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Mini Review

Antifungal Drugs and their Resistance Mechanism

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Introduction

Antifungal drugs are distinct in terms of effectiveness, spectrum of activity, therapeutic index, resistance mechanism, and mode of use. An important factor in the practicality of a compound is the mechanism by which it attacks the structure and function of the fungal cell. The target organelles have been established for most antifungal drugs [1].

Conventional Antifungal Drugs with Mechanism of Action and Drug Resistance

Depending on the drug and the *Candida* species, the mechanism of antifungal resistance can be inherent (without previous exposure) and acquired (with previous exposure) [2]. There are around 4 groups of antifungal drugs.

A. Polyenes: e.g. Amphotericin B- mechanism of action is through disruption of fungal cell membrane and resistance mechanism is by defective ergosterol biosynthesis, due to mutation in the ERG3 gene.

B. Azoles: Fluconazole, Itraconazole, Voriconazole, Posoconazole, Ravuconazole- inhibit ergosterol biosynthesis and resist this action by modifications in target enzymes due to point mutations in ERG11 and active efflux of the drug out of the cell via the activation of efflux transport proteins [1,3].

C. Flucytosine: Inhibit DNA and protein synthesis, fungi resist by alterations in the target enzymes (cytosine permease and cytosine deaminase), or increased production of pyrimidines.

D. Echinocandins: e.g. Caspofungin- inhibit b1, 3-D-glucan synthesis and drug resistance mechanism is by generating insufficient target enzyme b-1, 3-D-glucan synthase [2,4].

Candida Biofilm and New Antifungal Strategies

Emerging resistance to antifungal agents & toxicity of existing antifungal compounds leads the current science to search for highly effective with low toxicity natural products. Plants are good options for obtaining a wide variety of drugs [5,6] (Table 1). Another promising antifungal strategies are Silver nano particles (interfere with microbial DNA replication within bacteria and fungi), Anti-*Candida* antibodies (can reduce the binding of Candida to various surfaces), Photodynamic therapy (inactivation of the fungus) and Gold nano particle conjugate (mediated photodynamic therapy may be used against nosocomially acquired refractory *C albicansbiofilms*) [7-10].

Table 1: Antifungal activity of natural products against a variety of biofilms.

Natural Products	Biofilm
Peptide (18-amino acid cationic ApoEdpl-W)	**All species of *candida* except *C glabrata***
Peptide (Trapanatans)	*C tropicalis*
Romanian plant extracts	*C albicans*
Coriandrumsativum	*C albicans*
Cinnamon oil	*C parapsilosis*
Boesenbergia pandurate	*C albicans*
Piper sarmentosum	*C albicans*
Saponins	*C albicans*
Green tea	*C albicans*
Ocimumamericanum	*C albicans*
Caesalpiniaferrea	*C albicans*
Cassia spectabilis	*C albicans*
Usnic acid	*C parapsilosis and C orthoparapsilosis*
Croton cajucara	*C albicans*
Garlic extracts	*C albicans*

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