PHARM.D • YEAR 3

Medicinal Chemistry

CHAPTER 2.3

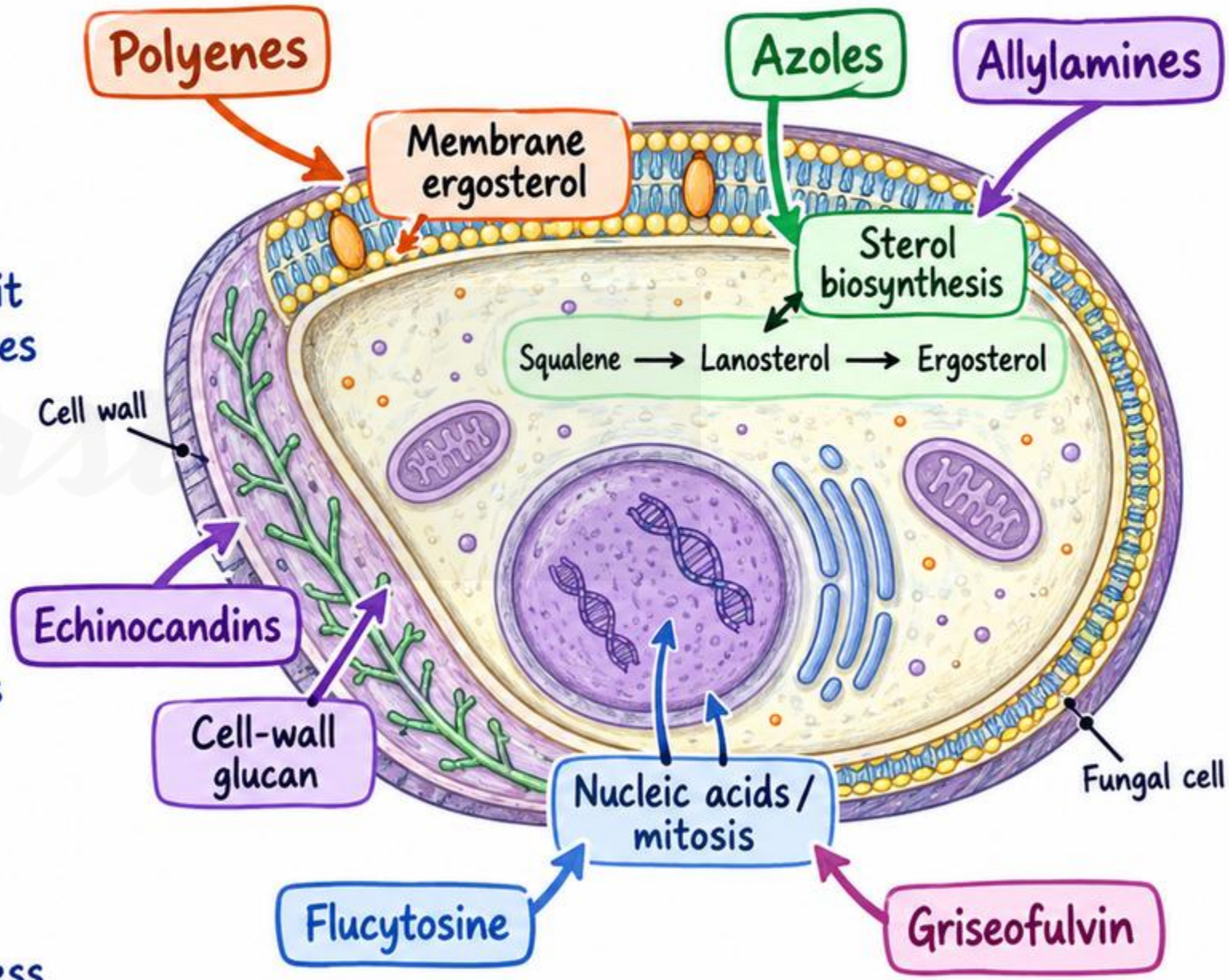
Antifungal Agents



PPT CHAPTER COVER

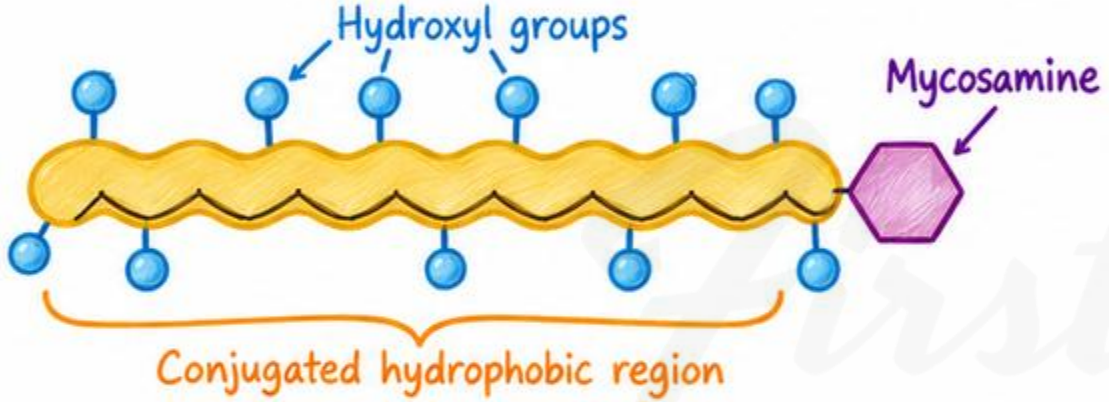
Antifungal targets and classification

- Fungal selectivity exploits targets that differ from human cells: ergosterol, the fungal cell wall and particular metabolic pathways.
- Polyenes bind ergosterol; azoles inhibit lanosterol 14α-demethylase. Allylamines inhibit squalene epoxidase, an earlier sterol-biosynthesis step.
