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Antifungal

An **antifungal medication**, also known as an **antimycotic medication**, is a pharmaceutical fungicide or fungistatic used to treat and prevent mycosis such as athlete's foot, ringworm, candidiasis (thrush), serious systemic infections such as cryptococcal meningitis, and others. Such drugs are usually obtained by a doctor's prescription, but a few are available over the counter (OTC).

Antifungal

Drug class

Canesten (clotrimazole) antifungal cream

Synonyms antimycotic medication

In Wikidata

Contents

Types of antifungal

There are two types of antifungals: local and systemic. Local antifungals are usually administered topically or vaginally, depending on the condition being treated. Systemic antifungals are administered orally or intravenously.

Of the clinically employed azole antifungals, only a handful are used systemically.[1] These include ketoconazole, itraconazole, fluconazole, fosfluconazole, voriconazole, posaconazole, and isavuconazole.[1][2] Examples of non-azole systemic antifungals include griseofulvin and terbinafine.

Classes

Polyenes

A polyene is a molecule with multiple conjugated double bonds. A polyene antifungal is a macrocyclic polyene with a heavily hydroxylated region on the ring opposite the conjugated system. This makes polyene antifungals amphiphilic. The polyene antimycotics bind with sterols in the fungal cell membrane, principally ergosterol. This changes the transition temperature (Tg) of the cell membrane, thereby placing the membrane in a less fluid, more crystalline state. (In ordinary circumstances membrane sterols increase the packing of the phospholipid bilayer making the plasma membrane more dense.) As a result, the cell's contents including monovalent ions (K^+, Na^+, H^+, and Cl^-) and small organic molecules leak, which is regarded as one of the primary ways a cell dies.[3] Animal cells contain cholesterol instead of ergosterol and so they are much less susceptible. However, at therapeutic doses, some amphotericin B may bind to animal membrane cholesterol, increasing the risk of human toxicity. Amphotericin B is nephrotoxic when given intravenously. As a polyene's hydrophobic chain is shortened, its sterol binding activity is increased. Therefore, further reduction of the hydrophobic chain may result in it binding to cholesterol, making it toxic to animals.

- Amphotericin B
- Candicidin
- Filipin – 35 carbons, binds to cholesterol (toxic)
- Hamycin
- Natamycin – 33 carbons, binds well to ergosterol
- Nystatin
- Rimocidin

Azoles

Azole antifungals inhibit conversion of lanosterol to ergosterol by inhibition of lanosterol 14α-demethylase.[4] These compounds have a five-membered ring containing two or three nitrogen atoms. The imidazole antifungals contain a 1,3-diazole (imidazole) ring (two nitrogen atoms), whereas the triazole antifungals have a ring with three nitrogen atoms.

Imidazoles

- Bifonazole
- Butoconazole
- Clotrimazole
- Econazole
- Fenticonazole
- Isoconazole
- Ketoconazole
- Luliconazole
- Miconazole
- Omoconazole
- Oxiconazole
- Sertaconazole
- Sulconazole

- Tioconazole

Triazoles

- Albaconazole
- Efinaconazole
- Epoxiconazole
- Fluconazole
- Isavuconazole
- Itraconazole
- Posaconazole
- Propiconazole
- Ravuconazole
- Terconazole
- Voriconazole

Thiazoles

- Abafungin

Allylamines

Allylamines[5] inhibit squalene epoxidase, another enzyme required for ergosterol synthesis. Examples include butenafine, naftifine, and terbinafine.[6][7][8]

Echinocandins

Echinocandins inhibit the creation of glucan in the fungal cell wall by inhibiting 1,3-Beta-glucan synthase:

- Anidulafungin
- Caspofungin
- Micafungin

Echinocandins are administered intravenously, particularly for the treatment of resistant *Candida* species.[9][10]

Triterpenoids

- Ibrexafungerp

Others

- Acrisorcin
- Amorolfine – a morpholine derivative used topically in dermatophytosis[11]

