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# PATENTS AND LITERATURE

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. Four major areas of biochemistry will be covered corresponding to enzymes, cells, bioproducts, and nucleic acids. The patent section will briefly cover each area in every issue of the journal. The literature section will focus on one area per issue.

# PATENTS

This section will identify patents and published patent applications from the international patent literature. The title, the name(s) of the inventor(s), the patent number, the date of filing, the assignee, and a short description of the invention will be given. Copies of US patents can be obtained for 50¢ each from the Commissioner of Patents and Trademarks, Washington, DC 20231.

# ENZYMES

## Process for Isomerizing Glucose to Fructose

*S. P. Barrett*
US 4,288,548 (Nov. 15, 1979)
Standard Brands Incorporated

A glucose-containing material is treated with an ion exchange resin in the bisulfite/sulfite form and the treated liquid is then contacted with immobilized glucose isomerase.


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## Immobilized Intracellular Enzymes

*S. M. Gestrelius*
US 4,288,522 (Apr. 11, 1979)
Novo Industria A/S

An intracellular, glutaraldehyde-sensitive enzyme can be immobilized with glutaraldehyde if a branched polyalkalene imine is added before or simultaneously with the glutaraldehyde.

## Microorganism and Proteolytic Enzyme Derived Therefrom

*A. Belloc; J. Florent; J. Lunel; J. Palla; D. Mancy*
US 4,288,556 (Aug. 16, 1977)
Rhone-Poulenc Industries

*Streptomyces caligosus* DS 14,486 produces a proteolytic enzyme with a molecular weight of 27,000, an isoelectric point of 3.7, a maximum activity on casein at pH 7.5, and a specific activity on the hair–skin bond that, when used in depilation, affords recovery of both intact hair and intact skin.

## High Loading of Immobilized Enzymes on Activated Carbon Supports

*J. E. Bailey; Y. K. Cho*
US 4,289,853 (May 7, 1980)
Illinois Water Treatment Company

When activated carbon is treated with an isoxazolium salt, it forms a complex; when the complex is reacted with an enzyme in solution, the enzyme displaces the isoxazolium salt and forms a carbon–enzyme complex that can be separated from the reaction media.

## Cellulase Treatment of Orange Material

*T. Mouri; H. Kayama*
US 4,299,849 (Jun. 14, 1978)
Toyo Seikan Kaisha Limited

Cellulase enzyme produced by *Aspergillus niger* or *Trichoderma viride* and having no enzyme component capable of disintegrating plant tissue is reacted with steamed and crushed whole orange or its rind at a temperature of 30–55°C.

### Method for the Quantitative Determination of Terminal Deoxynucleotidyl Transferase in Biological Samples

*M. Kit*
US 4,307,189 (Mar. 21, 1980)
Unassigned

Labeled oligodeoxynucleotide primers or substrates are chemically modified so they cannot form base pairs by hydrogen bonding. This modification renders the substrates selective to utilization by terminal deoxynucleotidyl transferase without interference by other DNA polymerases.

### Isomerization of Glucose to Fructose Using Glucose Isomerase from Ampullariella

*S. E. Foley; P. J. Oriel; C. C. Epstein*
US 4,308,349 (Mar. 9, 1978)
Dow Chemical Company

A microorganism from the genus *Ampullariella* produces glucose isomerase in recoverable quantity upon fermentation in an aqueous nutrient medium.

### Thermophilic Aspartase and Its Preparation

*K. Kimura* (First Author)
Jpn Kokai Tokkyo Koho 56-75097 (A)
Patent Application No. 54-152468 (Nov. 27, 1979)
Kyowa Hakko Kogyo K.K.

Thermophilic organisms from the genus *Bacillus* produce aspartase that can be recovered after cell extraction.

## Cells

### Microbiological Process for Removing Oleaginous Material from Wastewater and Microbiological Combination Capable of Same

*P. W. Spraker*
US 4,288,545 (Jan. 7, 1979)
Sybron Corporation

Wasterwater containing oleaginous material is treated with a combination of *Pseudomonas aeruginosa* $SGRR_2$ and a member of the genus *Bacillus* or *Pseudomonas* other than said strain.

