ANTI-FUNGAL

1. Drugs That Target the Fungal Cell Membrane

Drug Class	Drugs	Mechanism of Action	Indications	Pharmacokinetics/Notes	Side Effects/Adverse Effects
Terbinafine	**Terbinafine** (superficial/systemic)	Inhibits **squalene epoxidase**, **preventing ergosterol synthesis (fungicidal).**	**Systemic (oral**) and **topical for dermatophytes** (more effective than griseofulvin). takes **3 months** to finish the course.	• Oral active (**40%** bioavailability); due to 1st pass metabolism • 99% bound to plasma protein • deposited in **nails, skin, fats and milk** so contraindicated in pregnancy. • half-life **200–400** hours. • Metabolized in **liver** • Execrated in the **urine**.	• GIT and taste disturbances • **Hepatotoxicity** • Headache • visual disturbances.
Azoles	**Ketoconazole** (superficial/systemic) **Itraconazole** **Fluconazole** **Posaconazole** (systemic)	Inhibit fungal **cytochrome P450** (14α-demethylase), blocking ergosterol synthesis.	- **Ketoconazole**: • Mild deep fungal infections, • 2nd line to amphotericin, resistant dermatophytes to Griseofulvin and terbinafine • Candida infections. - **Fluconazole**: • Esophageal/oropharyngeal candidiasis • Secondary prophylaxis against cryptococcal meningitis. • Equivalent to amphotericin B in systemic candidiasis - **Posaconazole**: • **Prophylaxis during cancer chemotherapy** • **mucormycosis.**	**- Ketoconazole**: • oral • needs acidic media • plasma protein bounded • metabolized in liver • Do Not combine with: antiacids, h2 blockers or amphotericin B. - **Itraconazole/Fluconazole**: • more specific to fungal CYP450 - **Fluconazole**: • Safer, less hepatotoxic - **Posaconazole**: • Broadest-spectrum azole; inhibits **CYP3A4.** • Increases cyclosporine & tacrolimus	- **Ketoconazole**: • **Hepatotoxicity** • **CYP450 inhibition** • gynecomastia • **adrenal suppression (corticosteroids, testosterone, female sex hormones)** • drug interactions astemizole& terfenadine lead to arrythmia • increase level of oral anticoagulants -**Itraconazole/Fluconazole:** • Safer, fewer side effects.
Polyenes	**Amphotericin B** (systemic)	**Binds to ergosterol**, forming **artificial pores** in the fungal membrane, leading to leakage and cell death.	Severe **deep** systemic infections life-threatening meningitis	• **IV only**; not absorbed orally • Intrathecal for meningitis • avoid infusion related side effects by **slow infusion, pretreatment with antihistamine and antipyretics.** • To avoid nephrotoxicity, **decrease the dose**	• Infusion related: 1. Fever 2. rigors 3. vomiting 4. hypotension 5. shock after IV infusion • Dose related: nephrotoxicity • convulsions.
	Nystatin (superficial)	Binds to ergosterol, forming pores in fungal membranes, causing leakage and cell death.	• Oropharyngeal • Cutaneous • vaginal Candida infections (oral or topical).	**Too toxic for systemic use**; non-irritant when used topically. Used orally but not absorbed For vaginal candida both topically and orally; coz vaginal candida usually associated with GI candida … which act as a source of reinfection	Rarely causes allergy.

2. Drugs That Target the Fungal Cell Wall

Drug Class	Drugs	Mechanism of Action	Indications	Notes	Side Effects/Adverse Effects
Echinocandins	**Caspofungin**, **Micafungin** (systemic)	Inhibit **β-glucan** synthesis, weakening the fungal cell wall. By blocking **β 1,3 synthase** enzyme which responsible for β-glucan synthesis	- **Caspofungin**: Candidiasis, invasive **aspergillosis refractory to Amphotericin B.** - **Micafungin**: **Mucocutaneous candidiasis**, **prophylaxis of Candida infections in bone marrow transplant patients.**	IV use only.	• GIT upset • fever • headache • flushing (histamine release).

3. Drugs That Affect Fungal DNA/RNA or Cell Division

Drug Class	Drugs	Mechanism of Action	Indications	Pharmacokinetics/Notes	Side Effects/Adverse Effects
Antimetabolites	**Flucytosine** (systemic)	Cytotoxic; converted to **5-fluorouracil (5-FU), inhibiting nucleic acid synthesis.**	**Cryptococcal infections** (used with Amphotericin B or azoles).	Selective toxicity: mammalian cells cannot convert flucytosine into 5-FU. advantages of using Flucytosine & amphotericin B together: 1. decrease resistant to amphotericin 2. decrease amphotericin nephrotoxicity (by lowering it dose)	• Bone marrow suppression • Hepatotoxicity • hair loss.
Griseofulvin	**Griseofulvin** (superficial/systemic)	Fungistatic; **inhibits microtubules, preventing mitosis.**	• **Dermatophyte infections** • systemic use for resistant or widespread cases.	Deposited in newly formed keratin (nails, hair); treatment duration: **6–12 months**.	• Teratogenic • Carcinogenic • Hepatotoxicity • Nausea • mental confusion • enzyme inducer (reduces warfarin levels).

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