World Skill Development Institute

Biotechnology Based Bulk Drugs

Course Duration – 1 Year.

Biotechnology has played an essential role in the development of the healthcare chemical industries. The range of product includes diagnostic, prophylactic and therapeutic agents. The discovery of a potentially active compound starts a sequence of exhaustive chemical and biological testing that may culminate in manufacture of the agent or an improved analog. The role of biotechnology in this complex path to regulatory approval and marketing is diverse. Biotechnology is a field of applied biology that involves the use of living organisms and bioprocesses in engineering, technology, medicine and other fields requiring bio products. Biotechnology also utilizes these products for manufacturing purpose. Some of the examples of drugs produced through biotechnology are penicillin, lincomycin, streptomucin, tylosin, peptide antibiotics, cephalosporins, etc. Modern use of similar terms includes genetic engineering as well as cell and tissue culture technologies. Biotechnology draws on the pure biological sciences and in many instances is also dependent on knowledge and methods from outside the sphere of biology. Conversely, modern biological sciences are intimately entwined and dependent on the methods developed through biotechnology and what is commonly thought of as the life sciences industry. The development of biotechnology is taking place in almost all fields of human life. The recent advances in the field of basic genetics have opened up new vistas, potentials and possibilities.

Some of the fundamentals of this course include pharmaceutical industries marketing strategy, common features in the evolution of products and processes, process technology fermentation, product recovery, new trends in biotechnology, penicillins, biosynthesis and regulation of thienamycin, olivanic acids and epithienamycins, aminoglycoside antibiotics, streptidine and deoxystreptamine, streptomycin, neomycin, paromomycin, ribostamycin and,butirosin gentamicin, micronomicin and sisomicin, tylosin, peptide antibiotics, current applications of peptides, blasticidin S: an agricultural antibiotic bleomycin and bestatin: peptides used in anticancer therapy etc.

This course contains process of biotechnology based bulk drugs like penicillin, B lactam antibiotics, aminoglycoside antibiotics, peptide antibiotics, anti cancer agents,

lincomycin etc. This course is resourceful for entrepreneurs, technocrats and research scholars.

INTRODUCTION

The Pharmaceutical Industries

Marketing Strategy

Common Features in the Evolution of Products and Processes

Process Technology

Fermentation

Product Recovery

New Trends in Biotechnology

PENICILLINS

Historical Perspective History

Biosynthetic Penicillins

Process Overview

Fermentation Technology

The Culture: Strain Development

Mutation

Selection

Genetics

Fermetation Process : Flow Sheet

Facilities

Inoculum Development

Fermentation Stage: Medium

Process Control

Physiological Variables and Their Effect on Product Formation

Duration of the Fermentation

Recovery of Penicillin

Carbon Process (Obsolete)

Solvent Extraction Process (Industry Standard)

Process Overview

Filtration

Solvent Extraction

Carbon Treatment

Further Extraction

Crystallization

Drying

Further Processing

Penicillin Acid Process (State of the Art)

