



Article

The Effect of Posaconazole, Itraconazole and Voriconazole in the Culture Medium on *Aspergillus fumigatus* Triazole Resistance

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Abstract: Triazoles are the only compounds used as antibiotics in both medicine and agriculture. The presence of triazoles in the environment can contribute to the acquisition of azole resistance among isolates of *Aspergillus fumigatus*. The objective of this study was to investigate the effect of *A. fumigatus* exposure to triazoles on susceptibility to these compounds. Seventeen triazole-resistant and 21 triazole-sensitive *A. fumigatus* isolates were examined. The isolates were transferred 20 times on the Sabouraud medium supplemented with posaconazole, itraconazole or voriconazole, followed by five times on the medium not supplemented. The minimum inhibitory concentrations of antimycotics were examined according to the EUCAST broth microdilution method after the 20th transfer and also the 25th transfer. In addition, the expression levels of genes *mdr1*, *mdr2*, *mdr3*, *atrF*, *cyp51A* and *cyp51B* were determined. Cultivation of *A. fumigatus* on media supplemented with posaconazole, itraconazole and voriconazole resulted in the acquisition of resistance to the tested triazoles of all examined isolates. After recultivation on Sabouraud without azoles, most of the isolates lost their acquired resistance. The long-term use of triazole compounds in agriculture may result in the occurrence of triazole resistant *A. fumigatus* isolates in the environment, not only by induction or selection of mutations in the *cyp51A* gene, but also by contribution to changes in the gene expression.

Keywords: *Aspergillus fumigatus*; mechanism of azole resistance; azoles

1. Introduction

Aspergillus fumigatus is a saprophytic mold widespread in the environment. It lives among dead and decaying organic matter in the soil and plays an important role in carbon and nitrogen biogeochemical cycles [1]. In humans, *A. fumigatus* is an opportunistic microorganism that threatens immunocompromised patients. It is the most common clinical cause of a group of illnesses collectively called aspergillosis. These diseases manifest as allergy, colonization or invasive infection [2]. *A. fumigatus* primarily infects the lungs, but can also infect the ears, eyes, skin, mucous membranes and various systemic sites, e.g., urinary tract [3,4]. Invasive aspergillosis is the most serious form of aspergillosis, and has a mortality rate of up to 80% [3]. The estimated burden of disease is about 500,000 acute infections every year [5]. Additionally, 3 million patients suffer from chronic