APPLIED BIOCHEMISTRY AND BIOTECHNOLOGY 6, 339–351 (1981)

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

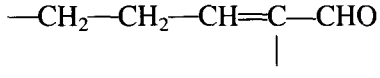
This section will identify patents and published patent applications from the international patent literature. The title, name(s) of the inventor(s), the patent number, the date of filing, the assignee, and a short description of the invention will be given. Copies of US patents can be obtained for 50¢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

Enzymes

Polyglutaraldehyde Synthesis and Protein Bonding Substrates

A. Rembaum
US 4,267,234 (Mar. 19, 1979)
California Institute of Technology

Microspheres are prepared having a diameter of 200 Å to 10 μm that consist of a repeating conjugated aldehyde unit with the formula:



Support Matrices for Immobilized Enzymes

R. P. Rohrbach
US 4, 268, 419 (Nov. 16, 1979)
UOP Inc.

An enzyme support matrice is prepared by depositing a polyamine binding layer on an alumina support and crosslinking it with glutaraldehyde.

Method for the Determination of Alpha-Amylase

S. Klose; H. G. Batz; M. Stoltz; A. Hagen; G. Weimann
US 4,268, 628 (Mar. 19, 1979)
Boehringer Mannheim GmbH

Alpha-Amylase splits a starch derivative and releases a low molecular weight aromatic fission product that can be reacted with a dyestuff forming component; the initial enzyme content is related to the amount of dyestuff formed.

Process for Isolation of Ribulose 1,5-Diphosphate Carboxylase from Plant Leaves

S. G. Wildman; P. Kwanyuen
US 4,268, 632 (Sept. 24, 1979)
Leaf Proteins, Inc.

Plant leaves are converted to a pulp that contains the enzyme in the liquid portion; after a heat denaturing step, the liquid portion is cooled and the enzyme crystallizes.

Regeneration of an Enzyme Immobilizate

G. Franzmann; H. L. Wulsmann
US 4,271,269 (May 15, 1979)
Dynamit Nobel Aktiengellschaft

Adsorbed inactivated enzyme is desorbed from its silicecous support by contacting it with a concentration of 10–40% inorganic ammonium sulfate or alkyl ammonium sulfate in a pH range of 5–11.

Acid Uricase and Process for the Production Thereof

T. Nakanishi; Y. Shigemasa
US 4,273,874 (Dec. 14, 1979)
Kyowa Hakko Kogyo Co., Ltd.

The oxidation of uric acid to allantoin is catalyzed by an acid uricase having an optimum pH in the range of 4.7–5.1.

Enzymatic Baiting Method

R. Monsheimer; E. Pfleiderer
US 4,273,876 (Dec. 18, 1979)
Rohm GmbH

Dehaired pelts are enzymatically baited at a pH between 3 and 6 with an acid protease and an amylase.

Glucose Isomerase Immobilized Product and Process for Preparing Same

T. Yoshioka; K. Teramoto; M. Shimamura
US 4,275,156 (Jan. 22, 1980)
Toray Industries, Inc.

Glucose isomerase is immobilized to a polymerized monovinyl aromatic compound through beta-aminopropionamidomethyl side chains.

Preparation and Use of Glucose Isomerase

C. K. Lee
US 4,283,496 (Sept. 19, 1977)
R. J. Reynolds Tobacco Company

Flavobacterium arborescens ATCC 4358 produces substantial amounts of glucose isomerase when cultivated in a nutrient medium with lactose as the sole carbon source.

Heat and Acid-Stable Alpha-Amylase Enzymes and Processes for Producing the Same

M. Tamuri; M. Kanno; Y. Ishi
US 4,284,722 (Nov. 13, 1979)
CPC International Inc.

An alpha-amylase from *Bacillus stearothermophilus* having a pH optimum between 4.0 and 5.2 is capable of retaining at least 50% of its initial activity when held at 90°C at a pH of 6.0 for 60 min in the absence of calcium ions.

Cells

Immobilization of Enzymes or Bacterial Cells

I. Kaetsu; M. Kumakura; M. Yoshida
US 4,272,617 (Jul. 26, 1979)
Japan Atomic Energy Research Institute

Enzymes and/or cells are insolubilized by mixing them with a hydrophobic vitrifiable monomer and the resulting mixture is polymerized by irradiation at a temperature of less than −10°C.

Method for Treating Dutch Elm Disease Using *P. syringae*

G. A. Strobel
US 4,277,462 (Nov. 19, 1979)
Endowment and Research Foundation at Montana State University

P. syringae NRRL B-12050 is applied in appropriate disease-controlling amounts to trees with Dutch elm disease.

Preparing Entomocidal Products with Oligosporogenic Mutants of *Bacillus thuringiensis*

D. E. Johnson
US 4,277,564 (Jan. 9, 1980)
United States of America

The vegetative cells of a *Bacillus thuringiensis* mutant produce spores and parasporal crystals in a spore : crystal ratio of less than 1 : 800.

