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PATENTS AND LITERATURE

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The objective of this section is to keep readers aware of significant inventions and trends in industrial research, as well as to highlight those areas of research that may lead to new biotechnological opportunities. Five subject areas will be covered in 1985: immobilized biocatalysts, applied immunology, nucleic acid technology, affinity separations, and bioassays. In each issue a new subject area will be introduced with a review of recent patents and literature. The subject of the first Patent and Literature Section of 1985 is Immobilized Biocatalysts.

Immobilized Biocatalysts

Patents

This section identifies and gives a brief description of patents from the US patent literature over the years of 1983 and 1984. The major search heading was *immobilized* (minor search headings included *adsorbed, entrapped, encapsulated, microencapsulated, bound,* and *cross-linked*) with the cross-terms: *enzymes* and *cells*. Both patent abstracts and titles were searched. Copies of US Patents can be obtained for $1.00 each from the Commissioner of Patents and Trademarks, Washington, DC 20231.

Arena, B. J., and Rohrbach, R. P. (Nov 22, 1983), SUPPORT MATRICES AND IMMOBILIZED ENZYME SYSTEMS. US 4416992.

Assignee: UOP Inc.

Support matrices are prepared by titanating the surface hydroxyl groups of refractory inorganic oxides with a titanium tetrahalide, such as

$TiCl_4$, reacting each of the remaining halogens of the surface-titanated oxide with one of the amino groups of diamine, and thereafter reacting the remaining amino group with one of the functional groups of a dialdehyde or diisocyanate. Such important matrices may be used to bind enzymes, affording effective immobilized enzyme systems.

Avrameas, S., Broun, G., Selegny, E., and Thomas D. (Aug 07, 1984), IMMOBILIZATION OF ACTIVE PROTEIN BY CROSS-LINKING TO INACTIVE PROTEIN. US 4464468.

Assignee: Agence Nationale de Valorisation de la Recherche (ANVAR)

A solution of an active protein substance and an inactive protein substance is reacted with a crosslinking agent, optionally in the presence of an inert carrier, under crosslinking conditions. The active protein substance comprises up to about 20% of the total protein substance, whereas the crosslinking agent comprises from 0.5 to 8% by weight.

Baret, J.L.A.G. (Jul 12, 1983), METHOD FOR DISINFECTING IMMOBILIZED ENZYMES. US 4393138.

Assignee: Corning Glass Works

Disinfecting of immobilized enzymes is carried out by contacting the immobilized enzymes with a dilute aqueous solution of at least one substituted diethylenetriamine (such as dioctyldiethylenetriamine) at a concentration and for a period of time sufficient to substantially kill the contaminating microorganisms without significant deleterious effects on the immobilized enzymes.

Buckmann, A. (Apr 17, 1984), PROCESS FOR THE PRODUCTION OF ADENINE RING SYSTEM CONTAINING CO-ENZYMES BOUND TO MACROMOLECULES. US 4443594.

Assignee: Gelleschaft fur biotechnologische forschung mbH (GBF)

The production of adenine ring system containing coenzymes bound to a macromolecular carrier comprising the steps of alkylating an adenine ring system containing coenzyme in the 1-position with an alkylating agent containing a terminal group capable of reacting with said macromolecular carrier. The alkylated coenzyme bound to a macromolecular carrier is subjected to a Dimroth rearrangement, and adenine ring system containing coenzyme bound to a macromolecular carrier recovered.

Cheetham, P.S.J. (Apr 17, 1984), STABILIZATION OF IMMOBILIZED ENZYMES WITH GLYCEROL. US 4443538.

Assignee: Tate & Lyle Public Limited Company

Enzyme-containing cells immobilized in an alginate gel are stabilized by contacting the gel with glycerol. The enzyme-containing cells preferably convert sucrose to isomaltulose.

Cheetham, P.S.J. (Jul 12, 1983), BACTERIAL ETHANOL PRODUCTION. US 4393136.