- Echinocandins inhibit β-1,3-glucan synthesis. Flucytosine interferes with nucleic-acid synthesis after fungal activation, while griseofulvin interferes with mitosis.
- Classification by target differs from classification by chemical family. Spectrum, infection site, dosage form and toxicity determine clinical usefulness.

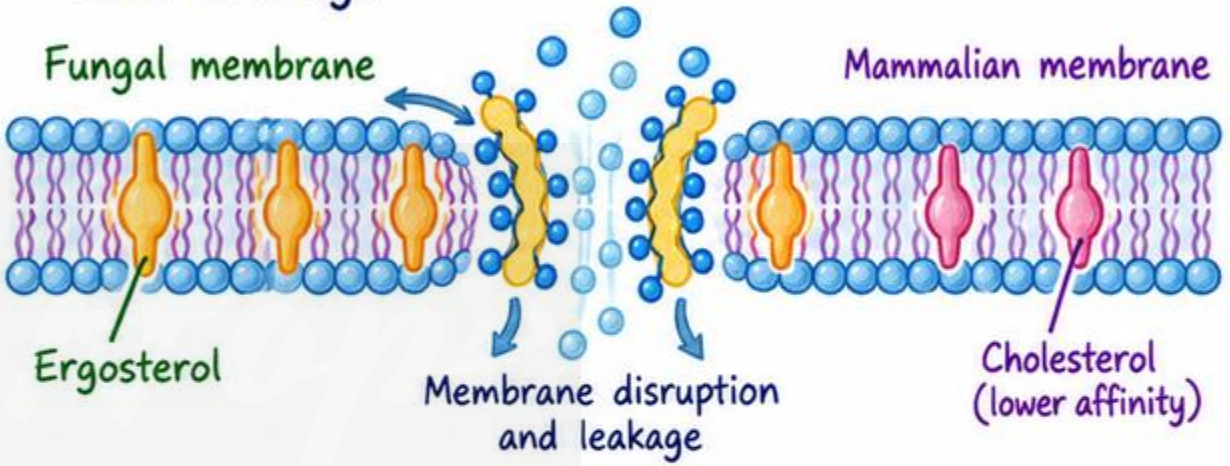


Polyenes: amphotericin B

- Amphotericin B is a large polyene macrolide with a conjugated hydrophobic region, multiple hydroxyl groups and the amino sugar mycosamine.