Mutant Microorganisms Useful for the Production of Single Cell Protein and Amino Acids

V. R. Srinivasan; Y. C. Choi
US 4,278,766 (Nov. 8, 1977)
Louisiana State University Foundation

Mutant microorganisms of *Cellulomonas* (ATCC 21399) excrete L-glutamic acid, L-lysine, or both when grown in a fermentation medium in the absence of yeast extract.

Method of Highly Concentrated Cultivation of Yeasts

H.Fukuda; T. Shiotani; W. Okada
US 4,284,724 (Jan. 22, 1979)

During the course of aerobic cultivation in a fermentor, yeast cells are removed continuously and separated into yeast cells and a filtrate containing growth inhibiting substances; the cells are recycled into the fermentor and the steps repeated to bring the final cell concentration to between 6 and 20%.

Method for Continuous Culturing of Microbes

R. A. Messing; R. A. Oppermann; L. B. Simpson; M. M. Takeguchi
US 4,286,061 (Jun. 23, 1980)
Corning Glass Works

Microbes immobilized on a porous inorganic support are kept in a logarithmic growth state by supply medium at a sufficient rate and by removing microbe-containing effluent at an equal rate; the pore size of the support varies according to whether bacteria, yeast, or fungus-like organism are grown and also depends on the smallest and largest dimensions of the organisms.

Bioproducts

Process for Obtaining Human Relaxin from Fetal Membranes

M. Bigazzi
US 4,267,101 (Feb. 1, 1980)
Serono Laboratories Inc.

A crude relaxin extract is obtained by homogenizing human fetal membranes and then precipitating and discarding tissue residues and cellular organelles.

Immunosuppresive Extracellular Product from Oral Bacteria

T. B. Higerd; J. M. C. Goust
US 4,268,434 (Jan. 9, 1979)

Streptococcus intermedius produces an extracellular protein with a molecular weight of 160,000 and an isoelectric point of 4.8; it has inhibitory activity against fibroidblastoid cells and against blast transformation of PHA-stimulated human lymphocytes.

Production of Angiogenic Factor by Cell Culture

W. R. Tolbert; M. J. Kuo; J. Feder
US 4,268,629 (Mar. 3, 1980)
Monsanto Company

Human diploid cell line IMR—90 is cultured in nutrient medium for a sufficient time to elaborate angiogenic factor that can be isolated from the cells or cell product.

Microbiological Production of Ketones from C_3–C_6 Alkanes

R. N. Patel; C. T. Hou; A. I. Laskin
US 4,268,630 (Mar. 30, 1979)
Exxon Research & Engineering Co.

Methylotropic microorganisms previously grown on nutrient medium containing methane are brought into contact with C_3–C_6 *n*-alkanes; under aerobic conditions, a portion of the alkane molecule is oxidized to the corresponding methyl ketone which can be isolated.

Preparation of L-Tryptophan by Fermentation

H. Yukawa; K. Osumi; Y. Takayama
US 4,271,267 (Dec. 6, 1979)
Mitsubishi Petrochemical Co., Ltd.

When cultivated on a medium containing ethanol as the main carbon source, *Serratia marcescens* MT-5 produces L-tryptophan.

Process for Producing D-Arabitol

A. Fujiwara; S. Masuda
US 4,271,268 (Sept. 8, 1978)
Hoffman-La Roche Inc.

When cultivated on a medium containing selected hydrocarbons and ethyl alcohol, *Pichia haplophila* produces D-arabitol.

HGI-Glycoprotein Capable of Stimulating Proliferation and Differentiation of Human Granulocyte, Process for Preparing Same, and Keukopenia Curative Containing Same

F. Takaku; K. Ogasa; M. Kuboyama; M. Saito; N. Yanai; M. Nishida
US 4,275,056 (Mar. 19, 1979)
Morinaga Milk Industry Co., Ltd.; The Green Cross Corporation

A glycoprotein that stimulates human bone marrow cells to form colonies of granulocytes is purified from normal human urine; it has a molecular weight of 75,000–90,000, an isoelectric point of pH 4.7, and contains 13–20% by weight of polysaccharide.

Method for the Production of L-Lysine

O. Tosaka; E. Ono, M. Ishihara; H. Morioka; K. Takinami
US 4,275,157 (Jul. 10, 1979)
Ajinomoto Co., Inc.

Mutants of the genus *Brevibacterium* or *Corynebacterium* are sensitive to fluoropyruvic acid and accumulate L-lysine in the culture medium.

Manufacture of Fatty Acids Having Straight and Long Carbon Chains Using a Microorganism

A. Taoka; S. Uchida
US 4,275,158 (Jan. 7, 1980)
Bio Research Center Company, Ltd.

When aerobically cultivated in a nutrient medium with straight chain C_{10}–C_{18} hydrocarbons, *Debaryomyces vanriji* (BR-308) ATCC 20588 produces mono- and dicarboxylic acids of the same carbon skeletal length.