Assignee: Talres Development (NA) NV

Glucose or other substrate is covered to ethanol with immobilized bacterial cells under conditions that prevent growth of the cells.

Chibata, I., Tosa, T., and Takata, I. (Feb 21, 1984), ENZYMATIC ACTIVE SUBSTANCE IMMOBILIZED IN A POLYSACCHARIDE GEL MATRIX. US 4433054.

Assignee: Tanabe Seiyaku Co. Ltd.

An immobilized enzymatic active substance with improved stability. An enzymatic active substance, such as microbial cells entrapped within a gel matrix of an unsubstituted, amino, monoalkylamino, or dialkylamino group, introduced polysaccharide having not less than 10 w/w% of sulfate (such as carrageenan). The immobilized enzymatic active substance is prepared by admixing the enzymatic active substance and aqueous solution of the polysaccharide and allowed to gel.

Cole, F.X. (Nov 20, 1984), IMMUNOASSAY WITH ANTIGEN OR ANTIBODY LABELED LIPOSOMES SEQUESTERING ENZYME. US 4483921.

Assignee: Collaborative Research, Inc.

An immunoassay method utilizes antigen tagged, enzyme encapsulating liposomes that are immunospecifically ruptured in the presence of cognate antibody and active complement. A homogeneous phase reaction occurs with the antibody and complement acting to release the enzyme if an immunospecific antigen–antibody complex is formed at the surface of the liposome.

Daniels, M. J., and Farmer, D. M. (Dec 20, 1983), IMMOBILIZATION OF ENZYMES. US 4421850.

Tate & Lyle Ltd.

An immobilized enzyme product is produced by contacting an inert particulate support with an aqueous enzyme solution containing at least 25% dissolved solids and with water-miscible organic solvent, and crosslinking the enzyme to insolubilize the enzyme on the support as a gel. The water-miscible organic solvent is in excess to the water mixed with the support. The resultant immobilized enzyme product has a bulk volume 5–300% greater than the bulk volume of the support material. A portion of the gel is external to the support and constitutes at least 3% by volume of the immobilized enzyme product.

Freedman, H. H. (Oct 23, 1984), PROCESS FOR CROSSLINKING POLYAMINES. US 4478938.

Assignee: The Dow Chemical Company

Polyalkylenepolyamines are crosslinked in a non-anhydrous environment to yield water-swellable, essentially water-insoluble gels. The polyalkylenepolyamine is contacted with a polyisocyanate at pH 5–8 and subjected to a high rate of agitation. The process of this invention can be employed to immobilize proteins, enzymes, antibodies, etc.

Gestrelius, S. M., and Kjaer, J. E. H. (Apr 19, 1983), METHOD OF

DEACIDIFYING WINE AND COMPOSITION THERFOR. US 4389552.

Assignee: Novo Industri A/S

Deacidifying wine by passage through an alginate gel containing living cells of *Leuconostoc oenos* therein. To ensure maximum viability, the alginate gel is stored in a resting medium, preferably sterile grape juice containing 5–12% ethanol. Before deacidifying wine the immobilized cells are conditioned to a wine millieu.

Hall, L. D., and Yalpani, M. (Jan 03, 1984). DERIVATIVES OF CHITINS, CHITOSANS AND OTHER POLYSACCHARIDES. US 4424346.

Assignee: Canadian Patents and Development Ltd.

Derivatives of chitins and chitosans in which the amine residues on the polyglucosamine have been modified to: (a)—N=CHR or —$NHCH_2R$; (b) —NHR′; (c) —NHR″; and (d) —$NHCH_2CO_2H$ or —NH—glyceryl where R is an aromatic moiety with one hydroxyl or carboxyl group, or a macrocyclic ligand, R′ is an aldose or ketose residue, and, R″ is an organometallic aldehyde residue. These derivatives are useful in chelating metals, in pharmaceutical formulations, in cosmetics, in chromatographic separations, in enzyme immobilization, as catalysts, etc. Galactomannans having selected amine-containing side chains have also been prepared by reductive amination.