## Process for Large Scale Production of Pituitary Hormones by Serial Secondary Suspension Cultures

*M. J. Narasimhan; J. A. Anderson*
US 4,288,546 (Nov. 6, 1978)

Pituitary prolactin is produced by serially subculturing cells in a medium supplemented with liver extract, insulin, and a substance with progesterone–androgenic activity.

## Anaerobic Thermophilic Culture System

*L. G. Ljungdahl; J. K. W. Wiegel*
US 4,292,406 (Sept. 11, 1979)
United States Department of Energy

A mixed culture system composed of *Thermoanaerobacter ethanolicus* (ATCC 31550) and *Clostridium thermocellulum* (ATCC 31549) produces ethanol upon fermentation in a medium containing cellulose material.

## Mass and a Method of Preparing Same of Living Cells of Organisms for Adsorbing Metal Ions from a Physiological Solution and Employment of the Mass for Enriching Metals

*U. Zimmermann; G. Pilwat*
US 4,292,408 (Mar. 12, 1979)
Kernforschungsanlage Julich Gesellschaft mit beschrankter Haftung

Chlorella algae, dunalliela algae, or sea water bacteria are exposed to an electric field for a period of time sufficient to increase the porosity of the cell membranes; the treated cells are suspended in an aqueous solution with metal ions including uranium ions that adsorb to the cells and are subsequently removed by centrifugation.

## Cell Culture Microcarriers

*D. W. Levine; W. G. Thilly; D. I. C. Wang; J. S. Wong*
US 4,293,654 (Jul. 2, 1979)
Massachusetts Institute of Technology

Beads of crosslinked dextran are soaked in an aqueous solution of a tertiary or quaternary amine and a base until they are substituted with amine groups to produce an exchange capacity of 0.1–4.5 mEq/l of dry dextran.

## Process of Treating Burn Victims

*M. G. Eisinger*
US 4.299,819 (Sept. 13, 1979)
Sloan-Kettering Institute for Cancer Research

Epidermal cells from human skin are cultured in the absence of dermal components into a pure epidermal sheet in a tissue culture medium having a pH of 5.6–5.9. The cell sheet is applied to an afflicted area on the burn victim.

## Asporogenous Mutant of *B. subtilis* for use as Host Component of HVl System

*F. E. Young; G. A. Wilson; S. L. Mottice*
US 4,302,544 (Oct. 15, 1979)
University of Rochester

*B. subtilis* RUB 331 (ATCC 31578) has the following characteristics: translucent phenotype on tryptose blood agar; a frequency of transformation with linear or covalently closed circular DNA of up to 2%; lyses in a complex medium; does not from colonies after drying at room temperature for 12 h and has a frequency of reversion to sporeformers of less than $10^{-7}$.

## Transplantable Sheets of Living Keratinous Tissue

*H. Green; O. Kehinde*
US 4,304,866 (Nov. 14, 1979)
Massachusetts Institute of Technology

Keratinocytes are cultured so as to produce a sheet of keratinous tissue upon the culture vessel surface. A neutral protease is used to detach the sheet from the vessel without disaggregation.

# Bioproducts

## Whey Protein Recovery

*M. Buhler; M. Olofsson; P. Fosseux*
US 4,291,067 (May 7, 1979)
Societe d'Assistance Technique pour Produits Nestle S.A.

Lactoserum is heat-treated to denature the proteins to an extent of about 35–70% by weight of proteins; the denatured proteins are separated by ultrafiltration and the retentate is subjected to another heat treatment to insure complete protein denaturation.

## Production of Fructose and Fructose-Base Syrups and Means for Carrying Out Such Production

*L. Degen; P. Branduzzi; R. Olivieri; N. Cimini*
US 4,291,123 (Jun. 8, 1978)
Snamprogetti, S.p.A.

Fructose and syrups containing fructose and glucose are prepared by contacting a solution of glucose with a *Streptomyces sp.* NRRL 11,120 or NRRL 11,121.

## Polysaccharide S-53 and Bacterial Fermentation Process for Its Production

*K. S. Kang; G. T. Veeder*
US 4,291,156 (Feb. 28, 1979)
Merck & Co., Inc.

Under appropriate culture conditions, bacteria produce a heteropolysaccharide composed of 4.8% pyruvate, 7% acetyl, 18–19% uronic acid, and the remainder being neutral sugars, glucose, and fucose.

