

# Unit 5

# PHARMACEUTICAL INDUSTRIES

**By**

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- Any substance or pharmaceutical product for human or veterinary use that is intended to modify or explore physiological systems or pathological states for the benefit of the recipient is termed as drug (WHO).
- The terms drug, medicine and pharmaceutical product are commonly used interchangeably.
- An Active Pharmaceutical Ingredient (API) is the chemical substance contained in a pharmaceutical, which is responsible for its therapeutic effect. Some pharmaceuticals contain more than one active ingredient (combination product).

# Classification of Drugs

- **Based on Pharmacological Effects**
- Pharmacology is the field of science that focuses on the study of drugs and their reactions in the human body.
- A drug creates a pharmacological effect, i.e. the effects of a drug on the human body. This effect will cure what is ailing the body and have a positive biological response.
- So they are classified on the basis of what kind of effect they have in the body. For example,
- **Analgesics relieve the body from pain**
- **An antibiotic drug will cure infections**
- **Antiseptics will kill germs and microorganisms**

- **Based on Drug Action**
- drugs will be classified according to their targets.
- For example **antihistamines** are taken to stop the production of histamines so that swellings and allergies can be controlled.

# Antibiotics

- help stop bacteria-caused infections. By destroying the bacteria or preventing them from cloning themselves or reproducing
- A chemical material produced by a living organism, normally a microorganism, which is harmful to other microorganisms.
- Antibiotics are further classified according to susceptible bacteria against which they are effective or their antibacterial spectrum.

# Classification of Antibiotics

- **Penicillin:**
- Penicillin V is an antibiotic in the penicillin group of drugs which helps to fight bacteria in the body system. Penicillin is used to treat many types of infections caused by bacteria an example of which is an ear infection.
- During the stage of active replication, penicillin G is bactericidal against microorganisms prone to penicillin.
- It works by inhibiting cell-wall mucopeptide biosynthesis.
- Common antibiotics in the penicillin class include:
  - **amoxicillin**
  - **Ampicillin**
  - **oxacillin**

- **Streptomycin:**

- Used to treat the symptoms of moderate-to-severe infections such as Tuberculosis. Streptomycin may be used alone or with other medications.
- Streptomycin belongs to a class of drugs called Aminoglycosides.