Han, M. H., Mheen, T. I., Seong, B. L., and Son, H. J. (Feb 14, 1984), BIOLOGICAL PROCESS FOR THE PREPARATION OF RIFAMYCIN DERIVATIVES. US 4431735.

Assignee: Korea Advanced Institute of Science and Technology

A process for converting rifamycin B to rifamycin O, rifamycin S, or rifamycin SV by treatment with whole cell, cell extract, or immobilized enzyme of Humicola spp. or Monocillium spp. is provided. The process also includes the recovery of rifamycin B in the fermentation broth after conversion to rifamycin O, rifamycin S, or rifamycin SV.

Hartmeier, W. (Jul 10, 1984), ENZYMES BONDED TO LIVING YEAST CELLS. US 4459312.

Assignee: C. H. Boehringer Sohn

An enzyme or enzyme mixture are coupled to living, fermentable yeast cells by contacting at least partially dehydrated living yeast cells with an aqueous enzyme solution to cause the yeast cells to rehydrate and a layer of enzyme to form on the surface of the yeast cells, and then contacting the rehydrated yeast cells with an enzyme-precipitating solution which optionally contains a crosslinking agent to cause the enzyme to become attached to the yeast cells. An aqueous solution of tannin is preferably the enzyme-precipitating solution and gluardialdehyde is preferably the crosslinking agent. Pepsin coupled to Saccharomyces yeast, when used to ferment grape must to produce wine, results in prac-

tically foam-free attenuation, quicker fermentation, and better self-clarification. Amgloglucosidase coupled thereto may be used to ferment beer wort to produce a diet beer.

Harvey, D.G., executrix by Harvey, D. C., and Harvey, C. D. (Apr 10, 1984), CONTINUOUS ENZYMATIC REACTOR FOR USE OF IMMOBILIZED ENZYME BEADS. US 4442216.

Continuous reaction with immobilied enzyme beads in an enzymatic reactor providing for continuous cleansing and continuous recycling of the cleansed immobilized-enzyme beads for reaction. A reaction chamber having a screw mounted coaxially within a shell having means at the first end for introducing immobilized enzyme beads and fluid reactant material, means at the second end for removal of product, means at the second end for lifting of immobilized enzyme beads and dropping them through a reaction chamber, and means for conveying cleansed immobilized enzyme beads from the cleansing to the means for introducing.

Ho, G.H., and Liao, C. C. (May 17, 1983), ACTIVATION OF A SILICEOUS CARRIER FOR ENZYME IMMOBILIZATION. US 4384045.

Assignee: Borden, Inc.

An improved immobilized enzyme composite is prepared by subjecting a siliceous carrier to an initial treatment with alkali, then acid, then reacting the carrier with an organosilane. The organosilane may then be coupled through a covalent coupling agent with an enzyme. The treated carrier is especially useful in the preparation of high performance immobilized enzyme compositions, particularly by multilayering immobilization, providing a very high amount of enzyme activity per unit volume.

Ikeda, M., and Tomizawa, T. (Nov 22, 1983), ARTIFICIAL CARRIER FOR IMMOBILIZATION OF BIOLOGICAL PROTEINS. US 4416813.

Assignee: Fujizoki Pharmaceutical Co. Ltd.

A novel artificial carrier is disclosed that is prepared from gelatin, a water-soluble polysaccharide, a sodium metaphosphate, and an aldehyde. The carrier can be used to immobilize antibodies, antigens, or enzymes. Immobilized antigens and antibodies can be used as a diagnostic reagent in assays involving antigen–antibody reactions.

Jost, L. I. (Sep 25, 1984), ANAEROBIC METHOD FOR PRESERVING WHOLE BLOOD, TISSUE AND COMPONENTS CONTAINING LIVING MAMMALIAN CELLS. US 4473552.