- Aurones – possess antifungal properties[12]
- Benzoic acid – has antifungal properties, such as in Whitfield's ointment, Friar's Balsam, and Balsam of Peru[13]
- Carbol fuchsin (Castellani's paint)
- Ciclopirox (ciclopirox olamine) – a hydroxypyridone antifungal that interferes with active membrane transport, cell membrane integrity, and fungal respiratory processes. It is most useful against tinea versicolour.[14]
- Clioquinol
- Coal tar
- Copper(II) sulfate[15]
- Crystal violet – a triarylmethane dye. It has antibacterial, antifungal, and anthelmintic properties and was formerly important as a topical antiseptic.[16]
- Chlorophetanol
- Diiodohydroxyquinoline (Iodoquinol)
- Flucytosine (5-fluorocytosine) – an antimetabolite pyrimidine analog[17]
- Fumagillin
- Griseofulvin – binds to microtubules and inhibits mitosis[18]
- Haloprogin – discontinued due to the emergence of antifungals with fewer side effects[19]
- Miltefosine – disrupts fungal cell membrane dynamics by interacting with ergosterol[20]
- Nikkomycin – blocks formation of chitin present in the cell wall of fungus.
- Orotomide (F901318) – pyrimidine synthesis inhibitor[21][22]
- Piroctone olamine
- Pentanenitrile
- Potassium iodide – preferred treatment for lymphocutaneous sporotrichosis and subcutaneous zygomycosis (basidiobolomycosis). The mode of action is obscure.[23]
- Potassium permanganate - for use only on thicker, more insensitive skin such as the soles of the feet.
- Selenium disulfide
- Sodium thiosulfate
- Sulfur
- Tolnaftate – a thiocarbamate antifungal, which inhibits fungal squalene epoxidase (similar mechanism to allylamines like terbinafine)
- Triacetin – hydrolysed to acetic acid by fungal esterases[24]
- Undecylenic acid – an unsaturated fatty acid derived from natural castor oil; fungistatic, antibacterial, antiviral, and inhibits *Candida morphogenesis*
- Zinc pyrithione

Side effects

Apart from side effects like altered estrogen levels and liver damage, many antifungal medicines can cause allergic reactions in people.[25] For example, the azole group of drugs is known to have caused anaphylaxis.

There are also many drug interactions. Patients must read in detail the enclosed data sheet(s) of any medicine. For example, the azole antifungals such as ketoconazole or itraconazole can be both substrates and inhibitors of the P-glycoprotein, which (among other functions) excretes toxins and drugs into the intestines.[26] Azole antifungals also are both substrates and inhibitors of the cytochrome P450 family CYP3A4,[26] causing increased concentration when administering, for example, calcium channel blockers, immunosuppressants, chemotherapeutic drugs, benzodiazepines, tricyclic antidepressants, macrolides and SSRIs.

Before oral antifungal therapies are used to treat nail disease, a confirmation of the fungal infection should be made.[27] Approximately half of suspected cases of fungal infection in nails have a non-fungal cause.[27] The side effects of oral treatment are significant and people without an infection should not take these drugs.[27]

Azoles are the group of antifungals which act on the cell membrane of fungi. They inhibit the enzyme 14-alpha-sterol demethylase, a microsomal CYP, which is required for biosynthesis of ergosterol for the cytoplasmic membrane. This leads to the accumulation of 14-alpha-methylsterols resulting in impairment of function of certain membrane-bound enzymes and disruption of close packing of acyl chains of phospholipids, thus inhibiting growth of the fungi. Some azoles directly increase permeability of the fungal cell membrane.

See also

- Fungicide
- Antimicrobial
- Etest

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External links

- Antifungal Drugs (http://www.fungalguide.ca/treatments/antifungal_drugs.html) – Detailed information on antifungals from the Fungal Guide written by R. Thomas and K. Barber
- "Clotrimazole" (https://www.canesten.com.ph/canesten-cream). *Clotrimazole (Canesten)*. Bayer Philippines.