

Microbiology is the study of microorganisms such as bacteria, protozoa, fungi and similar organisms that can't be seen with the naked eye. The need to study these minute organisms started when scientists discovered the association of microbes to specific diseases. The roles of microbiology on the advances in the healthcare industry, especially in pharmaceutical and medical industry have led to great discoveries, from vaccines to devices. The growth of cosmetic industries also paralleled microbiological innovations, which in fact, paved the way to the study of cosmetic microbiology.

By nature, cells fight microbes that enter our body and this is commonly exhibited by pus formation and inflammation of wounds. Macrophages play an important role in immune system because they are capable of ingesting microbes that enter our body through open wounds. However, microbes could adapt and mutate rapidly, which results to opportunistic infectious diseases, such as HIV. On the contrary, microbes can also help us in ways like the way the "good bacteria" lactobacillus functions in our digestive system.

Understanding the principles of microbiology and human cell mechanisms allows pharmacists to discover antimicrobial drugs that would prevent an escalating number of communicable diseases. Pharmacists and microbiologists work synergistically to ensure that drug therapies target the opportunistic microbes without harming its human host. Another important role in pharmaceuticals is the use of microbes for the medically important studies, such as Bacteriorhodopsin, a protein from the plasma membrane of *Halobacterium salinarum*.

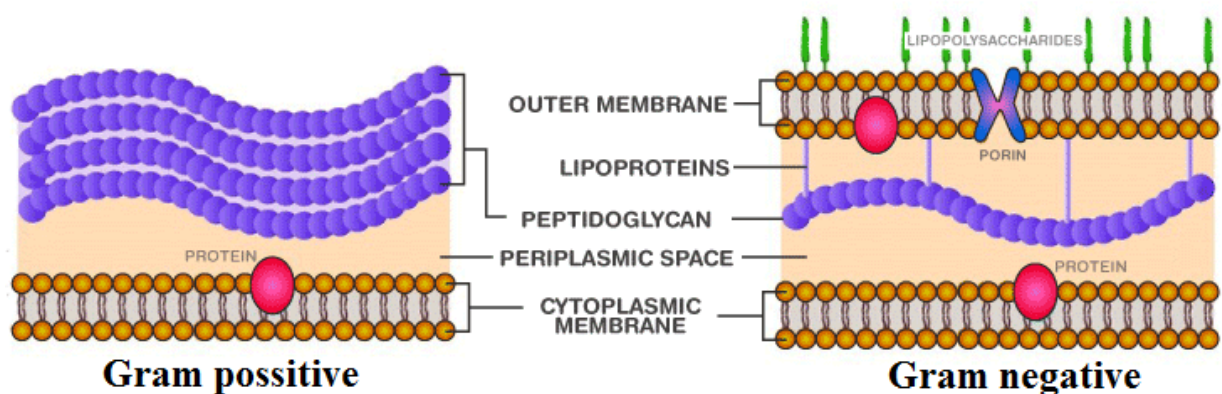
**Antibiotics-** Substance produced by a microorganism [or a similar product produced wholly (synthetic) or partially (semisynthetic) by chemical synthesis] that is capable, in low concentrations, of inhibiting the growth of or killing other microorganisms.

Or an antibacterial is an agent that inhibits bacterial growth or kills bacteria. The term is often used synonymously with the term *antibiotic(s)*. Today, however, with increased knowledge of the causative agents of various infectious diseases, *antibiotic(s)* has come to denote a broader range of antimicrobial compounds, including anti-fungal and other compounds.

The term *antibiotic* was first used in 1942 by Selman Waksman and his collaborators in journal articles to describe any substance produced by a microorganism that is antagonistic to the growth of other microorganisms in high dilution.

This definition excluded substances that kill bacteria, but are not produced by microorganisms (such as gastric juices and hydrogen peroxide). It also excluded synthetic antibacterial compounds such as the sulfonamides. Many antibacterial compounds are relatively small molecules with a molecular weight of less than 2000 atomic mass units. With advances in medicinal chemistry, most of today's antibacterials chemically are semisynthetic modifications of various natural compounds.[4] These include, for example, the beta-lactam antibacterials, which include the penicillins (produced by fungi in the genus *Penicillium*), the cephalosporins, and the carbapenems. Compounds that are still isolated from living organisms are the aminoglycosides, whereas other antibacterials for example, the sulfonamides, the quinolones, and the oxazolidinones—are produced solely by chemical synthesis. In accordance with this, many antibacterial compounds are classified on the basis of chemical/biosynthetic origin into natural, semisynthetic, and synthetic. Another classification system is based on biological activity; in this classification, antibacterials are divided into two broad groups according to their biological effect on microorganisms: bactericidal agents kill bacteria, and bacteriostatic agents slow down or stall bacterial growth.