An anaerobic method for preserving mammalian blood, tissue, or living cell-containing components in a state of suspended animation. The method involves adding the substance to be preserved to a receptable contianing anticoagulant and low molecular weight hydroxyethyl starch, hydroxypropyl starch, or polystarch at 35°F and storing the resulting mixture, which then preserves blood, tis-

sue, or a component indefinitely. The structure is lightly crosslinked with a water-soluble crosslinking agent of the acrylamide type, to form a gel structure. When it is desired to use the preserved material, the swelled starch derivative may be liquefied, or the gel may be broken whereupon the preserved material may be used in the same way as the freshly collected substance.

Kiel, J. L., and Everse, J. (Dec 04, 1984), INSOLUBLE CROSSLINKED CYTOTOXIC OXIDASE-PEROXIDASE SYSTEM. US 4486408.

A therapeutic preparation, and a process of using the preparation, for the control of tumor growth and immune diseases. The preparation is an immobilized cytotoxic enzyme system that is carried by an insoluble substrate and administered into the mammalian subject by injection or implantation. A polymerized albumin carrier containing immobilized glucose oxidase and peroxidase is prepared in the form of small particles that can be administered either by implantation or by injection into tumor-bearing mammals. To date, antibacterial activity has been demonstrated only in vitro. Several daily administrations are required to achieve complete destruction of the tumor. Additionally, the preparation is also active as a stimulant of the specific immune response to neoplasia. Its effect on the immune system could be useful in the stimulation of the immune system in diseases where the action of the endogenous immune system is insufficient.

Kim, L., and Ash, S. G. (May 17, 1983), PRODUCTION OF MICROBIAL POLYSACCHARIDES. US 4384044.

Assignee: Shell Oil Company

The production of a polysaccharide wherein a microorganism species that produces polysaccharide (preferably in the stationary phase of the growth cycle) is supported on a porous, particulate inert support, the pore size being greater than about 0.5 μm, to form an immobilized cell system, aqueous nutrient medium is passed through the immobilized system, and polysaccharide-containing medium is withdrawn from the system.

Lantero, Jr., O.J., and Oreste, J. (Jun 28, 1983), IMMOBILIZATION OF THE SUCROSE MUTASE IN WHOLE CELLS OF PROTAMINOBACTER RUBRUM. US 4390627.

Assignee: Miles Laboratories, Inc.

Sucrose mutase in whole cells of *Protaminobacter rubrum I* is immobilized by contacting the cells with tannic acid, polyethylenimine, and an adduct of glutaraldehyde and an epihalohydrin/polyamine copolymer. The reaction product has improved sucrose mutase activity and physical characteristics for use in a packed-bed reactor to convert sucrose to palantinose.

Lanterno, Jr., O. J. (Mar 20, 1984), IMMOBILIZATION OF BIOCATALYSTS ON GRANULAR CARBON. US 4438196.

Assignee: Miles Laboratories, Inc.

Enzymes are immobilized on activated granular carbon. The carbon is treated with a polyamine compound having pendant amino groups to cause the polyamine to adhere to the carbon leaving pendant amine groups free to further react. The free amine groups are derivatized by treatment with a difunctional compound having amine reactive moieties, so that free amine groups of the enzyme can be covalently bound to the polyamine via the amine reactive compound.

Lehmann, H. D., Krisam, G. G., and Golla, R. S. (Oct 25, 1983), METHOD OF BINDING A BIOLOGICALLY ACTIVE MATERIAL TO A CARRIER CONTAINING HYDROXYL GROUPS. US 4412000.

Assignee: Gambro Dialysatoren KG.

Biologically active material such as an enzyme is bonded to a carrier containing hydroxyl groups by binding an isocyanate compound to the carrier and bonding the biologically active material to the bound isocyanate compound. Binding of the isocyanate compound to the carrier is achieved with the use of a nontoxic titanium (such as tetrabutyltitanate) compound that catalyzes the formation of urethane bonds.

Lim, F. (Jul 05, 1983), MICROCAPSULES CONTAINING VIABLE TISSUE CELLS. US 4391909.

