

Enhanced Antifungal Efficacy of Amphotericin B Against Resistant *Candida albicans* Through Combination with 3-Hydrazinoquinoxaline-2-Thiol

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ABSTRACT

Candida albicans is a commensal and opportunistic fungus capable of causing severe infections under specific circumstances, *Candida albicans*, for example, is a commensal organism that can cause serious infections under certain conditions. Fungal infections, particularly, among immunocompromised individuals. *C. albicans* infections, have become a significant global health threat, with an estimated 1.7 to 2 million deaths annually. Despite advances in antifungal therapies, challenges remain in diagnosing and treating these infections effectively. This study aims to explore, for the first time, the potential synergistic effects of combining amphotericin B with 3-Hydrazinoquinoxaline-2-Thiol in vitro against clinical strains of *C. albicans*, with the objective of reducing treatment duration and minimizing the toxicity of amphotericin B. To our knowledge, this paper aims for the first time to explore the potential synergistic effects of combining amphotericin B with 3-Hydrazinoquinoxaline-2-Thiol in vitro against clinical strains of *Candida albicans*. 22 of Clinical strains of *Candida albicans* were tested for antifungal synergy between amphotericin B and 3-Hydrazinoquinoxaline-2-Thiol using broth microdilution and checkerboard assays. We've demonstrated that combining amphotericin B with 3-Hydrazinoquinoxaline-2-Thiol shows promising potential to boost antifungal effectiveness against *C. albicans*. Specifically, We found strong synergy against 20 strains, with a Fractional Inhibitory Concentration Index (FICI) consistently below 0.5, and additive effects against 2 strains. We observed no antagonistic interactions. This combination significantly lowered the MIC for both agents, with amphotericin B reducing the MIC of 3-Hydrazinoquinoxaline-2-Thiol by 64-fold, and the reverse by 32-fold, which underscore the potential for not only increased antifungal efficacy but also reduced drug toxicity through combination therapy. In summary, the pairing of amphotericin B and 3-Hydrazinoquinoxaline-2-Thiol presents a strong antifungal strategy against *C. albicans*. The consistent synergy and substantial MIC reductions highlight its promise in enhancing antifungal activity and addressing resistance, making it an area deserving of further research and clinical trials. For the first time we have showed that the combination of amphotericin B with 3-Hydrazinoquinoxaline-2-Thiol shows promising potential in enhancing antifungal efficacy against *Candida albicans* infections, but further tests are needed. This study evaluated the synergistic effects of Amphotericin B and 3-Hydrazinoquinoxaline-2-Thiol against 22 clinical *Candida albicans* strains. The combination demonstrated strong synergy in 20 cases, with a Fractional Inhibitory Concentration Index (FICI) consistently below 0.5, and additive effects in 2 cases. No antagonistic or indifferent interactions were observed. The combination reduced the MIC of both agents, with Amphotericin B lowering the MIC of 3-Hydrazinoquinoxaline-2-Thiol by 64-fold and vice versa by 32-fold. These findings highlight the potential for enhanced antifungal efficacy and reduced drug toxicity through combination therapy. In conclusion, combining amphotericin B with 3-Hydrazinoquinoxaline-2-Thiol shows strong potential as an antifungal strategy against *Candida albicans*. The consistent synergy and significant MIC reductions highlight its promise in enhancing antifungal efficacy and overcoming resistance, warranting further research and clinical trials.

Keywords: *Candida albicans*, Fractional Inhibitory Concentration Index, Infections, Fungus

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