**Gram positive and gram negative organisms** Gram staining is based on the ability of bacteria cell wall to retain crystal violet dye after common Gram-positive organisms: Common Gram-negative organisms: G during solvent treatment. The cell walls for Gram-positive microorganisms have a high peptidoglycan and lower lipid content than Gram-negative bacteria.



1. **Natural microbial production** using Fermentation technology. Example: Penicillin

2. **Semi synthetic production** (post production modification of natural antibiotics).

Example: Ampicillin

3. **Synthetic production** of antibiotics made synthetically in the lab. Example: Quinoline

### **Fermentation Technology**

The source microorganism is grown in large containers (100,000–150,000 liters or more) containing a liquid growth medium. Oxygen concentration, temperature, pH and nutrient levels must be optimum. As antibiotics are secondary metabolites, the population size must be controlled very carefully to ensure that maximum yield is obtained before the cells die.

#### **The fermentation process requires the following**

1. A pure culture of the chosen organism, in sufficient quantity.
2. Sterilized, carefully composed medium for growth of the organism
3. A seed fermenter, a mini-model of production fermenter to develop inoculums to initiate the process in the main fermenter.
4. A production fermenter, the functional large model and
5. Equipment for:
  - a) Drawing the culture medium in steady state
  - b) Cell separation
  - c) Collection of cell free supernatant
  - d) Product purification and
  - e) Effluent treatment.

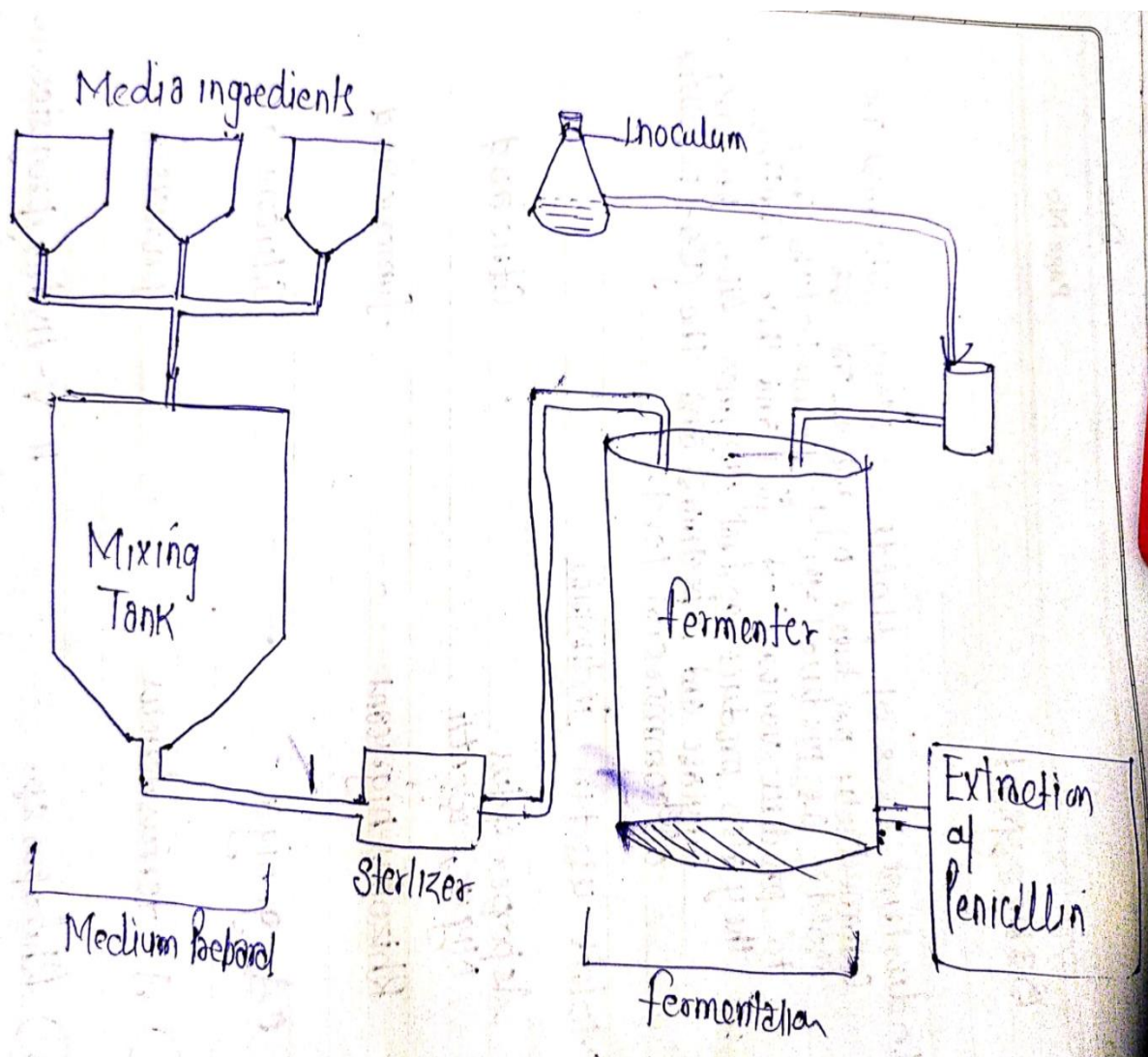
Step 1 to 3 constitutes the upstream and step 5 constitutes the downstream of the fermentation process.