Assignee: Damon Corporation

Tissue cells such as islet of Langerhans cells or liver cells are encapsulated within a spheroidal semipermeable membrane comprising a polysaccharide having acidic groups crosslinked with a polymer of molecular weight greater than 3000. The cells within the microcapsules are viable, healthy, physiologically active, and capable of ongoing metabolism. The encapsulated cells are useful for implantation in a mammalian body to produce substances and effect chemical changes characteristic of the cells in vivo tissue.

Lim, F. (Oct 04, 1983), REVERSIBLE MICROENCAPSULATION OF A CORE MATERIAL. US 4407957.

Assignee: Damon Corporation

Microencapsulation of a core material and subsequent release was achieved by selective disruption of the membranes of the microcapsules. The encapsulation technique involves the formation of a semipermeable membrane, e.g., around a droplet, through the formation of multiple ionic salt bonds between a polyionic polymer in the droplet and a crosslinking polyionic polymer that possesses multiple ionic groups of opposite charge. The membrane can be selectively disrupted by exposing it first to a solution of competing crosslinking multivalent (preferably di- or trivalent) ions followed by a solution of a competing polyionic polymer of the same charge as the polymer in the original droplet. The process may be used to encapsulate and subsequently release cell cultures without damage to the cells.

Lim F. (Oct 11, 1983), PREPARATION OF SUBSTANCES WITH ENCAPSULATED CELLS. US 4409331.

Assignee: Damon Corporation

A process for producing substances produced in cells such as antibodies and biological response modifiers. Producing cells are encapsulated within semipermeable membranes having an upper limit of permeability sufficient to allow traverse of cell nutrients and then suspended in a culture medium. Serum components and other high molecular weight materials needed for ongoing viability may be included within the intracapsular volume and may be excluded from extracapsular medium by limiting the permeability of the membranes. The substance of interest collects either in the intracapsular volume or the extracapsular medium, depending on the degree of permeability of the membranes and on the molecular weight of the substance.

Matsumoto, K., Izumi, R., Seijo, H., and Mizuguchi, H. (Feb 01, 1983), IMMOBILIZATION OF BIOLOGICAL MATERIAL WITH AN ACRYLONITRILE POLYMER. US 4371612.

Assignee: Toyo Jozo Company, Ltd.

Enzymes are immobilized by adsorption or covalent bonding to a microporous water-insoluble acrylonitrile polymer containing from 20 to 1000 μm of amino groups/g of polymer. Covalent bonding may be carried out with a crosslinking or condensing agent. The amino groups may be introduced into the polymer by reduction of nitrile groups with lithium aluminum hydride, in an inert nonsolvent.

Matsuo, T., Sawamura., N., Hashimoto, Y., and Hadhida, W. (Nov 22, 1983), METHOD FOR ENZYMATIC TRANSESTERIFICATION OF LIPID AND ENZYME USED THEREIN. US 4416991.

Assignee: Fuji Oil Company, Limited.

A method for the enzymatic transesterification useful for modification of a lipid, which comprises continuously or repeatedly contacting an enzyme or an enzyme preparation having transesterification activities with a fresh supply of a dried fatty ester substrate such as fats and oils of glycerides. The enzyme preparation is prepared by dispersing, adsorbing or bonding an enzyme having lipolytic activities in or to a carrier and drying the resulting mixture at an adequately slow initial drying rate to activate or increase the transesterification activities of the enzyme.

Mimura, A., Yuasa, K., and Shibukawa M. (May 22, 1983), IMMOBILIZATION OF MICROORGANISMS IN A POLYMER GEL. US 4450233.

Assignee: Asahi Kasei Kogyo Kabushiki Kaisha

Microorganisms are immobilized by adding cells to an aqueous solution of a mixture of a polymerizable starch and a polymerizable monomer to prepare a polymer gel with entrapped cells. The polymerizable starch

is prepared by introducing an acrylamidomethyl group into starch. The polymer gel has high mechanical strength and can be used repeatedly over long periods of the time while maintaining at high levels the reactivity of the microorganism enclosed therein.

