; US 4357357 (Nov. 2, 1982), Novo Industri. Rennet from *Mucor miehei* and *M. pusillus* is oxidized by an active chlorine agent (e.g., sodium hypochlorite, *N*-chlorosuccinimide, chloramine-T, trichloroisocyanuric acid, and chlorine) to a loss of less than 50% activity (10–30% preferred). The destabilization reduces thermal stability by at least 5°C.

Thermal Collagenase, Thermophillic Bacteria Capable of Producing Thermophilic Collagenase, and Process for Producing Said Collagenases; MIWA, N., MASUDA, Y., KAWARABUKI, S., SAI, T., SAITO, T.; US 4315988 (Feb. 16, 1982), Mitsubishi Petrochemical Co., Ltd.

Immobilized Carboxypeptidase; Pentel Co., Ltd., JP 82125692 (Aug. 5, 1982). Leucine production by nylon immobilized carboxypeptidase.

Lipases

Preparation of Immobilized Enzymes for Use in a Nonaqueous Reaction System; Ajinomoto Co., Inc.; Kansai Paint Co., Ltd.; JP 82118792 (Jul. 23, 1982). A photopolymerizable resin based on a vinyl group-terminated polyalkylene glycol is used in immobilization of a fungal lipase to perform transesterification in hexane.

Other Enzymes

Process for Obtaining Cholesterol Oxidase; GAUHL, H., SCHAWOHL, G., SEIDEL, H., BEAUCAMP, K.; US 4334023 (June 8, 1982, Boehringer Mannheim GmbH. Enzymes from *Streptomyces griseofuscus* DSM 40191, *Streptomyces hygroscopicus* 40771, *Streptomyces acidomyceticus* DSM 40798, and *Arthrobacter paraffinens* DSM 312 were used.

Process for Producing L-Amino Acid Oxidase; YOSHINO, E., ISHIKAWA, H., INOUE, F., TAKADA, M., MISAKI, H.; US 4357425 (Nov. 2, 1982), Toyo Jozo Co. Ltd. L-Amino acid oxidase from *Colletotrichum* sp. M5073, FERMP 5441 was used.

Stabilization of Peroxidase; DAWSON, E. C.; HOMAN, J. D. H.; VAN WEEMAN, B. K.; US 4331761 (May 25, 1982), Akzona Inc. The novel peroxidase contains metal ions from Groups 3 and 4 of the periodic table, e.g., Al, Zn, Mg, Fe, and Cu.

Process for Production of Ascorbate Oxidase; MATSUMURA, E., ISHIKAWA, H., MISAKI, H.; US 4331763 (May 25, 1982), Toyo Jozo Kabushiki Kaisha. Ascorbate oxidase from the plant *Sechium edule* Sw. is extracted in an aequeous alkaline medium.

Enzyme Deesterification of Cephalosporin Methyl Esters; ABBOTT, B. J., BERRY, D. B.; US 4316955 (Feb. 23, 1982), Eli Lilly & Co. Enzyme from *Streptomyces capillispira* is used.

Stabilization of Cholinesterase, Detector Kit using Stabilized Cholinesterase and Methods of Making and Using the Same; GOODSON, L. H., GOODMAN, A.; US 4324858 (Apr. 13, 1982), Midwest Research Institute.

Immobilized Thermophillic Acetate Kinase; Unitika Ltd. and Kazutomo Imabori; JP 8233597 (Feb. 23, 1982). Acetate kinase from *Pseudomonas thermoamino-lyticus* and *Clostridium thermoaceticum* are immobilized on Sepharose.

Process for Preparation of L-Tryptophan by Enzyme; ASAI, Y., SHIMADA, M., SODA, K.; US 4335209 (Jun. 15, 982), Mitsui Toatsu Chemicals, Inc., L-Serine and indole are reacted in the presence of tryptophan synthetase or tryptophase to yield L-tryptophan. D-Serine in DL-serine is racemized partly to L-serine by a racemase prior to the said process.

Preparation Process of Optically Active alpha-Aminated Acids by Biological Hydrolysis of Nitriles; JALLAGEAS, J. C., ARMAUD, A., GALZY, P., US 4366250 (Dec. 28, 1982), Anvar. Racemic D,L-alpha-amino amides can be hydrolyzed by L-stereospecific amidase for the preparation of alpha-amino acids. A general nitrilase is used to prepare the alpha-amino amides.

Immobilized Restriction Endonucleases; CHIRIKJIAN, J. G., US 4342833 (Aug. 3, 1982), Bethesda Research Laboratory.

Techniques

Preparation and Use of Enzymes Bound to Polyurethane; WOOD, L. L., HARTDEGEN, F. J., HAHN, P. A., US 4312946 (Jan. 26, 1982), W. R. Grace. An aeueous dispersion of an enzyme is mixed with an isocyanate-capped polyurethane. The subsequent foaming traps the enzyme.