#### **Strains used for production –**

1. Species are often genetically modified to yield for maximum amounts of antibiotics.
2. Mutation is often used -introducing mutagens such as ultraviolet radiation, x-rays Selection and further reproduction of the higher yielding strains can raise yields by 20-fold or more.
3. Another technique used to increase yields is gene amplification, where copies of genes coding for enzymes involved in the antibiotic production can be inserted back into a cell, via vectors such as plasmids.

#### **Raw material-**

- A. The compounds that make the fermentation broth are the primary raw materials required for antibiotic production.
- B. The broth is an aqueous solution made up of all of the ingredients necessary for the proliferation of the microorganisms.
- Typically, it contains; Carbon source: molasses, or soy meal, acetic acid, ♦ alcohols, or hydrocarbons • These materials are needed as a food source for the organisms.
  - Nitrogen Source : Nitrogen is another necessary compound in the metabolic cycles of the organisms. ammonia salt is typically used.
  - Other Elements Trace elements needed for proper growth of ♦ antibiotic producing microorganisms such as: phosphorus, sulfur, magnesium, zinc.
  - Anti foaming agents to prevent foaming during fermentation such as lard oil.



**Isolation & Purification-** After 3-5days, the maximum amount of antibiotic will have been produced. The isolation process can begin. The isolation depend on the specific antibiotic produced, the fermentation broth is processed by various purification methods.

- A. **Water soluble antibiotics** Antibiotic compounds that are water soluble, an ion-exchange method is used for purification. The compound is first separated from the waste organic materials in the broth. Then sent through equipment, which separates the other water-soluble compounds from the desired one.
- B. **Oil soluble antibiotics** - Solvent extraction method is used for the isolation of oil soluble or organic antibiotics. The broth is treated with organic solvents such as butyl acetate or methyl isobutyl ketone, which can dissolve the antibiotic. The dissolved antibiotic is then recovered using various organic chemical means. At the end of this step a purified powdered form of the antibiotic is obtained which can be further refined into different product types.
- C. **Refining/Packaging-** Antibiotic products can take on many different forms. They can be sold in solutions for intravenous bags or syringes, in pill or gel capsule form, or powders, which are incorporated into topical ointments.

Various refining steps may be taken after the initial isolation.

For intravenous bags, the crystalline antibiotic can be dissolved in a solution, put in the bag, which is then hermetically sealed. •

For gel capsules, the powdered antibiotic is physically filled into the bottom half of a capsule then the top half is mechanically put in place.

When used in topical ointments, the antibiotic is mixed into the ointment