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Classification and pharmacology feature of antifungal drug: A review

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Abstract
There has been high in severity of infection causes fungas in present time. Antifungal require prolonged treatment some of the systemic fungal infection may be life threatening. Antifungal drug have positive effect as well as negative effect including on heart and liver Failure They have need to testing every 4 to 6 weets For kidney, liver & heart damage depending on antifungal pills Sometime infection reverse after treatment. For Mucosal & systemic yeast infection Floconazole is widelyused, drug is widely used. For the nail infection, terbinafine drug is used. For the oral thrush nystatin drug is used & For the vaginal thrush Floconazole is used. [3]

Keywords: antifunfal, squalene epoxide, azole, toxicity

Introduction

Medicine that kill the growth of fungi are known as Antifungal that cause infections. Antifungal are also called antimycotic agents. Clotrimazole, econazole, miconazole, terbinafines Fluconazole, ketoconaz ole, nystatin, amphotericin aze the common names for anti-Fungal medicines. Antifungal creams, liquid or Sprays are available to treat the Fongal infections. polyers, azoles, allylamines & echinocandins are the classes of antifungal drugs. Amphotericin B deoxycholate is the

Fiest antifungal was introduce in 1958. In 1973, Flucato sine, a pyrimidine analogue was introduced it is active against candida cryptococcus. In 1990 the 1st gemation azo of azole drugs became available & these agent ef have the advantages of oral administration & have good activity against yeast pathogens. The and genration of azole in 2000s. The ad which includes voriconazole drog are intoduce and İsavu conazole w. The advantages of these agent is posaconazole extended spectrum of activity against Filamentous fungi. Symptoms of Fungal infections are itchy red color patches, hair loss as well as crusted patches

In year 1950s, more than 200 polyenes with antifungal activity have been discovered. Fungal infection can affect the circulatory system. There are 4 main classes of antifungal drug they are Follows polyenes, azoles, allylamines and echinocandians. There are 10 antifungal drugs are approved by Food & Drug administration for the systemic Fungal infection.

Antifungal drug have positive effect aswell as negative effect including on heart and liver Failure They have need to testing every 4 to 6 weets For kidney, liver & heart damage depending on antifungal pills Sometime infection reverse after treatment.

For Mucosal & systemic yeast infection Floconazole is widelyused, drug is widely used. For the nail infection, terbinafine drug is used. For the oral thrush nystatin drug is used & For the vaginal thrush Floconazole is used. [2, 3, 5]