Immobilized Intracellular Enzymes; GESTRELIUS, S. M.; US 4288552 (Sep. 8, 1982), Novo Industri. Intracellular enzymes sensitive to glutaraldehyde are immobilized in the presence of poly(alkylenimine) in the ratio of 0.01 : 1 to 10 : 1 (primary amine : aldehyde).

High Loading of Immobilized Enzymes on Activated Carbon Supports; BAILEY, J. E., CHAO, Y. K.; US 4289853 (Sep. 15, 1982), Illinois Water Treatment Company. Enzymes are immobilized on active carbon treated with solution of an isoxazolium salt. A carbon–enzyme complex is formed on the carbon surface at the displacement of the isoxazolium salt.

Kefir Granules as Immobilized Lactase; Snow Brand Milk Products Co., Ltd., JP 8204312 (Jan. 25, 1982).

Immobilized Nonproteolytic Enzymes; Denki Kagaku Kogyo K. K., JP 8243687 (Mar. 11, 1982). Glucoamylase from *Aspergillus* is immobilized on gelatin.

Immobilized Enzymes or Microorganisms; Mitsubishi Rayon Co., Ltd., JP 82105189 (Jun. 30, 1982). Glucoseamylase from *Saccharomyces cerevisiae* was immobilized by microencapsulation on cellulose triacetate.

Preparation of Immobilized Enzymes for Use in a Nonaqueous Reaction System; Ajinomoto Co., Inc.; Kansai Paint Co., Ltd. Lipases are immobilized in polyalkylene glycol films for the synthesis of triglycerides.

Enzymes Bound to Polyurethane and Their Use; WOOD, L. L., HARTDEGEN, F. J., HAHN, P. A.; US 4312946 (Jan. 26, 1982)., W. R. Grace & Co.. Penicillin amidase entrapped in polyurethane.

Polymer Beads and Their Use in Immobilization; SANNER, A.; MARCINOWSKI, S., TSCHANG, C. J.; EP49385 (Apr. 14, 1982), BASF A.-G. Invertase was immobilized on abraded polymer beads of styrene and methacrylate.

Enzyme Immobilized on Glass Derivatives; BISSE, E., DE 3033076 (Apr. 29, 1982). Glucose oxidase immobilized on propylamine glass for glucose determination.

Polymeric Pariculate Carrier; ROYER, G. P., US 4326009 (Apr. 20, 1982). Polyethylenimine support with glutaraldehyde as crosslinking agent.

Immobilization of Biocatalysts; HERSHBERGER, D. F., STERNBERG, M. M.; US 4337313 (Jun. 29, 1982), Miles Laboratories, Inc. Enzymes or microorganisms are immobilized with tannin, a long-chain polyamine, and a crosslinking agent.

Immobilization of Enzymes; CREMONESI, P., US 4338401 (Jul. 6, 1982) Italfarmaco S.p.A. Enzymes are immobilized on a polysaccharide–vinyl monomer copolymer formed by UV-activation. The monomer can be methyl-acrylate, glycidylmethacrylate, acrylonitrile, bis-acyloylpiperazine or symmetrical N,N',N''-trisacryloyl-hexahydrotriazine.

Immobilization of Biologically Active Substances in a Porous Support, ROSEVEAR, A.; US 4323650 (Apr. 6, 1982), United Kingdom Atomic Energy Authority. Glucose isomerase and lactase immobilized on porous titania spheroids, crosslinked by glutaraldehyde.

Regeneration of an Immobilized Enzyme System; ROHRBACH, R. P., LEVY, J., LEE, G. K., ZA8100013 (Jan. 27, 1982), UOP Inc. Enzymes immobilized by amino-crosslinking to the support are regenerated.

Stabilized Liquid Enzyme and Coenzyme Compositions; MODROVICH, I. E., CA 1127005 (Jul. 6, 1982).

Coenzyme Immobilized Electrode; NAKAMURA, K.; NANKAI, S.; IIJIMA, T.; US 4321123 (Mar. 23, 1982), Matsushita Electric Industrial Co., Ltd. Electrodes with tin oxide layer are used for immobilization of NAD-dehydrogenase for the analysis of ethanol, glutamate, and lactate.

Preparation of Immobilized Enzymes; NITTO ELECTRIC INDUSTRIAL CO., LTD. JP 8208785 (JAN. 18, 1982). An enzyme is immobilized with a free aldehyde group-containing polymer carrier especially ethylene–vinyl acetate copolymer.

Immobilized Enzymically Active Substance; KLEIN, J., WANGER, F.;US 4334027 (Jun. 8, 1982). Pressed yeast is mixed with sodium alginate and precipitated with calcium chloride, shrunk by drying, and then hardened in a bath containing $Al_2(SO_4)_3$.

Preparation of Membranes for Immobilization of Enzymes; TOYOBO CO., LTD., JP 82122797 (JUL. 30, 1982). Glucose oxidase is immobilized on cellulose acetate-containing membranes.

II. Literature Survey

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