Antifungal agents
Systemic & Topical

By: Assist. Prof. Dr. Nawar Alsalih

Antifungal drugs & site of action

SITE OF ACTION	DRUGS
Cell membrane	
Ergosterol binding	Amphotericin B, Natamycin and Nystatin
Ergosterole synthesis inhibitors (Squalene epoxidase inhibitor)	Allylamines (Amorolfine, Terbinafine etc.)
Ergosterol synthesis inhibitors (lanosterol to ergosterol)	Azoles (Ketoconazole, Miconazole etc.)
Cell wall	
β glucan synthase inhibitor	Echinocandins
Intracelluler	
Pyrimidine analogue	Flucytosine
Mitotic inhibitors	Gresiofulvin
Other site	Benzoic acid , salicylic acid, tolnaftate, castor oil etc.

Antifungal Agents

- **Polyene antibiotic**
- The polyene antibiotics bind with sterols in the fungal cell membrane, principally ergosterol. This causes the cell's contents to leak out and the cell dies. Animal cells contain cholesterol instead of ergosterol and so they are much less susceptible.
  - Nystatin
  - Amphotericin B (may be administered liposomally)
  - Natamycin
  - Rimocidin
  - Filipin
  - Pimaricin

Amphotericin B

- **Source –Streptomycesnodosus**
- **Mechanism of action –Increases permeability of cell membrane by binding to ergosterol**
- **Antimicrobial spectrum –broad spectrum**
- **Resistance –when less ergosterolin membrane**
- **Pharmacokinetics –poorly absorbed from GIT, do not cross BBB**
- **Adverse effects -Nephrotoxicity**
- **Drug interaction –**
- **1. with miconazoleantagonistic effect**
- **2. with flucytosinesynergistic effect**

Nystatin: The first antibiotic against fungi

- **Like many other antimycotics and antibiotics, nystatin is of bacterial origin. It was isolated from *Streptomyces noursei* in 1950 by Elizabeth Lee Hazen and Rachel Fuller Brown.**
- **Source :**
- **Streptomyces noursie**
- **Streptomyces aureus**
- **Mechanism of action –**
- **It binds toergosteoland forms pores in cell membrane**

Antifungal Agents

- **Imidazole and triazole**
- The imidazole and triazole groups of antifungal drugs inhibit the enzyme cytochrome P450 14α-demethylase. This enzyme converts lanosterol to ergosterol, and is required in fungal cell membrane synthesis. These drugs also block steroid synthesis in humans.
- **Imidazoles:**
  - Miconazole
  - Ketoconazole
  - Clotrimazole
  - Mebendazole
  - Isoconazole
  - Sertaconazole
  - Thiabendazole
  - Bifonazole
  - Butoconazole
  - Econazole
  - Fenticonazole
  - Oxiconazole
  - Sulconazole
  - Tiaconazole

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- The triazoles are newer, and are less toxic and more effective:
  - Fluconazole
  - Itraconazole
  - Ravuconazole
  - Posaconazole
  - Voriconazole

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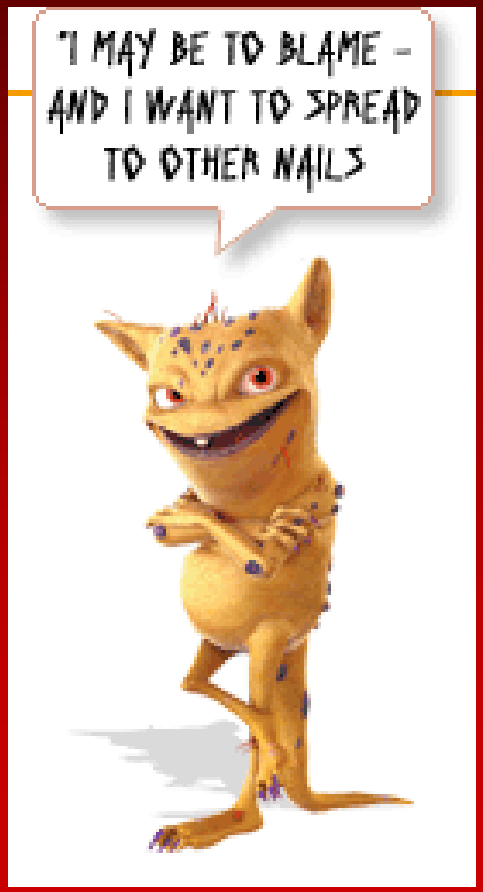
- **Allylamines**
- Allylamines inhibit the enzyme squalene epoxidase, another enzyme required for ergosterol synthesis:
- **Terbinafine - marketed as Lamisil**
- **Amorolfine**
- **Naftifine**
- **Butenafine**



Antifungal Agents

- **Echinocandin**
- Echinocandins inhibit the synthesis of glucan in the cell wall, probably via the enzyme 1,3-β glucan synthase:
  - **Anidulafungin**
  - **Caspofungin**
  - **Micafungin**

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Flucytosine

- Mechanism of action
- 1. It is converted to 5 furouracilwhich inhibit thymidylatesynthetase enzyme
- 2. It inhibits transcription as 5FUTP(5 flurouracilribose triphosphate)is an antimetabolite.

Griseofulvin

- Source –Penicillium griseofulvinum
- Mechanism of action –inhibit mitosis by interfering spindle fiber formation
- Antimicrobial spectrum
- Resistance –due to reduced drug uptake
- Pharmacokinetics –low water solubility, bind with keratin layer
- Adverse effects –in cat leucopenia, neurotoxicosisand increased hepatic enzyme activity, avoid in pregnant animals

Others

- Fluocinonide
- Tinactin or Tolnaftate
- Potassium Iodide
- In combination of benzoic acid and Salicylic Acid are used as antifungal ointment known as “Whitfield’s ointment”

Thank you