Antimycotic or Antifungals

Antimycotic, or antifungal, drugs are used to treat fungal infections.

The major antifungal drug groups include:

- polyen
- Azoles and Triazole Antifungal Agents(Ergosterol Biosynthesis Inhibitors
- glucan synthesis inhibitors
- synthetic allylamine derivatives.
- Others like Flucytosine

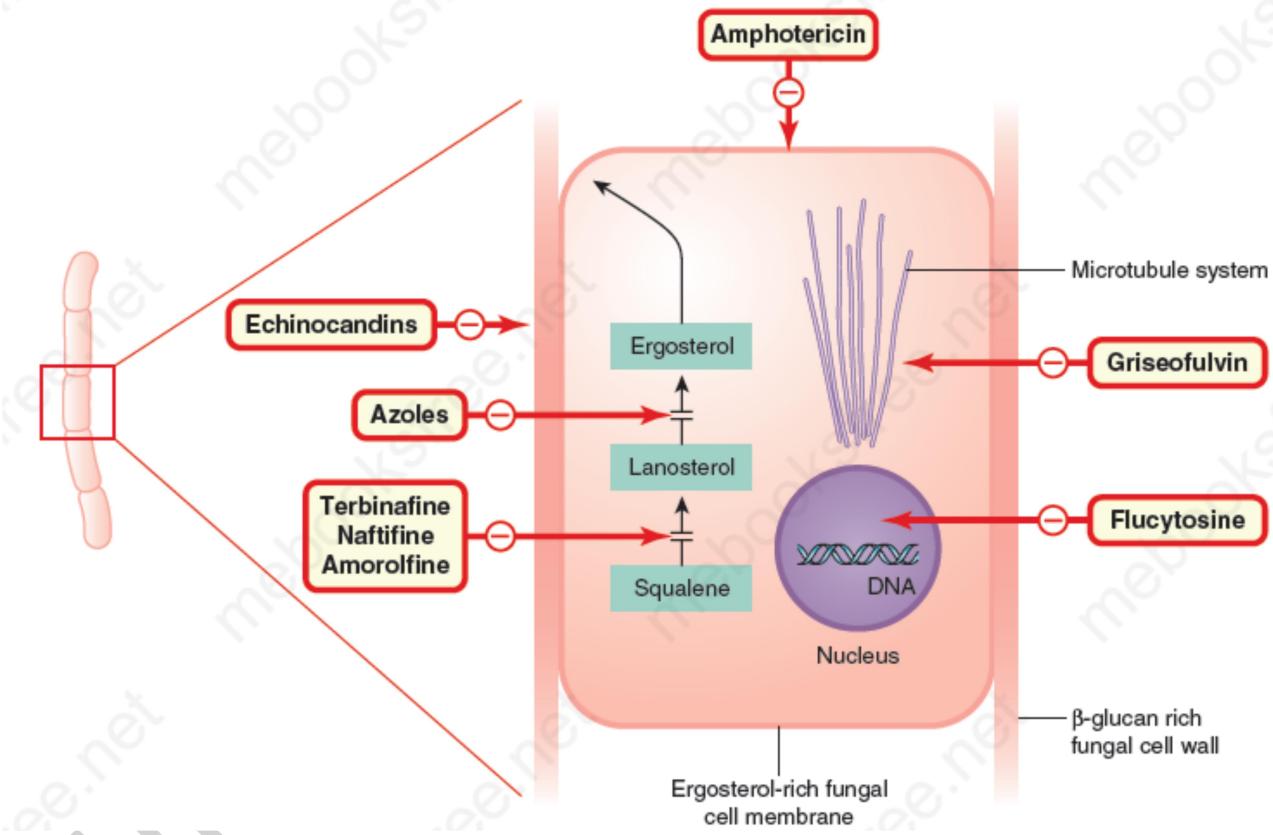


Fig. : Sites of action of common antifungal drugs.

Mechanisms of action of the antifungal agents

There are three general mechanisms of action for the antifungal agents:

- cell membrane disruption
- inhibition of cell division
- inhibition of cell wall formation.

1.The polyenes

The polyenes include **amphotericin B** and **nystatin**.

Amphotericin B potency has made it the most widely used antimycotic drug for severe systemic fungal infections. Amphotericin B, causes cell death by binding to by binding to sterol (a lipid) in the fungal cell membrane, altering cell permeability and allowing intracellular components to leak out. Because amphotericin B is highly toxic, its use is limited to the patient who has a definitive diagnosis of life-threatening infection and is under close medical supervision.

NOTE: 1. Magnesium and potassium levels and kidney function must be monitored frequently in patients receiving amphotericin.

2.The risk of kidney toxicity increases when amphotericin B is taken with aminoglycosides, cyclosporine, or acyclovir.

Nystatin,

Nystatin (also called fungicidin) is a polyene macrolide antibiotic similar in structure to amphotericin and with the same mechanism of action. It is given orally, but is not absorbed through mucous membranes or skin, and its use is mainly limited to Candida infections of the skin, mucous membranes and the GI tract. Unwanted effects may include nausea, vomiting and diarrhoea.

2. Azoles and Triazole Antifungal Agents(Ergosterol Biosynthesis Inhibitors):

The azoles inhibit synthesis of ergosterol, a key constituent of the fungal cell membrane.

- **Miconazole, econazole, clotrimazole and ketoconazole** are relatively toxic and therefore mainly administered topically.
- **Ketoconazole** may be given orally, but causes hepatitis in ~1:15000 cases

- **Triazoles** are preferred for systemic administration because of their reduced toxicity.
- **Fluconazole** is effective against yeasts only (Candida and Cryptococcus spp.).
- **Itraconazole** is lipophilic and distributes extensively, including to toenails and fingernails. Oral absorption is erratic and formulation-dependent, which necessitates monitoring of blood levels.