Monsan, P. (Sep 20, 1983), ENZYMES IMMOBILIZED ON A SOLID SUPPORT CONTAINING CELLULOSE AND LIGNIN. US 4405715.

Assignee: Beghin-Say, SA

Enzymes are immobilized on a solid support material containing cellulose and lignin by a process involving oxidation of the support to provide aldehyde groups, amination of the oxidized support by reacting a diamine with the aldehyde groups, reduction of the aminated support to produce stabilized aminated groups, activation of the aminated groups by reacting the groups with a dialdehyde and immobilization of an enzyme by covalent coupling.

Muetgeert, J., Otto, P. H. L., and Flippo, F. A. (Nov 29, 1983), ENZYME IMMOBILIZATION IN A STARCH GEL. US 4418147.

Assignee: Nederlandse Organisatie Voor Toegepast-Natuurwetenschappelijk Onderzoek Ten Behoeve Van Nijverheid, Handel En Verkeer

Cell-free enzymes are immobilized by mixing the enzymes with a starch sol or a partially gelled starch gel to form a mixture containing 20 to 60% starch, gelling the mixture, extruding the gelled mixture to form strands, drying the strands, and breaking the dried strands into pieces to form shaped structures having improved mechanical strength.

Nakamura, K., Nankai, S., and Iijima, T. (Mar 15, 1983), COENZYME IMMOBILIZED ELECTRODE. US 4376689.

Assignee: Matsushita Electric Industrial Co. Ltd.

Improvements in a coenzyme electrode used to electrochemically measure the activity of enzyme or substrate concentration of the enzyme easily. The coenzyme is immobilized, without using a semipermeable membrane on the electron collector directly with the chemical bond, whereby the activity of the oxide-reductase requiring the coenzyme can be measured. In addition, the oxide-reductase requiring the coenzyme is also immobilized together with such immobilized coenzyme to improve the characteristics of the conventional enzyme–coenzyme immobilized electrode.

Nakamura, K., Nankai, S., and Iijima, T. (Jul 12, 1983), ELECTROCHEMICAL MEASURING APPARATUS COMPRISING ENZYME ELECTRODE. US 4392933.

Assignee: Matsushita Electric Industrial Co. Ltd.

An immobilized enzyme electrode effective in measurement of the substrate concentration of the enzyme and in conversion from enzyme reaction energies into electric energies. The immobilized enzyme, of an oxidase system, and a metal oxide capable of constituting a redox system

that is reduced through coupling with these enzyme reactions and is electrochemically oxidized (anodic oxidation) are combined with each other. The use of the enzyme electrode allows the determination quantity of the enzyme substance at extremely low concentration.

Nankai, S., Imai, A., and Iijima, T. (Feb 14, 1984), ENZYME ELECTRODE. US 4431507.

Assignee: Matsushita Electric Industrial Co. Ltd.

An improved enzyme electrode which includes a first electrode having at least one kind of an enzyme immobilized on it for electrochemically detecting a substance to be produced in association with a reaction based on the enzyme, and a second electrode for electrochemically removing materials that interfere with the detection by the first electrode. The second electrode is disposed at the side of a test solution containing a substrate of the enzyme with respect to the first electrode.

Nankai, S., Nakamura, K., and Iijima, T. (Feb 28, 1984), ENZYME IMMOBILIZATION WITH AN IMMOBILIZING REAGENT IN VAPOR PHASE. US 4434229.

Assignee: Matsushita Electric Industrial Co. Ltd.

Immobilization of enzymes by covering the surface of a solid support with an enzyme and then contacting the enzyme with an immobilizing reagent in the vapor phase. The immobilizing reagent is preferably an aldehyde or a polymerized aldehyde. By having the immobilizing reagent in vapor phase, the immobilizing reagent concentration can be easily controlled by the vapor pressure. A uniform covering of immobilized enzyme on the support is obtained and support surfaces that are uneven or curved can be covered with immobilized enzyme regardless of size.