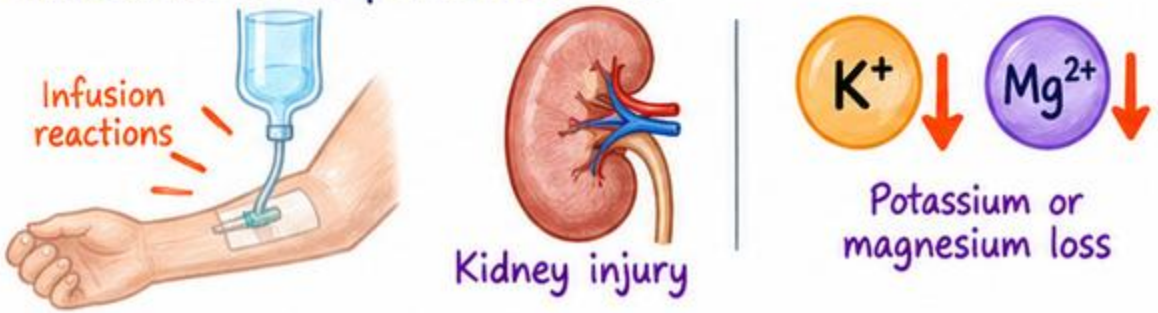
- It binds fungal ergosterol and disrupts membrane function. Its affinity for sterols explains both antifungal activity and important host toxicity.



- It is used for selected serious fungal infections. Formulation changes, including lipid-based preparations, alter disposition and tolerability.



- Infusion reactions, kidney injury and potassium or magnesium loss require attention. Lipid formulations are not simply interchangeable dose-for-dose with conventional amphotericin B.

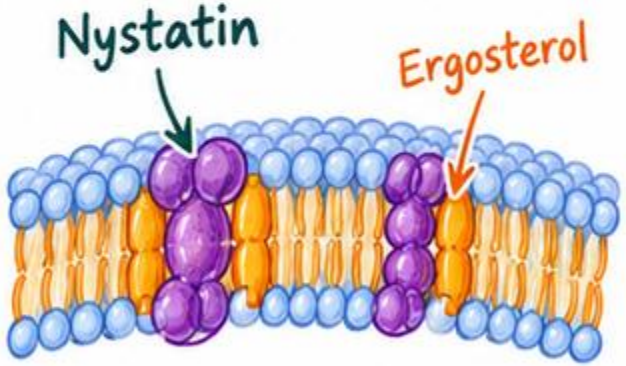


Nystatin and natamycin

Nystatin and natamycin are polyene antifungal antibiotics, but their indications and formulations differ.

Nystatin

Nystatin acts by ergosterol-associated membrane disruption and is used locally for susceptible Candida infections. Poor gastrointestinal absorption supports local intestinal action rather than systemic treatment.



Fungal cell membrane



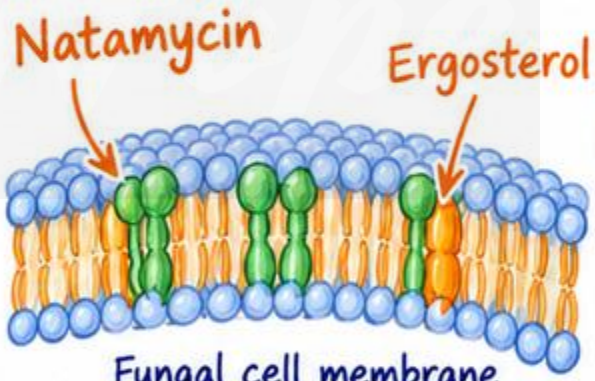
Local use for Candida infections



Poor gastrointestinal absorption supports local intestinal action rather than systemic treatment.