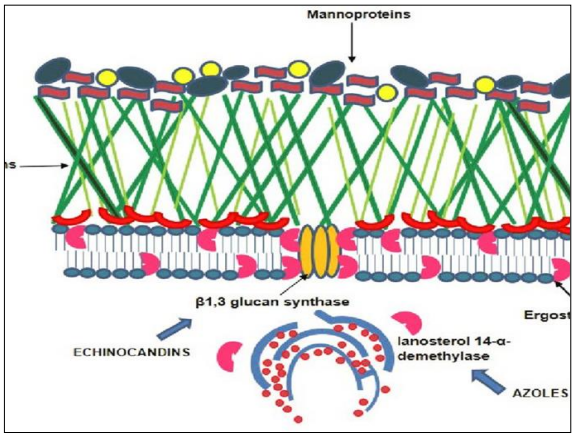

Fig 1: Traditionally antifungal drug

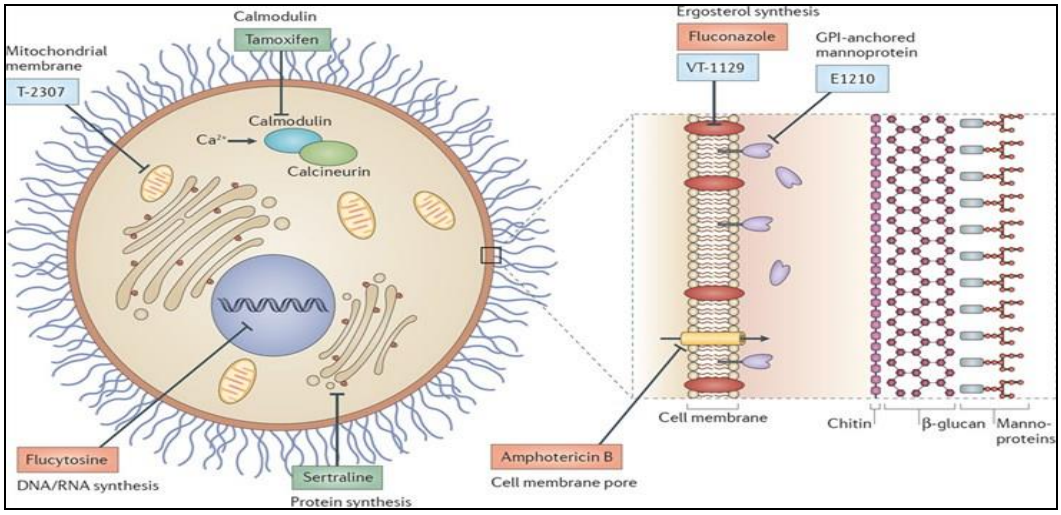

Fig 2: role of antifungal drug

Classfication of antifungal drug [1, 5]

Antifungal drugs classified into 5 types

1. Antibiotics
2. Antimetabolites
3. Azoles
4. Allylamine
5. Topical Agents

1. Antibiotics

Antibiotics also classified into 3 types.

A. Polyenes
B. Echinocandins
C. Heterocyclic benzofuran

A. Polyenes

- Amphotericin B
- Nystatin
- Hamycin

B. Echinocondins

- Caspofungin
- Micafungin
- Anidulafungin

C. Heterocyclic Benzofuran

- Griseofulvin

2. Antimetabolites

- Flucytosine

3. Azoles

Azoles having 2 types

A. Imidazoles
B. Triazoles
C. Imidazoles

Having 2 Subtype

a. Topical
- Clotrimazole
- Econazole
- Miconazole
- oxiconazole

b. Systemic
- Ketoconazole

B. Triazoles
- Fluconazole
- Itraconazole
- voriconazole
- posaconazole

4. Allylamine
- Terbinafine

5. Topical Agents
- Tolnaftate
- Undecylenic acid
- Benzoic acid
- Cicloplrox olamine
- Butenafine
- Quiniodochlor
- Sod. thiosulfate

Drug acting on cell membrane.

1. Amphotericin -B
- Fungicidal
- Systemic antifungal

Mechanism of Action

Binds to ergsterol (main component required for cell wall synthesis)
To forms a pores
Cell content leak out
Then cause cell death
Pharmacokinetcs
Orally not absorbed so available only in form of IV preparation.

Uses

To treat fungal infection.
Choice for all life-threatening mycotic infections In cystitis
= To prevent relapse of cryptococcosis and his toplasmosis in patients with AIDS
Given orally in fungal infection of the gut
Used topically in candidiasis

2. Nystatin

= Acting on cell membrane
= Topical (bcause it showes toxic effect)

Pharmacokinetics
- Absorption = poorly absorbed
- Distribution = UK
- Metabolism t 1/2 = UK
- Excretion = In feces unchanged

Contraindication

= Hypersensitivity
= Pregnancy

Uses

= Vaginitis
= Oral condidiasis

3. Griseofulvin

= Acting on nucleus
=Systemic antifungal
=Fungistatic
=It causes disrption of mitotic spindle formation by interacting with polymerised microtubule

Drug interaction

Increase activity of warfarin, intolerance with alcohol, absorption improved by taking it with fatty food

MOA
Griseofulvin binds to microtubular protein in the nucleus, disrupts the mitotic spindle and inhibits mitosis in the fungus.
It gets deposited in the newly forming skin, binds to keratin and protects the skin from getting newly infected.
Pharmacokinetics
= Poorly water soluble
= Poor bioavailability
= microsomal enzyme inducer.

Uses
= Used orally in superficial dermatophytosis
= Suitable for ringworm infection of skin and nails.

4. Ketoconazole
=Acting on cell membrane
=First oral azole
=Well absorbed from the gut (need acidic PH for absorption)
= Food and low gastric PH enhance absorption.

MOA
Preventing the synthesis of ergosterol, the fungal equivalent of cholestrol, therefore increse membrane fluidity and preventing growth of the fungus
Pharmacokinetics
=Variable oral absorption, depends on PH
=t 1/2 = 7-10 Hours
=Protein binding > 99%
= Hepatic, bile and kidney elimination.

