Production of Griseofulvin

Introduction

- **Griseofulvin** is a natural **antifungal antibiotic** produced by certain species of *Penicillium*.
- It was **first discovered in 1939**, but its therapeutic use was established in the 1950s.
- **Mode of action**: Griseofulvin interferes with **fungal mitosis** by binding to **tubulin** and disrupting microtubule function.
- It is used to treat **dermatophytic fungal infections** (skin, hair, nails), such as **ringworm, athlete's foot, jock itch**.

Microorganisms Used

- Main producers:
  - *Penicillium griseofulvum*
  - *Penicillium patulum* (syn. *P. urticae*)
- Mutant and improved strains are used for **higher yield**.

Raw Materials (Fermentation Media)

- **Carbon sources**: Glucose, starch, sucrose, glycerol.
- **Nitrogen sources**: Corn steep liquor, peptone, ammonium salts, soybean meal.
- **Inorganic salts**: Potassium, phosphates, magnesium, sulfates.
- **Precursors**: Some fatty acids and organic acids can enhance production.

Fermentation Process

1. Inoculum Preparation

- Pure culture of *Penicillium griseofulvum* grown on agar slants.
- Transferred to seed medium → seed tanks → production fermenters.

2. Production Fermentation

- Method: **Submerged fermentation** (large-scale).
- Conditions:
  - Temperature: 25–28°C
  - pH: 6.0–7.0
  - Aeration: Moderate (oxygen required)
  - Duration: 5–7 days
- Some processes use **surface fermentation** (older method, less common today).
- During fermentation, the fungus secretes **griseofulvin into the broth**.

Recovery and Purification

1. **Filtration** – fungal mycelium separated from broth.
2. **Extraction** – griseofulvin extracted with organic solvents (e.g., chloroform, butanol).
3. **Concentration** – solvent evaporated under vacuum.
4. **Purification** – recrystallization, chromatography.
5. **Final product** – purified griseofulvin as crystalline powder.

Flowchart – Industrial Production of Griseofulvin

Penicillium griseofulvum (strain)
↓
Inoculum preparation
↓
Fermentation (submerged, 25–28°C, 5–7 days)
↓
Griseofulvin secreted into broth
↓
Filtration (remove mycelium)
↓
Solvent extraction
↓
Concentration & purification
↓
Crystallization
↓
Griseofulvin (pure antibiotic)

Applications of Griseofulvin

1. **Medical Applications**
   - Used against **dermatophytes** (fungi infecting skin, hair, nails).
   - Treats **ringworm (tinea corporis), athlete's foot (tinea pedis), jock itch (tinea cruris), and onychomycosis (nail infection)**.
   - Not effective against **systemic fungal infections** (e.g., Candida, Aspergillus).
2. **Veterinary Applications**
   - Used in animals for treatment of fungal infections of skin and hair.
3. **Research Use**
   - Used in cell biology studies as a **mitotic inhibitor** (blocks spindle formation).

Advantages of Microbial Production

- Economical and large-scale feasible.
- Uses simple, cheap substrates.
- Fermentation process well-optimized.
- High demand in medicine ensures industrial importance.

Conclusion

- **Griseofulvin** is an important **antifungal antibiotic** obtained from **Penicillium species**.
- Produced mainly by **submerged fermentation**, followed by extraction and purification.

- It plays a vital role in the treatment of **superficial fungal infections** of skin, hair, and nails.
- Industrial microbiology has made it possible to supply griseofulvin worldwide for both **medical and veterinary applications**.