Nees, S. (Feb 08, 1983), DEVICE FOR CULTIVATION OF MATRIX-BOUND BIOLOGIC CELL SYSTEMS. US 4373029.

Improved apparatus for cultivation of matrix-bound cell systems on microcarrier particles within a replenishable nutrient medium providing controlled three dimensional displacement of a culture vessel and its contents to effect uniform cell exposure to available nutrient material.

Novak, I. and Berek, D. (May 03, 1983), PROCESS FOR PRODUCING XEROGEL OF SILICIC ACID WITH HIGH VOLUME OF PORES. US 4382070.

A product which can be applied as a column packing for high performance liquid chromatography. This material is further useful as a catalyst carrier, as a sorbent for selective concentrating diluted compounds for analytical purposes, and for immobilizing enzymes and the like.

Peters, P. J. H. and Kerkhoofs, P. L. (Aug 09, 1983), PREPARATION AND IMMOBILIZATION OF INULINASE. US 4397949.

Assignee: Stamicarbon, B. V.

Enzyme preparation from *Aspergillus phoenicis* having high inulinase activity, a very low Michaelis constant, thermal stability, optimum

inulinase activity across a wide pH range, and little sensitivity to heavy metal ion inhibition may be immobilized on an organic macroporous polymer or in an alginate gel.

Rosevear, A. (Jan 10, 1984), IMMOBILIZATION OF BIOLOGICALLY ACTIVE SUBSTANCES. US 4425434.

Assignee: United Kingdom Atomic Energy Authority.

The preparation of discrete particles having immobilized in the pores a biologically active substance (e.g., an enzyme). The method includes precipitating a biologically active substance in the pores of the particles of support material, by use of a precipitating agent comprising or including a water miscible organic liquid, and treating the biologically active substance precipitated in the pores to cause crosslinking.

Schmer, G. (Feb 14, 1984), BIO-ARTIFICIAL ORGAN USING MICROENCAPSULATED ENZYMES. US 4431428.

Assignee: Trimedyne, Inc.

A bioartificial organ containing a biochemically active matrix comprised of biochemically active enzyme-containing microcapsules entrapped within a gel matrix. An extracorporeal blood flow can be passed through the organ and over the biochemically active matrix to permit the enzyme to perform its enzymatic function on a substrate in the blood.

Schmer, G. (Mar 20, 1984), BIOCHEMICALLY ACTIVE MATRIX FOR USE IN A BIO-ARTIFICIAL ORGAN. US 4438198.

Assignee: Trimedyne, Inc.

A biochemically active matrix for use in a bioartificial organ comprised of an enzyme covalently bonded to a matrix of organochemically crosslinked fibrin. The matrix may be suspended in a medium of agarose which irreversibly solidifies below 37°C. The bioartificial organ is useful for extracorporeal treatment of blood to remove excess substrate from the blood.

Shigesada, S., Kitagawa, H., Mihara, T., and Ishimatsu, Y. (Oct 25, 1983), IMMOBILIZATION OF ENZYMES ON GRANULAR GELATIN. US 4411999.

Assignee: Denki Kagaku Kogyo Kabushiki Kaisha

An immobilized enzyme composition produced by simultaneously reacting a nonproteolytic enzyme and a water-soluble multifunctional reagent with a nonhardened granular gelatin in an aqueous medium. The nonproteolytic enzyme forms a uniform film on the surface of the granular gelatin and the bond between the nonproteolytic enzyme and the granular gelatin is strengthened by the water soluble protein polymer.

Shimizu, J., Suzuki, M., and Nakajima, Y. (May 31, 1983), METHOD OF PRODUCING PALATINOSE WITH IMMOBILIZED ALPHA-GLUCOSYL TRANSFERASE. US 4386158.

Assignee: Mitsui Sugar Co. Ltd.

Palatinose is produced from sucrose with an immobilized bacteria containing alpha-glucosyl transferase. The bacteria is immobilized by entrapping the bacteria in calcium alginate gel granules and treating the granules with polyethyleneimine and glutaraldehyde. Palatinose is efficiently produced by packing the bacteria-containing granules in a column and passing a sucrose solution through the column at high velocity.

