Pyrvinium: A Novel Antifungal Agent With Unique ROS-Dependent Autophagy Induction in Candida albicans

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Azole antifungals have served as frontline therapies for Candida infections. However, increasing azole-resistant Candida species presents a real clinical challenge requiring alternative antifungal strategies. Pyrvinium pamoate, an FDA-approved anthelmintic drug, has shown potent antifungal activity in Candida albicans by inducing an acute autophagy response independent of metabolic starvation. However, the intracellular mechanisms underlying its antifungal effect remain poorly understood.This study focuses on elucidating the pathways that mediate pyrvinium-induced fungal cell death with emphasis on the role of autophagy. Autophagy is a conserved eukaryotic stress-response pathway essential for cellular homeostasis and survival. One possible mechanism of acute autophagic induction is mediated through reactive oxygen species, ROS. I hypothesized that pyrvinium triggers ROS-dependent autophagy which reduces viability of C. albicans. To test this, I analyzed autophagy induction and quantitation, ROS production, mitochondrial activity, synergistic effect with rapamycin and cell viability with pyrvinium combined with blue light using various biochemical and cellular assays. Pyrvinium treatment rapidly increased autophagic activity and intracellular ROS levels by approximately 88% within 15 min. Mitochondrial levels were constantly elevated regardless of pyrvinium treatment. While pyrvinium combined with rapamycin showed no synergistic growth inhibition, pyrvinium combined with blue light significantly reduced C. albicans viability, demonstrating a synergistic anti-fungal effect consistent with ROS-mediated autophagy. These results support my hypothesis in which pyrvinium pamoate induces acute excessive ROS-mediated autophagy in C. albicans and subsequent cell death.

Awards Won:
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