## ● Tetracycline

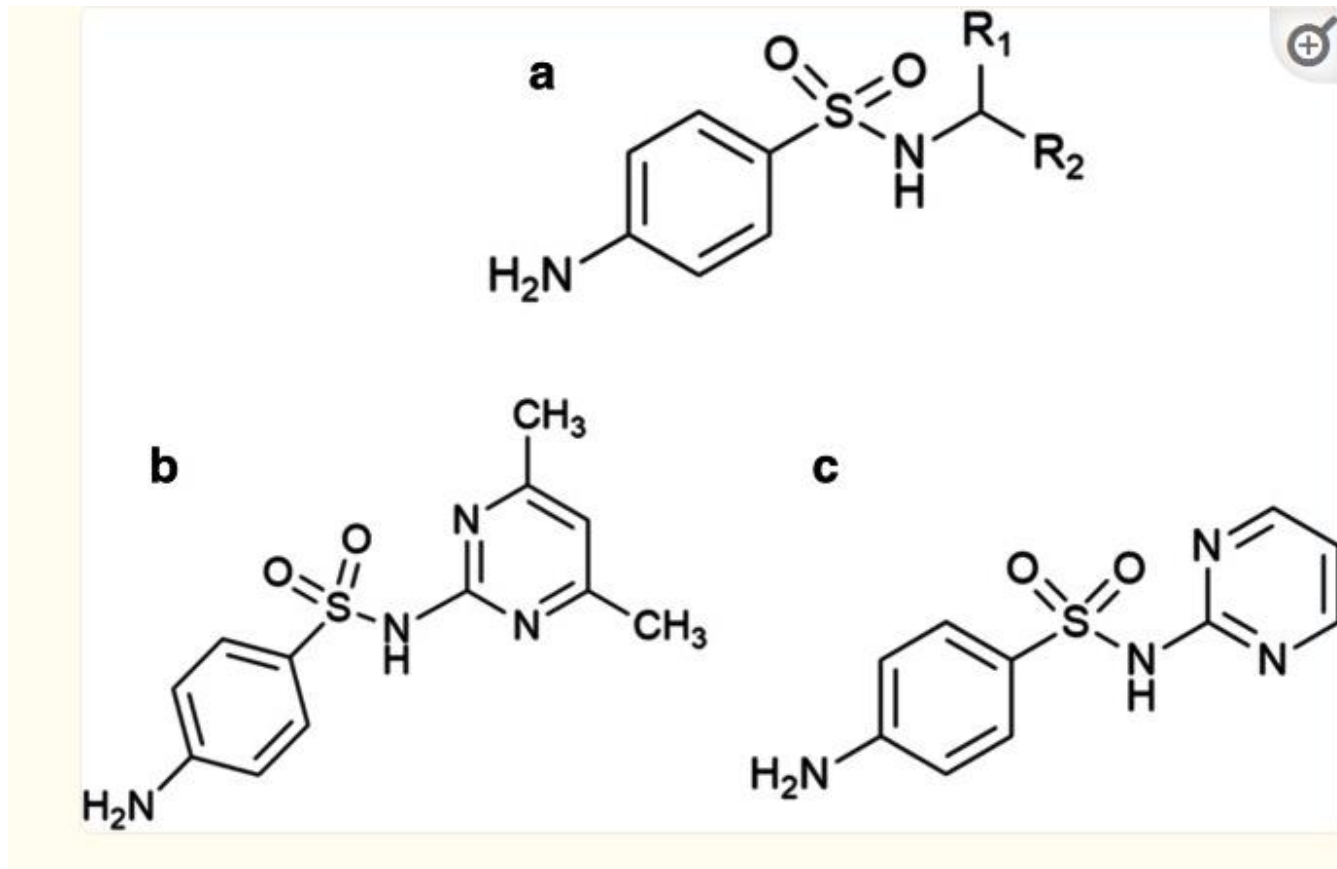
- Tetracycline is used to treat infections caused by bacteria including pneumonia and other respiratory tract infections
- infections of skin, eye, lymphatic, intestinal, genital and urinary systems
- and certain other infections that are spread by lice, mites, and infected animals. It is also used along with other medications to treat acne.



# Synthetic Drugs:

- **Synthetic drugs** refer to substances that are artificially modified from naturally-occurring drugs and are capable of exhibiting both therapeutic and psychoactive effects.
- Examples:
  - Sulfa drugs
  - Anti TB drugs
  - Antileprotic drug
  - Analgesics
  - Anesthetics
  - Gastrointestinal drugs

- **Sulfa drugs:**
- Sulfonamides (SN) or sulfanilamides belong to an important class of synthetic antimicrobial drugs that are pharmacologically used as broad spectrum for the treatment of human and animal bacterial infections
- The typical structure of a SN involves a **central sulfur atom**, with **two doubly bonded oxygen**, that is also **bonded to a nitrogen atom** (existing as a substituted amine) and **an aniline group**



- **a**. sulfonamide (SN), **b** sulfamethazine (SMZ), and **c** sulfadiazine (SDZ)

- **Anti TB drugs**
- Antitubercular medications: rifampin, isoniazid, pyrazinamide, and ethambutol are FDA approved to treat Mycobacterium tuberculosis infections.
- **Antileprotic drug:**
- A **leprostatic agent** is a drug that interferes with proliferation of the bacterium that causes leprosy
- **leprostatic agents:**<sup>[3]</sup>
  - acedapsone
  - clofazimine
  - dapsone

- **Anesthetic**, also spelled **anaesthetic**, any agent that produces a local or general loss of sensation, including pain.
- Anesthetics achieve this effect by acting on the brain or peripheral nervous system to suppress responses to sensory stimulation. The unresponsive state thus induced is known as anesthesia.
- General anesthesia involves loss of consciousness, usually for the purpose of relieving the pain of surgery.
  - **Desflurane (common)**
  - **Halothane (inexpensive)**
  - **Isoflurane (common), Methoxyflurane, Nitrous oxide.**

## ● Analgesics

- Analgesics are medications that relieve pain inflammation.
- For example:
  - After surgery.
  - Due to injury, such as a fractured bone.
  - For acute (sudden, short-term) pain, such as a twisted ankle or headache
  - For aches and pains like menstrual cramps or muscle soreness.
  - For chronic painful conditions such as cancer or back pain.