Natamycin

Natamycin binds ergosterol and disrupts important membrane-associated functions. Its effects should not be reduced to universal pore formation.



Fungal cell membrane

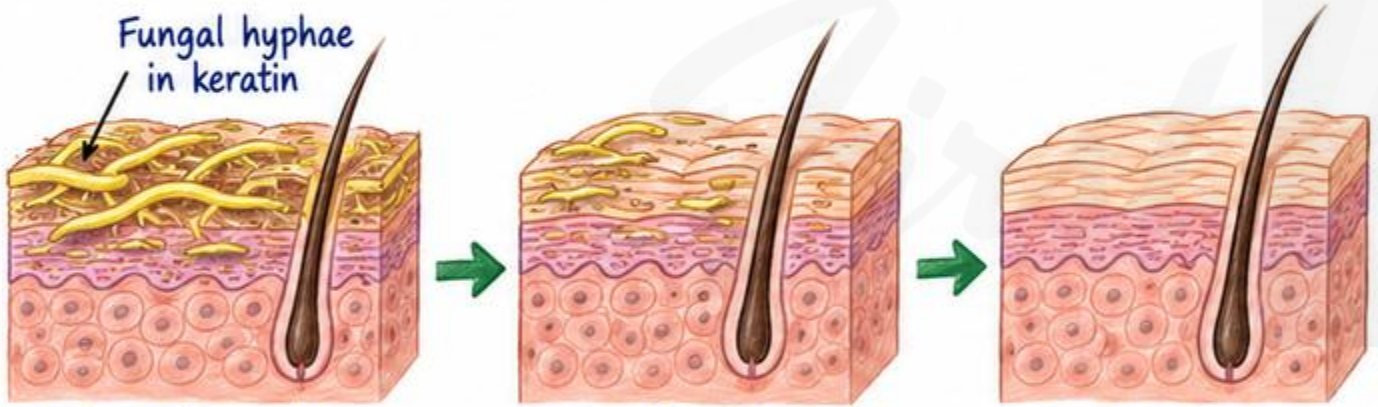


Natamycin ophthalmic preparations are used for appropriate fungal keratitis. A topical polyene is not a substitute for systemic therapy when the infection is deep or disseminated.

Griseofulvin

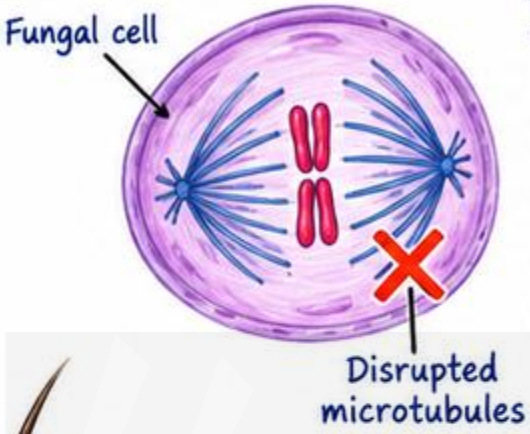
Chemistry

Griseofulvin is a chlorinated, methoxylated spirocyclic antifungal antibiotic. Its chemistry is distinct from polyenes and azoles.



Tissue response

Growth of uninfected keratin gradually replaces affected tissue; treatment duration therefore depends on the site.



Action

It interferes with fungal microtubules and mitosis and becomes associated with newly formed keratin. Its principal activity is against dermatophytes rather than *Candida*.

Absorption

Absorption is influenced by formulation and food.



Cautions

Hepatic effects, photosensitivity and enzyme-inducing interactions are important cautions. It is not a general treatment for every fungal skin or nail disorder.



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