Semisynthetic Penicillins

6-Aminopenicillanic Acid

Enzymic Cleavage of Penicillins to Yield 6-Aminopenicillanic Acid

Chemical Preparation of 6-Aminopenicillinic Acid

Synthesis of Clinically Useful Penicillins and Closely Related Congeners

Automation

Process Economics

Costs

NOVEL LACTAM ANTIBIOTICS

Thienamycin

Discovery

Chemistry

Pharmacological Activity

Chemical Synthesis

Biosynthesis and Regulation of Thienamycin

Biosynthesis

Regulation

Classical Fermentation Process

Introduction

Seed Stages

Production Stage

Fermentation Process Development

Strain Improvement

Fed-Batch Techniques

Synthetic Media

Novel Fermentation Processes

Ultrafiltration Coupled Fermenter

Immobilized Cells

Thienamycin Purification

Future Prospects

Market Projections

Clavulanic Acid

Introduction

Production

Market

Olivanic Acids and Epithienamycins

Nocardicins

Introduction

Production of Nocardicin A

Market Projections

Monobactams

AMINOGLYCOSIDE ANTIBIOTICS

Streptidine and Deoxystreptamine

Streptomycin

Neomycin, Paromomycin, Ribostamycin and Butirosin

Gentamicin, Micronomicin and Sisomicin

Fortamine and Fortimicins

Mutasynthesis

A-Factor

Metabolic Grid

Manufacture

Fermentation

Microorganisms

Equipment

Inoculum Development

Media

Procedures

Isolation

Strain Improvement

TYLOSIN

Production Technology

Structure of Tylosin and Related Compounds

Biosynthetic Pathway

Growth of Producer Microorganisms

Product Recovery and Purification

Product Development

Development in the Genetic Improvement of Producing Strains

Developments in Fermentation Technology

PEPTIDE ANTIBIOTICS

Current Applications of Peptides

Blasticidin S : an Agricultural Antibiotic

Bleomycin and Bestatin: Peptides used in Anticancer Therapy

Cyclosporin: an Immunosuppressor

Structural Types of Peptides

Biosynthesis of Peptide Antibiotics

Ribosomal and Nonribosomal Mechanisms

Reactions Involved in Enzymatic Peptide Formation

Carboxyl Activation

Peptide Bond Formation

Modification Reactions

Production of Peptides

Fermentation

Product Recovery

Other Major Aminoglycoside Antibiotics

Screening and Genetic Engineering of Strains for New Aminosides

Screening of new strains

Use of Idiotrophic Mutants

Structural Modification of Known Aminosides

Hemisynthesis

Bioconversion

Chemical Synthesis of New Aminosides

Streptothricins, Aminoglycoside-like Antibiotics

Structure

Physicochemical and Biological Properties

Production by Fermentation and Isolation

Uses

Marketing Prospects

CEPHALOSPORINS

Mode of Action of Cephalosporins

Structure and Biosynthesis of Bacterial Cell Wall

Sensitivity and Resistance

Structure/Activity Relationships

Cephalosporin Market

Biosynthesis of Cephalosporins

Biosynthesis Pathway

Regulation of Cephalosporin Biosynthesis

Aminoadipic Acid

Valine

Cysteine

Effect of Oxygen Tension

Catabolite Repression

Specific Growth Rate

Fermentation Process

The Fermenter-Its Design and Instrumentation

Fermentation Microbiology

Production Kinetics

Strain Development

Fermentation Development

Alternative Process-DAC Process

Recovery Process

Purification of Cephalosporin C

Cleavage of Cephalosporin C to 7-ACA

COMMERCIAL PRODUCTION OF CEPHAMYCIN ANTIBIOTICS

Cephamycin Product Description

Discovery

Mode of Action

Cefoxitin

Physicochemical Characteristics

Cephamycin C Assay Techniques

Fermentation Microbiology

Introduction

Metabolic Origins

Carbon Metabolism

Nitrogen Metabolism

Sulfur Metabolism

Phosphate Metabolism

Cephamycin Production Technology

Inoculum Development Stage

Antibiotic Production Stage

Isolation and Purification Stage

Conclusions and Implications

LINCOMYCIN

Discovery

Chemistry

Spectrum

Mode of Action

Lincomycin Assays for Fermentation Development and Production

Production Technology

Lincomycin Biosynthesis

Fermentation

Lincomycin Production by Other Actinomyces Species

Fermentation Power Requirements

Isolation

Chemical Derivatives of Lincomycin

Commercial Markets

Current Manufacturers

Product Outlook

PHARMACOLOGICALLY ACTIVE AND RELATED MARINE MICROBIAL PRODUCTS

Pharmocologically Active Compounds From Marine Microorganisms

Products From the Culture of Microalgae in Coastal Ponds

Agricultural Applications

Conclusions

ANTICANCER-AGENTS

The Drug Development Process

Market Information

Containment Technology for Cytotoxic Agents

Containment of Process Equipment

Personnel Protection

Decontamination of Waste Streams

Microbial Process Examples

Fermentation Processes for Production of Anthracyclines

Strain Improvement

Batch Fermentation Processes

Isolation and Purification

Fermentation Processes for Production of Nucleosides

Strain Improvement

Batch Production Process

Therapeutic Enzymes

Batch and Continuous Fermentation Processes

Isolation and Purification

Examples of Products of Mammalian Cells in Culture

Interferon Production

Fibroblast Processes (HuIFN-ï• ¢)

Leukocyte Processes (HulFN-a)

Lymphoblastoid Processes (Hu Ly, IFN)

Immune Interferon Processes (HulFN-Y)

Future Technologies: Lymphokines and Monoclonal Antibodies

Summary

SIDEROPHORES

The Need for Iron-Solubilizing Agents

The Role of Siderophores

Uptake and Release of Iron from the Siderophore Complex

Production of Siderophores

Conditions for Siderophore Production

Extraction

Adsorption

Ion-exchange Chromatography

Restricted Growth

Protein Binding of Contaminant Iron

Range of Molecular Structures

Hydroxamates

Catecholates (sometimes referred to as phenolates)

Siderophores with Antibiotic Activity

Sideromycins

Interference with Iron Uptake

Siderophore Analogues

Sideromycins

Extraction and Purification of Siderophores

Mycobactin

Enterochelin

Ferrichrome

Commercial Production of Desferrioxamine B (Desferal)

Uses of Siderophores

Iron Metabolism in the Body

Iron Poisoning and Chelation Therapy

Haemochromatosis and Chelation Therapy

Chelation Therapy

Other Medical Application for Siderophores

Applications for Siderophores Outside Medicine

Future Trends

STEROID FERMENTATIONS

Bioconversions of Practical Importance

Bioconversions of Limited or Potential Practical Importance

Progesterone Side Chain Cleavage

Ring A Aromatization

17 and 21-Hydroxylations

Alternative Bioconversion Methods

Sterol Degradation

Steroid Solubility

Methods of Steroid Addition

Steroid Conversion in Organic Solvents

Future Trends in Steroid Bioconversions

Recovery of Steroids

Split Process

Whole-beer Process

Cake-extraction Process

Products of Commercial Importance

Summary

RODUCTS FROM RECOMBINANT DNA

Production Technology

Methods for Cloning and Expression

Range and Relative Advantages of Host Microorganisms

Stability of Strains and Plasmids

Product Recovery and Purification

Commercial Markets

Markets for Recombinant Products