## ● Acetaminophen

## ● Aspirin

- Nonsteroidal anti-inflammatory drugs(NSAIDs), such as ibuprofen and naproxen.

- **Vitamins:**

- Vitamins are substances that are required in very small amounts, for healthy growth and development.
- They occur naturally in certain foods but are not synthesized by humans and therefore it is essential to include it in the diet.
- Vitamins are either water soluble or fat soluble. Inadequate intake of any particular vitamin in the diet causes specific vitamin deficiency disease.
- Vitamin supplements are taken to correct inadequate intake in diet and to treat the deficiency.

- **Synthetic hormones**
- Bioidentical hormones are **artificial hormones that are similar to the hormones produced by the human body**. They are used as treatment for people whose own hormones are low or unbalanced.
- **Glucocorticoids**: alclometasone, prednisone, dexamethasone, triamcinolone
- **Mineralocorticoid**: fludrocortisone
- **Vitamin D**: dihydrotachysterol
- **Androgens**: apoptone, oxandrolone, oxabolone, testosterone, nandrolone (also known as anabolic steroids)
- **Oestrogens**: diethylstilbestrol (DES)
- Progestins



- Drugs of vegetable origin:

1. Quinine : antimalarial drug
2. Strychnine and brucine
3. Emetine
4. Digitalis glycosides: cardiac drug

# Vaccines

- A **vaccine** is a biological preparation that provides active acquired immunity to a particular infectious or disease
  - Diphtheria antitoxin
  - Polio oral vaccine
  - Insulin
  - Covaccin

# Penicillin Production Process

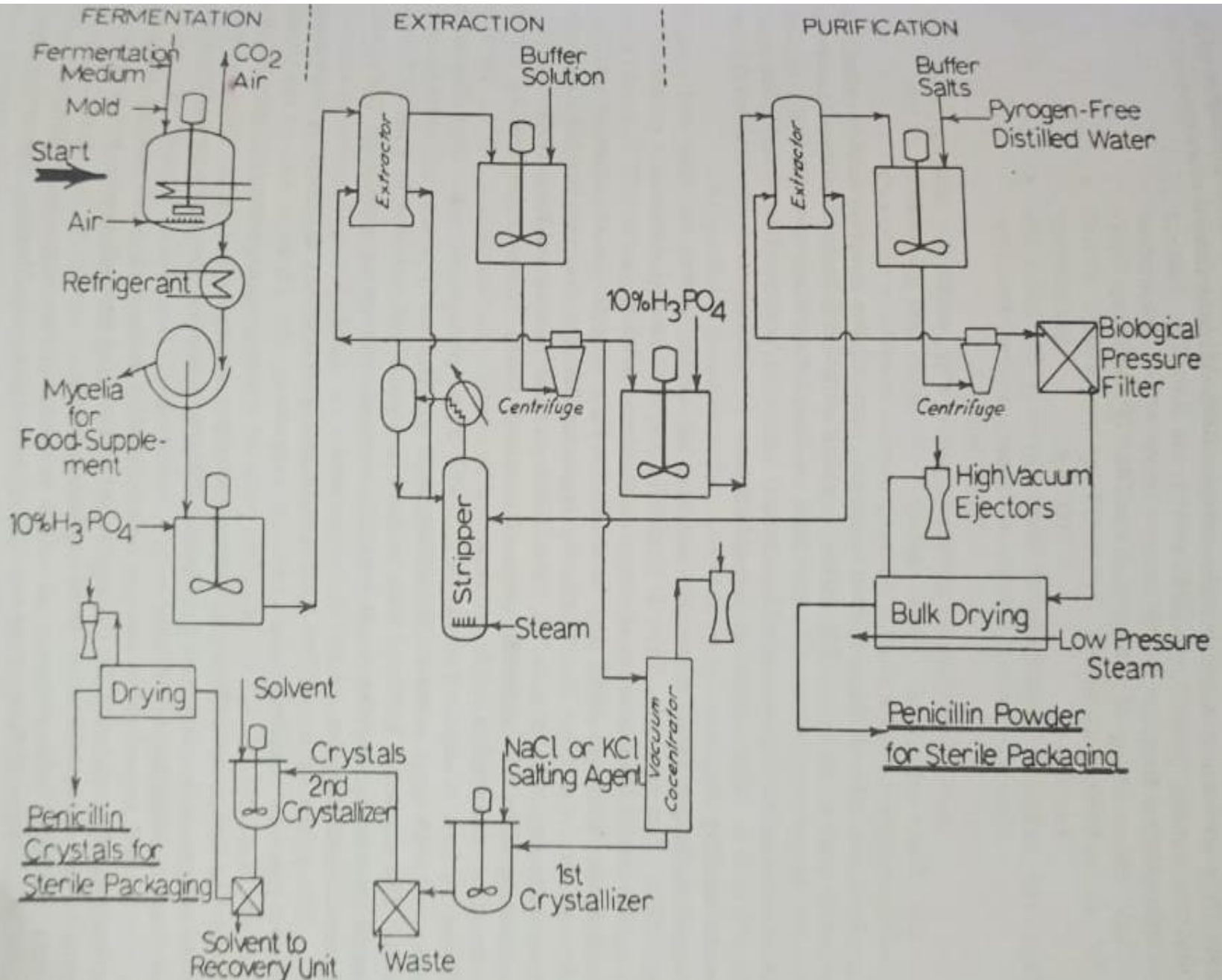
- The processes which are required to produce penicillin is generally microbial processes as this antibiotics are microbial.
- *Penicillium notatum* hindered and stopped the basic growth of infectious bacteria, *Staphylococcus aureus*.
- **Penicillin is produced by the process of fermentation.**

