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Amphotericin B: spectrum and resistance.

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Source

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Abstract

Amphotericin B is a polyene macrolide antibiotic derived from the actinomycete *Streptomyces nodosus*. Of the 200 known polyene agents, amphotericin B is the only one with toxicities that are sufficiently limited to permit intravenous administration. All polyenes have a common mechanism of action in that they preferentially bind to ergosterol, the primary sterol in the fungal cell membrane. The consequence of this binding includes disruption of the osmotic integrity of the membrane, with leakage of intracellular potassium and magnesium, and also the disruption of oxidative enzymes in target cells. Amphotericin B has a relatively broad spectrum of action and is useful in treating cases of candidosis, cryptococcosis, histoplasmosis, blastomycosis, paracoccidioidomycosis, coccidioidomycosis, aspergillosis, extracutaneous sporotrichosis and mucormycosis, and some cases of hyalohyphomycosis and phaeohyphomycosis. Resistance (MIC > 2 mg/L) tends to be species-dependent and emerges uncommonly and slowly in isolates from patients treated with amphotericin B. These include some individual strains of *Candida albicans*, *Candida tropicalis*, *Candida parapsilosis* and *Candida lusitanae*, which may acquire resistance during treatment. Some isolates of *Scedosporium apiospermum*, *Fusarium* spp. and *Sporothrix schenckii* also show primary resistance, whereas all strains of *Scedosporium prolificans* demonstrate resistance. The main problems associated with the use of conventional amphotericin B have always been due to its poor aqueous solubility and toxicity rather than antifungal resistance.

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