Industrial Examples

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Introduction

• Successful application of biocatalyst for organic transformations in industries depends on factors that include
  – availability of suitable enzyme,
  – ease of up- and downstream processing,
  – competition with established chemical methods,
  – time required for process development,
  – biocatalyst disposal,
  – possible perception of the technologists and engineers, and
  – government regulations
Introduction

• Most of the applications for biocatalysts at industrial scale are for low volume, high-value products
• Bioethanol comes from fermenting sugars, which are generated by breaking down starches from corn, potatoes, sugar cane, or wheat.
• Amino acid?

MANUFACTURE OF AMINO ACIDS

• Production of L-Aspartic Acid
• Production of L-Alanine
• Production of glutamic acid
• D-Aspartic Acid
• L-Maleic Acid
L-aspartic acid

• L-Aspartic acid is used in medicines and in food additives as artificial sweetener, which can be produced by reacting fumaric acid with ammonia in the presence of aspartase.

• Tanabe Seiyaku Co. Ltd. first reported the industrial production of L-aspartic acid using E. Coli B immobilized with polyacrylamide gel.

• Mitsubishi Petrochem Co. developed a process for production of L-Aspartic acid using native strain Brevibacterium flavum MJ 233.

D-Aspartic Acid

• Tanabe Seiyaku Co. has been producing biocatalytically 9.5 t of D-aspartic acid and 5.1 t of L-alanine per month simultaneously from 1988.

• The enzyme used is P. dacunhae cells (L-aspartase-h-decarboxylase) immobilized on a support
Production of L-Alanine

• L-Alanine, an amino acid used in medicines and food additives, is produced industrially since 1965 by Tanabe Seiyaku Co. from L-aspartic acid
• Continuous production of L-alanine from ammonium fumarate was commercialized in 1982 at a scale of 100 t/month of acid and 10 t/month of L-alanine using 1000 l and 2000 l reactors, respectively

L-Maleic Acid

• L-Maleic acid, a food additive, is industrially produced from fumaric acid using lactobacillus traditionally in a batch reactor.
• Tanabe Seiyaku Co. has been manufacturing since 1980 using immobilized B. flavum cells at the rate of 30 t/month with 70% yield.
• The novelty of the process is the use of microbial cells itself, rather than using the purified enzyme, thereby saving on the cost.
• A possible disadvantage of this approach is the formation of side products, in this case succinic acid.
MANUFACTURE OF ANTIBIOTICS

• 6-APA
  – 6-Amino penicillanolic acid (APA) is used in the production of semisynthetic penicillin, such as amoxicillin and ampicillin and more than 6200 t of 6-APA is produced annually worldwide (Asahi chemicals, Beechams, Pfizer, and Gist-Brocades).

• 7-ACA
  – 7-Aminocephalosporanic acid (ACA) is an intermediate in the production of medically important semisynthetic cephalosporins. Toyo Jozo and Asahi Chemicals industry, Montedison Group (Italy)

MANUFACTURE OF TRIGLYCERIDES

Cocoa Butter Equivalent

• Unilever and Fuji oil manufacture cocoa butter equivalent using 1,3-selective lipases replacing palmitic acid with stearic acid. Cocoa butter imparts the “mouth feel” in food products

• Unilever subsidiary Quest-Ioders Croklaan (Netherlands) use palm oil middle fraction or higher oleate sunflower oil as the starting material.
AMIDES

• About 30,000 t/annum of acrylamide is manufactured by Nitto Chemicals (Yokohama, Japan) using R. rhodochrous J1.
• Lonza (Switzerland) in their plant in Guangzhou, China make 3000 t/annum of nicotine amide (vitamin, animal feed supplement) from 3-cyano pyridine using R. rhodochrous J1.

SPECIALTY CHEMICALS

• Enzyme cyclodextrin glycotransferase can be used to convert simple starch molecules into cyclodextrin. Maxygen (Calif) has a process for reducing carboxylic acids into aldehydes.
• Thermogen (Chicago, Ill.) uses ehydrogenases to convert ketones to Chiral alcohols.
• Energy Biosystems (Woodlands, Tex.) has developed oxidases enzyme to convert crude oil into water-soluble molecules so that they can be separated from oil base.
CHIRAL DRUGS AND INTERMEDIATES

• Chiral drugs business in 2001 reached $100 billion, representing one-third of all drugs sales worldwide.

• Monsanto’s NSC Technology produces D-phenylalanine and D-tryrosine (intermediates for a series of derivative products that have use in HIV treatment, oncology, and cardiovascular drugs) using D-amino acid transaminase enzymes.

• BASF is producing vitamin B2 through fermentation