USE
=Mucocutaneous candidiasis and dermatophytosis
= In Cushing's syndrome= Deep mycoses
= Effective in cutaneous leishmaniasis

5. Flucanazole
= Acting on cell membrane
=Is a flourinated triazole is water soluble, well absorbed from the gut
Pharmacokinetcs
= Bioavailability > 90%
=Not dependant on gastric PH or food
=Metabolism = Not metabolised
= Excretion = Kidney
= T1/2 = 27 -34 hours

MOA
Interferes with synthesis of ergosterol to inhibit fungal growth (Inhibit cytochrome P- 450 3-A dependent enzyme) 14 - alpha demethylase

USE
=Cryptococcal meaningitis
=Coccidioidal meaningitis
=Candidiasis
=Other fungal infections
= leishmaniasis

Mechanism of action [3, 1]
Antifungal deugs are used for superficial fungal infections. More than 200 polyene with antifungal activity has been discovered in 1950s many antifungals topicals are applicable in antiseptic era. There are two important amphotericin B e griseofulvin. The medication of invasive fungal
infections [19] amphotericin B. single polyene drug are choose for the treatment of Cancer 5- Flucytosine drug metabollite used are 1st exposed drug.
The antineoplastic action is low, Now 5-FC Serves in combinational antifungal remedy [20]. Fluconazole (FLC) and itraconazole (GTC). Are 1st formation triazoles. Voriconazole (VOR), posaconazole (POS) & isavuconazole (50) [21] are the Second formation triazoles. The modern class of peptide antifungals known as echinocandins include capofungin (CSF) micafungin (MCF) and anidulafungin (ANF).

Amphotericin B cyclic heptaene is generated by the Gram-positive bacterium streptomyces nodosus. They are two mechanism of action, 1st is, some Fragment of Amphotericin B integrate into bind to ergosterol the fungal lipid bilayer. By an ergosterol disolation pores is formed the pair of ions like ca²-, ma2+, k+,cl- & electrolyte glucose are free And the second AMB encourage the aggregation of reactive oxygen species (ROS) resulting in DNA, mitochondrial damage, proteins [24].The critical positions for the AMB biological activity is structural part of mycosamine and hydroxyl group at C8, Cg C35 location. 5- Flucytosine are Synthetic analogue of cytosine After authority, 5 FC is taken up by cytosine permease into the Fungal cell 5- Fluorouracil 5- Fluorouracil into the fungal cell and deaminated to 5-fluorouracil is converted 5-fluorouridine triphosphate. likewise, 5-Fluorouracil are metabolised to 5-Fluorodeoxy uridine monophosphate by uridine monophosphate pyrophosphorylase. This compound incourage the primary origin of thymidine in DNA biosynthesis thymidylate synthetase to remove the Fluorine atom [25]. The mechanism action of triazoles is depend on the incourage of the microsomal Cytochrome p450 monoxygenase depend 14 alpha demethylase. The combo of accumulation OF harmful 14 alpha- methylsterols and depletion of ergosterol results in the fungistatic effect [26].