Suzuki, S., Aizawa, M., Koyama, M., Sato, Y., and Koezuka, J. (Jun 14, 1983), ELECTROCHEMICAL MEASURING APPARATUS PROVIDED WITH AN ENZYME ELECTRODE. US 4388166.

Assignee: Tokyo Shibaura Denki Kabushiki Kaisha

An electrochemical measuring apparatus comprised of an asymmetric semipermeable membrane mounted on an immobilized enzyme membrane of an enzyme electrode. This membrane being formed of a thin semipermeable layer exposed to the outside for contact with a liquid to be measured and an inner adjacent thick porous layers, and can measure an organic ingredient such as glucose contained in blood or serum with high sensitivity in a short time and moreover has a prominent durability.

Symon, T., and Barszcz, C. F. (Nov 15, 1983), SUPPORT MATRIX FOR IMMOBILIZED ENZYMES. US 4415663.

Assignee: UOP Inc.

A support matrix comprising a porous support impregnated with a polyamine substantially all of whose nitrogens bear pendant epoxide groups can be readily used to immobilize enzymes. Immobilization results from formation of a hydrolytically stable carbon–nitrogen single bond.

Watanabe, I., Sakashita, K., and Ogawa, Y. (Dec 20, 1983), PRODUCTION OF ACRYLAMIDE USING IMMOBILIZED CELLS. US 4421855.

Assignee: Nitto Chemical Industry Co. Ltd.

A process for producing acrylamide from acrylonitrile using an immobilized microorganism containing gel, which comprises immobilizing microorganism having nitrilasic activity with a cationic acrylamide-based polymer gel and bringing acrylonitrile into contact with the immobilized microorganism gel in an aqueous medium containing substantially no salt.

Wood, L. L., and Calton, G. J. (Mar 13, 1984), IMMOBILIZED MICROBIAL CELL COMPOSITION FOR MAKING L-ASPARTIC ACID. US 4436813.

Assignee: Purification Engineering, Inc.

Microbial cells having L-aspartase activity are immobilized for producing L-aspartic acid. The cells are immobilized by mixing the cells with a curable prepolymer material and curing the prepolymer material to form a crosslinked polymer. Suitable prepolymer materials are polyazetidine prepolymers, carboxymethyl cellulose that can be cross-

linked with polyvalent ions, polyurethane hydrogel prepolymers, and polymethylene isocyanates.

Yamaguchi, T. (Oct 04, 1983), POLYMERIC MEMBRANE HAVING MALEIC ANHYDRIDE RESIDUES. US 4407975.

Assignee: Agency of Industrial Science and Technology

A polymeric membrane having maleic anhydride residues that comprises a blend of a maleic anhydride copolymer and a support polymer. This blend partially crosslinked with a bifunctional crosslinking reagent. When hydrolyzed, this membrane turns into an ion exchange membrane or a membrane on which an enzyme is immobilized.

Yamaguchi, Y., Watanabi, I., and Satoh, Y. (Apr 03, 1984), PROCESS FOR THE CONTINUOUS PRODUCTION OF ACRYLAMIDE OR METHACRYLAMIDE USING MICROORGANISMS. US 4440858.

Assignee: Nitto Chemical Industry Co. Ltd.

A process for the continuous production of acrylamide or methacrylamide from acrylonitrile or methacrylonitrile by use of a microorganism capable of promoting the hydration of acrylonitrile or methacrylonitrile into the corresponding amide. Immobilizing the microorganism or extracted enzyme, continuously bringing the acrylonitrile or methacrylonitrile into contact with the immobilized microorganism or enzyme to cause the hydration reaction, and recycling in a part of the reacted solution to dilute the unreacted acrylonitrile or methacrylonitrile.

Literature

This section surveys the literature in the area of immobilized enzymes and cells published in 1983 and 1984. This section is not intended to be all encompassing and lists only some of the major articles and reviews which appeared during this time period.

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