## Sweetening Compositions Containing Peptide Sweeteners and a Method for Their Manufacture

*Z. Latymer*
US 4,292,336 (Feb. 1, 1980)
Talres Development (N.A.) N.V.

Gelatin is mixed with either monellin or thaumatin to form sweetening compositions.

## Sugar-Free Confectionery Material Based on Xylitol and Sorbitol

*G. Andersen*
US 4,292,337 (Mar. 25, 1980)
August Storck KG

A sugar-free swelling agent is mixed with xylitol, sorbitol, water, and selected additives to from a chewy confectionery material.

## Microbiological Recovery of Metals

*W. Drobot*
US 4,293,333 (Feb. 12, 1980)
Engelhard Minerals & Chemicals Corporation

A process for removing selected metals from an aqueous medium by contacting them with a live fungus from the molds family for a period of time sufficient to allow the fungus to extract the metal from the solution in a water insoluble form.

## Method of Dissolving Collagen-Containing Tissues

*R. Monsheimer; E. Pfleiderer*
US 4,293,647 (Feb. 28, 1978)
Rohm Gmbh

Collagen-containing tissue is hydrolyzed into soluble products of low viscosity by treatment with an acid protease in the presence of urea.

## Method of Producing High Purity Maltose

*H. Hidaka; T. Kohno; T. Eida*
US 4,294,623 (Dec. 5, 1979)
Meiji Seika Kaisha, Ltd.

Saccharified liquor is passed through columns of granular activated carbon of different micropore diameters to produce a solution having more than 97% maltose content.

## Method for Improving Xanthan Yield

*W. P. Weisrock*
US 4,301,247 (Dec. 8, 1980)
Standard Oil Company (Indiana)

Deoxycholic acid, cholic acid, and salts thereof are added to a nutrient medium to improve heteropolysaccharide production from Xanthomonas microorganisms.

## Antigenic Modification of Polypeptides

*V. C. Stevens*
US 4,302,386 (Jan 16, 1980)
Ohio State University

Proteins and polypeptides with biological functions that are not normally immunogenic in mammals are chemically modified in vitro. When the modified form is administered to the mammal, it elicits the production of antibodies capable of inhibiting the biological function of the endogenous unmodified protein.

## Process for the Production of Erythropoietin

*K. Takezawa; H. Hiratani*
US 4,303,650 (Oct. 2, 1980)
Ajinomoto Co. Inc. and Chemical Research Co.

Human urine adjusted to a pH range of 6–8, is contacted with polystyrene-based adsorbent resin, chitosan, or diatomaceous earth in a manner to adsorb the erythropoietin that can be eluted after the depleted urine has been washed through.

## Process for the Continuous Enzymatic Change of Water Soluble α-Ketocarboxylic Acids into the Corresponding Amino Acids

*C. Wandrey; R. Wichmann; W. Leuchtenberger; M. Kula; A. Buckmann*
US 4,304,858 (Jul. 25, 1980)
Degussa Aktiengesellschaft

α-Ketocarboxylic acids are converted to their corresponding amino acids in a membrane reactor in the presence of a substrate-specific dehydrogenase, ammonium ions, and coenzyme. The coenzyme is linked to a water-soluble polyoxyethylene polymer and is simultaneously regenerated by means of formate ion in the presence of formate dehydrogenase.

## Method for Increasing the Diacetyl Production of a Diacetyl-Producing Bacteria

*J. Troller*
US 4,304,862 (May 19, 1980)
The Procter & Gamble Company

*S. diacetylactis, S. cremoris, S. lactis,* and mixtures thereof produced increased amounts of diacetyl when inoculated into a medium containing selected amounts of sucrose and diacetyl precursor.

## Method for Preparing a Carboxylated Chitin and a Derivative Thereof

*J. Koshugi*
US 4,304,905 (Dec. 17, 1979)
Kureha Kagaku Kogyo Kabushiki Kaisha

An aqueous highly concentrated alkali solution of chitin is frozen and then dispersed into an organic solvent containing an etherifying agent composed of a chlorine or bromine atom attached to a carboxylated alkane.