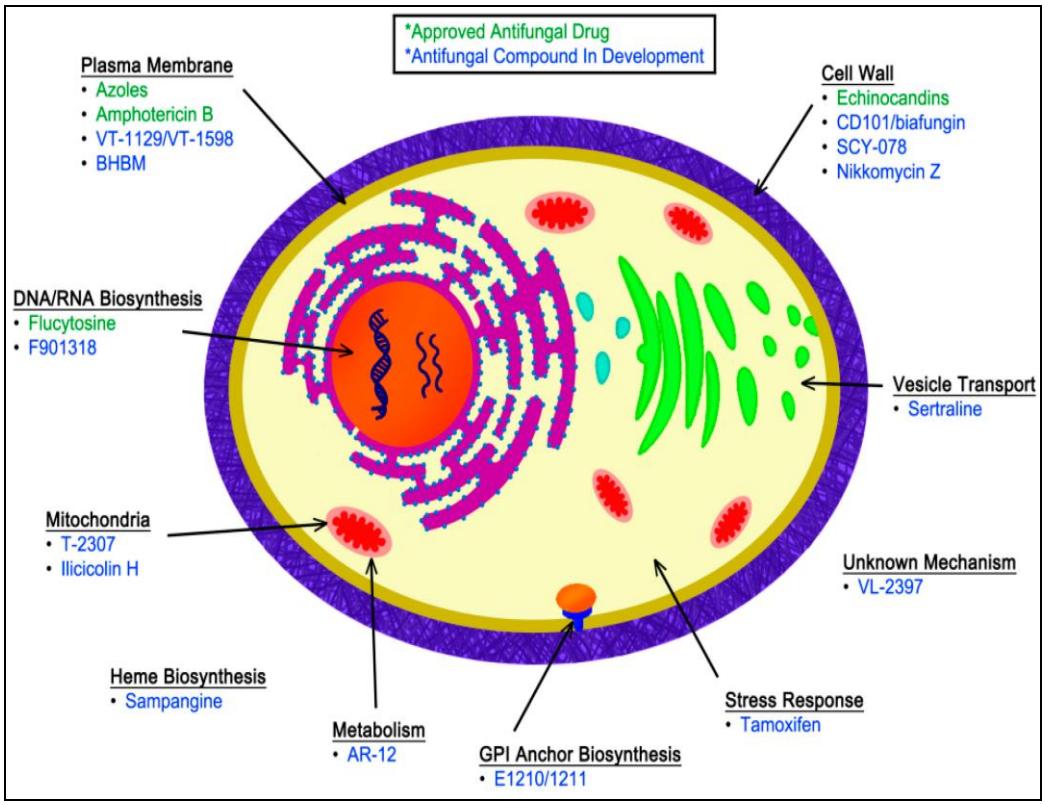

Fig 3: mechanism of action of antifungal drug.

Treatment of Antifungal drug. [6]

Antifungals treat these types of fungal skin infections: Athlete's foot, jock itch and ringworm. Dandruff (seborrheic dermatitis).Fingernail infection or toenail fungus. Thrush and esophageal candidiasis (yeast infection in the mouth, throat or esophagus).Vaginitis and vaginal yeast infection.

Cology and Toxicology of Antifungal drug. [3]

Properties of Echinocandins

- For the successful medication adequate antifungal dosing arrangement the type of medication, patient population and including patient physical condition are changes by optimal antifungal doseges.

Hence, dosage proposal are written in several guidlines and review articles, in that include aspergillosis and candidiasis in neonates [42], pediatrics [43], and adults [44, 45]. The embryotic effect are challenge due to limited information for pregnant women in antifungal prescription.

For the treatment of systematic fungal infection the safest drug is used AMB. The rest of antifungals have a worst credit because of indication or positive evidence of fetal risk bases on animal studies.

For dose development is also essential for obese population due to their drug development studies are result in limited pharamacological data for antifungal.

Whereas, FLC, MCF and CSF are co-ordinate with complete body weight, dosing, variations are not essential for AMB, ANF and POS.

Properties of Triazoles: The metabolism of voriconazole are on the affect of genetic polymorphisms of CYP 2C19 and CYP3 A4.

In VOR occurs hepatotoxicity is the most common serious side effect. Although ISV abbreviate the QT interval (time is between the start of ventricular depolarization & end of the ventricular repolarization), the triazole are slow down act as across way.
Regrettably, triazoles are many possible drug-drug
interation due to attraction for CYP-450 isoenzyme.
Echinocandin are 50 for been authorized for only intravenous administration.

Excessive protein binding
and insignificant metabolism by CYP-450 are ordinary among then, by other way their degradation process and half-life are distinct.
The peptide hydrolysis and N-acetylation these two inactive metabolites are degraded by the caspofungin has the least half-life & after involuntary opening of the peptide ring.
Ultimately, the metabolism of micafungin forms 3 meta by catechol o-methyltransfererase (COMT), CYP3A side- chain hydroxylation and aryl sulphate.
For the degradation CSF product are excreted by the urine.

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1. Gayatri Bhagat
2. Nikita kokare
3. Mahek Shaikh
4. Ajay kalekar.

Conclusion
Beside the design of structurally new antifungals based on new target promising strategics to combat antifungal drug resistance seem to be design of efflux inhibitor. Fungal infection in immunocompromise hosts associate with high mortality.

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