

ANTIFUNGAL DRUGS

PART I. FUNGAL CELL STRUCTURE, FUNCTION AND SUSCEPTIBLE TARGETS FOR ANTIFUNGAL AGENTS. REVIEW

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Summary. The aim of this review is to discuss the critical points of current knowledge about pathogenic fungi cell structure, function and susceptible targets for antifungal agents. Unlike bacteria, both fungi and mammalian are eukaryotic cells. Thus, fungal and mammalian cells are comparable at the molecular level and protein synthesis function. However, the antifungal agents develop a toxic effect on mammalian cells. The main difference between fungal and mammalian cells is that animal cells do not have a cell wall, they are enclosed by a plasma membrane, and fungal cell has a cell wall, which is an obvious target for antifungal agents. Cellular differences between fungal and mammalian cells gave the opportunity to modify well-known or design new antifungal agents, that would kill off the fungal organism without dangerous effects on the host. The identification of new susceptible targets in fungal cell lead to development of effective and less toxic to the host antifungals. The fungal cell wall is a dynamic organelle that must provide the cell with sufficient mechanical strength. Fungal cell wall is structurally unique, is comprised of glycoproteins and polysaccharides, mainly glucan and chitin, which are cross-linked together to form a complex network, which forms the structural basis of the cell wall. Ergosterol is an essential component of the fungal cell membrane, required to maintain cellular rigidity and integrity. Ergosterol biosynthesis pathway is a specific branch of the mevalonate pathway and is fungal-specific and unique, there are several enzymatic steps that are attractive targets for antifungal drugs. Azoles, allilamines, thiocarbamates and morpholines inhibit the synthesis of ergosterol. Since the (1,3)- β -glucan structure is not found in mammalian cells, enzyme (1,3)- β -glucan synthase has become a target for echinocandins and pneumocandins. The search for new antifungal drugs and strategies, that will focus on inhibition of ergosterol, glucan, chitin synthesis and more targets, continues. Antifungal agents, their mode of action and application will be reviewed in the next edition.

Key words: fungal cell, susceptible targets, the mode of action of antifungal drugs.