## Inhibitors Obtained from Bacilli for Glycoside Hydrolases

*W. Frommer; L. Muller; D. Schmidt; W. Puls; H. Krause; U. Heber*
US 4,307,194 (Dec. 6, 1977)
Bayer Aktiengesellschaft

In nutrient solution, microorganisms from the genus *Bacillus* produce a glycoside hydrolase inhibitor having the characteristics of l-desoxynojirimycin.

## Preparation of Opium Alkaloid by Tissue Culture of *Papaver Somniferum* Plant

*T. Furuya*
Jpn Kokai Tokkyo Koho 56-61994 (A)
Patent Application No. 54-138575 (Oct. 26, 1979)
Unassigned

Cells of *Papaver somniferum* are put into tissue culture to cause callus formation. The callus is cultivated at low temperature under light irradiation in a nutrient medium supplemented with dichlorophenoxyacetic acid and coconut milk.

### Culture of Mycelium Type Yeast and Fermentative Production of High-Molecular Weight Substances

*Y. Tani* (First Author)
Jpn Kokay Tokkyo Koho 56-68389 (A)
Patent Application No. 54-143628 (Nov. 5, 1979)
Unassigned

*Candida tropicalis* loses its ability to hold high molecular weight intracellular substances when it is cultivated in an inositol-deficient medium containing 1–3% ethanol. If a carbon supply is available, the intracellular substances continuously accumulate in the medium.

## Nucleic Acids

### Method for Synthesizing DNA Sequentially

*S. N. Cohen*
US 4,293,652 (May 25, 1979)
Cetus Corporation

A predetermined fragment of chemically synthesized double-stranded DNA is inserted into a cloning vector having a single restriction site. After placing the vector into a host to amplify and purify the inserted fragment, the process is repeated for other portions of the gene immediately adjacent the previously cloned fragment until the gene is complete.

### Transfer and Detection of Nucleic Acids

*G. M. Wahl; G. R. Stark*
US 4,302,204 (Jul. 2, 1979)
The Board of Trustees of Leland Stanford Junior University

A solid substrate having polynucleotides covalently affixed is contacted with a hybridization solution containing labeled polynucleotides suspected of being complementary to the affixed nucleic acids. A mixture of double-stranded DNA can also be detected by annealed, labeled polynucleotides by first electrophoresing the DNA and then denaturing it.

## Selective Determination of Nucleotides in Viable Somatic and Microbial Cells

*S. E. Kolehmainen; V. Tarkkanen*
US 4,303,752 (Nov. 30, 1979)
Unassigned

Microbial cells are treated with a mixture of ionic surface active agents to selectively release ATP without rupture of microbial cell membranes and cell walls. The concentration of ATP released is measured by means of a firefly bioluminescent assay and the number of viable microbial cells is thereby determined.

## Process for the Production of Hybrid Bacteria

*J. Collins; B. Hohn*
US 4,304,863 (Mar. 30, 1979)
Gesellschaft fur Biotechnologische Forschung mbH

A hybrid plasmid is prepared from a foreign DNA fragment and a bacterial plasmid having only one cos site of a lambda phage. The hybrid plasmid is packaged with the lysate of a lambda phage and transduced into *Escherichia coli* whereby hybrid bacteria are formed.

## Novel Recombinant Containing Reverse Transcriptase Gene

*H. Sugano* (First Author)
Jpn Kokai Tokkyo Koho 56-87600 (A)
Patent Application No. 54-164017 (Dec. 12, 1979)
Gan Kenkiyuukai

Avian DNA containing the reverse transcriptase gene is inserted into a lambda phage vector that can be grown in *Escherichia coli*.

## Preparation of L-Valine by Fermentation

*Y. Matsui* (First Author)
Jpn Kokai Tokkyo Koho 56-85289 (A)
Patent Application No. 54-161974 (Dec. 13, 1979)
Ajinomoto K. K.

DNA for the synthesis of L-valine is extracted from a valine analog-resistant organism from the genus *Escherichia*. The DNA is inserted into a vector that is then introduced into another *Escherichia* organism that accumulates L-valine in the growth medium.

# Literature Survey

The objective of the literature survey is to make a thorough, recent review of publications in one specific area. This issue's survey will be on enzymes. Further surveys will be on cells, bioproducts, and nucleic acids. The articles will be chosen for their impact on current biotechnology processes and for their potential to break new ground that may lead to new applications. The entries are listed in alphabetical order by the first author's name.

# Enzymes

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