- **Quantitative requirement:**
- Basis: 1 kg of penicillin
  - Broth : 135 kg
  - Lactose : 100 kg
  - Calcium Carbonate: 35 kg
  - Process Water: 3 tones
  - Air: 7000 Nm<sup>3</sup>
  - Small quantities of nutrients, precursors, mold
- **Plant capacities:** 10-50 kg/day

# Process Description

- An aerobic batch fermentation is carried out.
- Maize steep liquor or similar base is diluted with water to a 4-5% solids, fortified with 4-5% lactose solids and nutrients such as magnesium, zinc and/or sodium sulfate, ammonium acetate, and potassium dihydrogen sulfate in amount of less than 0.2%.
- Calcium carbonate is added to adjust the pH to 5-6.
- The various types and amount of nutrients and alkali added depends on the starting liquor.

- Organic precursor chemicals are also added to control the type and yield of penicillin. For example, Type II Penicillin requires phenyl acetic acid precursor
- The batch fermentation medium is sterilized with steam at 115°C for 1/2 hour, cooled with water to 25°C and inoculated with a specific mold culture, *Penicillium chrysogenum* for Type II.
- Sterile air is blown through the tank for 4-5 days under temperature control of  $\pm 1/2^\circ\text{C}$ .
- Penicillin yield is maximized by periodic assay.



- Separation of penicillin from fermented broth is accomplished by solvent extraction.
- Suspended solids are removed by continuous filtration at 1-2 C.
- The clear filtrate or beer is adjusted to pH of 2.5 with dilute phosphoric acid,
- Penicillin salt is extracted with amyl acetate.
- The raffinate or water phase is sent to a solvent recovery still.
- The extract is buffered with sodium phosphate salt solution in a continuous mixer and the crude penicillin returns to the aqueous phase. The mixture is centrifuged and the solvent is recirculated.



- The penicillin is purified by a second acidic extraction, followed by reversion to a pyrogen-free distilled water solution containing the alkaline salt of the desired elements, i.e., Na, K, Ca or Al.
- The purified aqueous concentrate is separated from solvent in a super centrifuge and then pressurized through a biological filter to remove final traces of bacteria and pyrogens.
- This solution can be concentrated by freeze drying or vacuum spray drying.

- crystalline penicillin salts can be obtained by salting out a saturated solution with a neutral salt containing the cation desired in the final penicillin salt.
- It can be further purified by recrystallization from organic solvents.
- The oil-soluble procaine penicillin is made by reacting a penicillin concentrate (20-30%) with a 50% aqueous solution of procaine hydrochloride.
- procaine penicillin crystallizes from this mixture.

- Major Engineering Problems:

- Design of 100-200 m<sup>3</sup> fermenters to provide uniform and efficient air-liquid contact.
- Sterile operations
- Recovery of penicillin—solvent extraction method has replaced original activated carbon adsorption-elution procedure