3.Synthetic allylamine derivatives

The allylamines have a more limited spectrum of activity than the azoles and triazoles and are only effective against dermatophytes. They are employed in the treatment of fungal infections of the skin and nails. Terbinafine, the most commonly used synthetic allylamine derivative

Mechanism of Action: These antifungal agents are reversible, noncompetitive inhibitors of the first step in ergosterol biosynthesis, the conversion of squalene to squalene-2,3- epoxide by squalene epoxidase. The buildup of squalene in the cell membrane is toxic to the cell, causing pH imbalances and malfunction of membrane bound proteins.

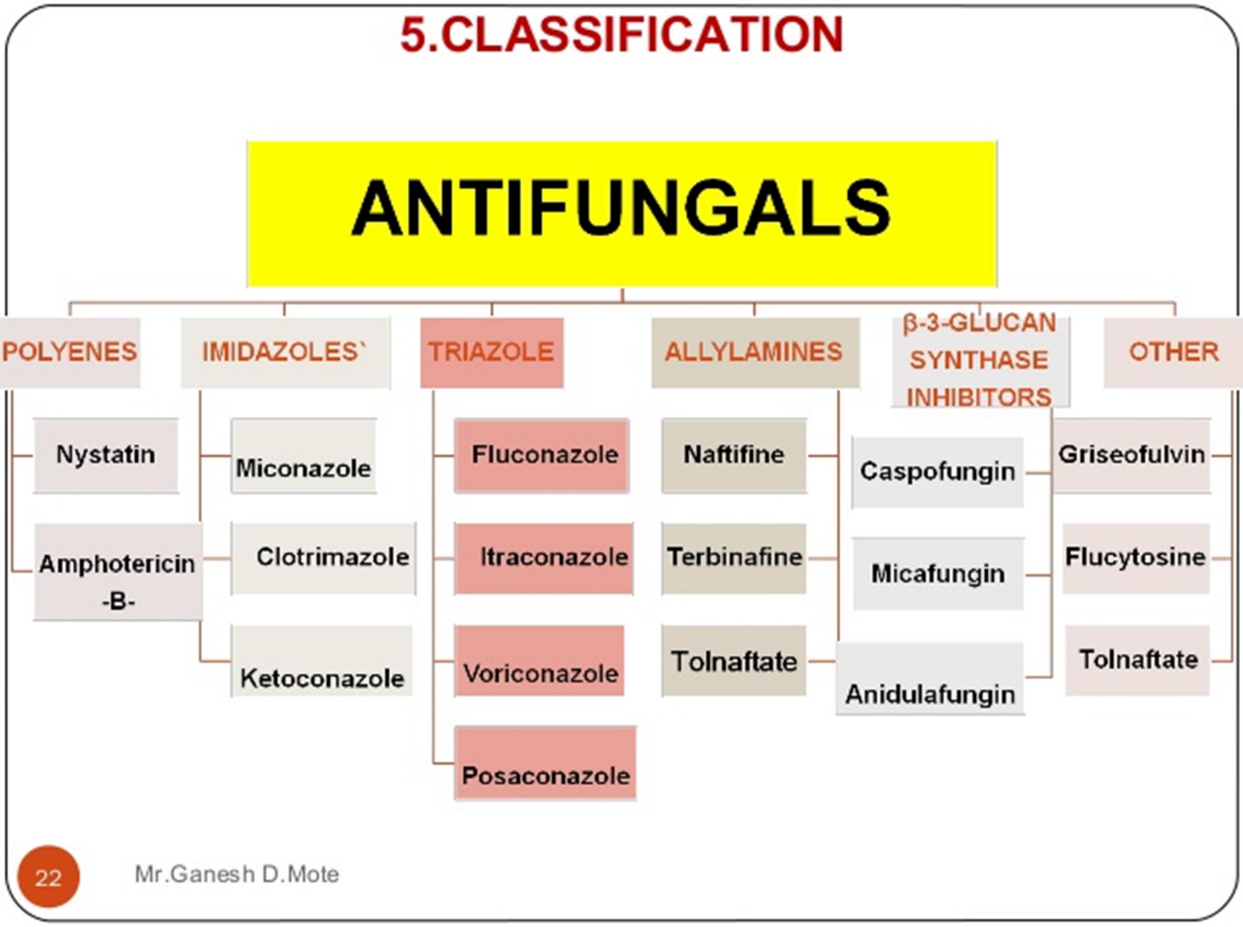
4.Glucan synthesis inhibitors

Caspofungin is a drug in a new class of agents known as glucan synthesis inhibitors (also called echinocandins). Its major use is in the patient who hasn't responded to other antifungal therapies, such as amphotericin B or itraconazole.

Caspofungin inhibits the synthesis of beta (1,3) D-glucan, an integral component of the fungal cell wall.

5.Flucytosine

Flucytosine is the only antimetabolite (a substance that closely resembles one required for normal physiologic functioning and that exerts its effect by interfering with metabolism) that acts as an antimycotic. It's a purine and pyrimidine inhibitor that's used primarily with another antimycotic drug, such as amphotericin B, to treat systemic fungal infections.


5.CLASSIFICATION
ANTIFUNGALS
POLYENES
IMIDAZOLES`
TRIAZOLE
ALLYLAMINES
β-3-GLUCAN SYNTHASE INHIBITORS
OTHER
Nystatin
Amphotericin -B-
Miconazole
Clotrimazole
Ketoconazole
Fluconazole
Itraconazole
Voriconazole
Posaconazole
Naftifine
Terbinafine
Tolnaftate
Caspofungin
Micafungin
Anidulafungin
Griseofulvin
Flucytosine
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