Process for the Production of Xylose by Enzymatic Hydrolysis of Xylan

J. Puls; M. Sinner; H. H. Dietrichs
US 4,275,159 (Jul. 30, 1979)
Projektierung Chemische Verfahrenstechnik GmbH

Xylanase, beta-xylosidase, and a uronic acid-splitting enzyme are purified from crude enzyme solution by a series of ultrafiltration steps.

Preferential Degradation of Lignin in Gramineous Materials

D. T. Wicklow; R. W. Detroy
US 4,275,167 (Jun. 18, 1980)
United States of America

Plant material is enriched in cellulose content by fermenting it with the fungal microorganism *Cyathus stercoreus* that preferentially degrades lignin.

Preparation of High Fructose Syrups from Sucrose

R. E. Heady
US 4,276,379 (Jun. 9, 1978)
CPC International Inc.

A cell-free fructosyl transferase enzyme derived from *Pullularia pullulans* converts sucrose to a mixture of glucose, fructose, and polysaccharides; the mixture is treated with glucose isomerase and then the polysaccharides are hydrolyzed in the absence of the isomerase enzyme.

Production of L-Amino Acids

H. Yukawa; K. Osumi; T. Nara; Y. Takayama
US 4,276,380 (Feb. 13, 1980)
Mitsubishi Petrochemical Co., Ltd.

Acinetobacter calcoacetocum YK-1011 produces and accumulates L-valine in a culture medium in which ethanol is the main carbon source.

Purification of Interferon

E. Knight, Jr.
US 4,278,661 (Oct. 12, 1979)
E. I. Du Pont de Nemours and Company

Impure serum-free human interferon is adsorbed on Cibacron Blue F3G-A and eluted with a buffer containing 35–45% ethylene gylcol; this results in an interferon preparation of greater than 95% purity.

Process for Treating Cellulosic Materials and Obtaining Glucose Therefrom

G. T. Tsao; M. R. Ladisch; C. M. Ladisch; T. A. Hsu
US 4,281,063 (Oct. 3, 1979)
Purdue Research Foundation

Cellulose-containing material is fractionated into a solid cellulose- and lignin-containing fraction and a liquid fraction containing hemicellulose; the cellulose in the solid fraction is removed from the lignin, reprecipitated, and then hydrolyzed to yield glucose.

Homogenous Fibroblast Interferon and Method for Manufacture Thereof

H. J. Friesen; S. Pestka
UK Patent Application GB 2,055,384 A (Jul. 30, 1980)
F. Hoffman-La Roche & Co.

Human fibroblast interferon purified by affinity chromatography and high pressure liquid chromatography has a specific activity of 4×10^8 units/mg, an apparent molecular weight of 20,500, and a maximum of three residues of glucosamine and no residues of galactosamine or mannosamine per molecule.

Nucleic Acids

Plasmid and Process of Isolating Same

J. J. Manis
US 4,273,875 (Mar. 5, 1979)
The Upjohn Company

Streptomyces espinosus biotype 23724a contains 20–40 copies of a 6 megadalton plasmid (pUC6) per cell.

Method for Preparing Strains That Produce Amino Acids

V. G. Debabov; J. I. Kozlov; N. I. Zhdanova; E. M. Khurges; N. K. Yankovsky; M. R. Rozinov; R. S. Shakulov; B. A. Rebentish; V. A. Livshits; M. M. Gusyatiner; S. V. Mashko; V. N. Moshentseva; L. F. Kozyreva; R. A. Arsatiants
US 4,278,765 (Jun. 28, 1979)

A hybrid DNA molecule is prepared by combining an amplifiable plasmid with a DNA fragment containing genes controlling the synthesis and feedback regulation of a particular amino acid; the hybrid molecule is used to transform recipient bacteria with appropriate mutations.

Purification of Nucleotide Sequences Suitable for Expression in Bacteria

H. M. Goodman; J. Shine; P. Horst
US 4,283,489 (Nov. 23, 1979)
The Regents of the University of California

The purity of a specific desired nucleotide sequence in a preparation of DNA fragments can be measured using restriction endonucleases, and separating DNA subfragments according to their length.

Microbial Expression of Quasi-Synthetic Genes

D. V. Goeddel; H. L. Heyneker
UK Patent Application GB 2,055,382 A (Jul. 3, 1980)
Genentech, Inc.

Methods are described for the construction and microbial expression of quasisynthetic genes arising out of the combination of organic synthesis and enzymatic reverse transcription from messenger RNA sequences that are incomplete from the standpoint of the desired protein product.

Genetically Modified Escherichia Coding for L-Lysine

K. Sano; T. Tsuchida
UK Patent Application GB 2,055,849 A (Jul. 22, 1980)
Ajinomoto Co., Inc.

A DNA fragment from a donor strain resistant to an L-lysine analog is inserted into a hybrid plasmid that is incorporated into a host cell; the fragment can control the production of L-lysine during fermentation.

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 nucleic acids. Further surveys will be on enzymes, cells and bioproducts. 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.

Nucleic Acids

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