

AMPHOTERICIN-B: A DRUG APPROACH IN FUNGAL TREATMENT

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Abstract—Amphotericin B (AmB) is a polyene macrolide class of antifungal agent and it is the drug of choice for systemic fungal infection, but unfortunately, oral bioavailability of this drug is negligible due to its low aqueous solubility. Amphotericin-B is a potent and effective antifungal medication used for serious fungal infections. It is used to treat aspergillosis, blastomycosis, candidiasis and cryptococcosis and many other fungal infection. It is typically given by injection into a vein, now a day's it used topically like-cream and gel. Common side effects fever, chills, headaches and Nephrotoxicity (kidney problem). Amphotericin-B act as forming pores in cell membrane that causes leakage of monovalent ions and subsequent fungal cell death.

Keywords— Antifungal, Polyene Macrolide, Blastomycosis, Bioavailability, Leishmaniasis, Aspergillosis.

I. INTRODUCTION

We Fungi are large organisms that typically survive on dead rotting animal and plant matter. They are found mostly in soil, an object contaminated with soil, on plants and animals skin, and that they may additionally be airborne. Fungi may exist as yeasts or molds and will alternate between the 2 forms, looking on environmental conditions. Yeasts are simple cells, 3 to 5 micrometres (0.0001 to 0.0002 inch) in diameter. Molds include filamentous branching

structures (called hyphae), 2 to 10 micrometres in diameter, that are formed of several cells lying end to finish.[1-6] Fungal diseases in humans are called mycoses; they include such disorders as histoplasmosis, coccidioidomycosis, blastomycosis, Mucormycosis.

A. Transmission

Fungi cells always reproduced by spreading single celled spores. The structure of a fungus is long and cylindrical, with small filaments branching from the body. Many fungal infections develop on the upper most layers of the skin, and some reached and spread in the deeper layers. Inhaled yeast or mold spores can sometimes lead to fungal infections, like pneumonia, or infections throughout the body. These also are called systemic infections. [7-12]

B. Antifungal Drugs

The most frequently used polyene macrolides are amphotericin-B and nystatin. These drugs act by binding to ergosterol in cell membranes increasing permeability, disrupting metabolism and causing death of cell. Amphotericin-B is a broad spectrum of activity against most species of Candida and Aspergillus. Amphotericin-B has been available since last four decade and exists in many type of formulations; however, because the oral bioavailability of amphotericin-B is less than

5%. So oral formulations are difficult to make. Intravenous formulations of amphotericin-B are used in the management of systemic fungal infections. [14-18]

C. Allylamines

The allylamine terbinafine inhibits squalene epoxidase, which acts in ergosterol depletion, membrane disruption and death of fungus cell.¹⁹ Terbinafine has activity against dermatophytes, low activity against *Aspergillus* spp. and other filamentous fungi but limited activity against *Candida* spp. The drug is registered for topical and oral treatment of cutaneous and nails dermatophyte infections, because terbinafine is lipophilic and keratinophilic, it accumulates in sebum, hair and nails. Terbinafine has been used alone or together with amphotericin-B or azoles for the treatment of invasive fungal infections. [19-22]

D. CHEMISTRY

Amphotericin-B is crystalline in bright yellow color having solid state. It shows crystalline solid at room temperature that shows physical characteristics of the drug. Amphotericin-B is water insoluble potent antifungal drug which belongs to the amino benzimidazole family drug. [24]

E. Amphotericin-B

Molecular weight: 924.09g/mol

Molecular Formula: C₄₇H₇₃NO₁₇

Melting point: 170°C

Boiling point: 100°C

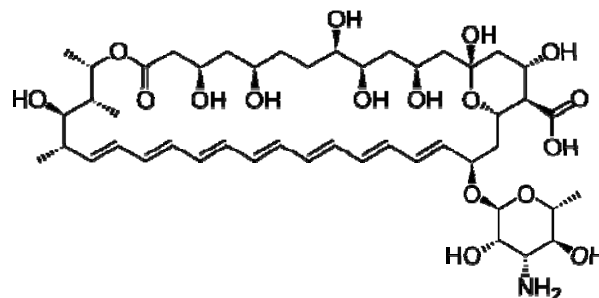
Density: 0.9g/cm³

Flash Point: 163°C

Solubility: Amphotericin-B is bright yellow crystalline powder soluble in DMSO, Lipids and insoluble in water.

Storage: Store at well closed amber colored container.

II. CHEMICAL STRUCTURE & PROPERTIES



CHEMICAL PROPERTIES

Appearance- Amphotericin-B is solid crystalline powder in nature with bright yellow colour.

Solubility- Amphotericin-B is slightly soluble in DMSO (di-methyl-sulfoxide), but is insoluble in water.⁵⁻⁹

III. PHARMACODYNAMICS/MECHANISM OF ACTION

Amphotericin-B is an antifungal medication used for serious fungal infections and leishmaniasis. It is accustomed to treat aspergillosis, blastomycosis, candidiasis and cryptococcosis. It is typically given by injection into a vein. Common side effects are fever, chills, headaches and kidney problems.²⁵⁻²⁸

Mechanism of action:

polyene antifungals, amphotericin B associates with ergosterol, the main component of fungal

cell membranes, forming a transmembrane channel that acts as monovalent ion (K⁺, Na⁺, H⁺ and Cl⁻) leakage, which is the primary effect resulting in fungal cell death. Recently, however, researchers found evidence that pore formation isn't necessarily linked to cell death. The particular mechanism of action is also more complex and multifaceted. 29-32

Pharmacokinetics:

Amphotericin B is very poorly absorbed when given orally, and this route is employed just for treating fungal infections of the upper alimentary canal. It is often used topically for local infection on skin. For systemic infections it's generally administered by slow injection complexed with liposomes or other lipid-containing preparations. This improves the pharmacokinetics and reduces the considerable burden of side effects. Amphotericin B is extremely highly protein bound. It penetrates tissues and membranes (such as because the blood-brain barrier) poorly, although it's found in fairly high concentrations in inflammatory exudates and should cross the blood-brain barrier more readily when the meninges are inflamed, and intravenous Amphotericin-B is employed with flucytosine to treat cryptococcal meningitis. It's excreted very slowly via the kidney, traces being found within the urine for two months or more after administration has ceased.

Medicinal uses:-

Antifungal Activity-

Amphotericin B is an antifungal used to treat fungal infections in neutropenic patients, cryptococcal meningitis in HIV infection, fungal infections, and leishmaniasis.

Black fungus treatment-

Amphotericin-B is widely used to treat post-covid symptoms black fungus (Mucormycosis) by inhibiting the synthesis of ergosterol, the most component of fungal cell membranes. 18-21

Side effects

Amphotericin-B has some following common side effects.

- Fever and chills.
- increased or decreased urination.
- irregular heartbeat.
- muscle cramps or pain.
- nausea.
- pain at the place of injection.
- unusual tiredness or weakness.
- vomiting.

Adverse drug reactions:

The adverse reactions most ordinarily observed are:

General (body as a whole): fever, malaise, weight loss.

hypotension tachypnea, anorexia; nausea; vomiting; diarrhea

Hematologic: normochromic anemia, normocytic anemia, Local: pain at the injection site, generalized pain, including muscle and joint pains.

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