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Effect of Cold Atmospheric Plasma on *Hsp90* Gene Expression in Terbinafine-Resistant Fungal Strains of the *Trichophyton mentagrophytes* Complex

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ABSTRACT

Introduction: The *Trichophyton mentagrophytes* complex, particularly terbinafine-resistant fungal strains, has emerged as a major cause of chronic and recurrent dermatophytosis, which is increasingly difficult to treat. These dermatophytes cause persistent infections of the skin, nails, and hair, often accompanied by inflammation, severe itching, keratin degradation, and reduced quality of life. In fungi, the molecular chaperone *Hsp90* is essential for stress tolerance, morphogenesis, and antifungal resistance. Cold atmospheric plasma (CAP), a non-thermal ionized gas, has recently gained attention for its notable antifungal activity. This study investigates the effect of CAP on *Hsp90* gene expression in terbinafine-resistant isolates of the *T. mentagrophytes* complex.

Materials and Methods: Fifty isolates of the *T. mentagrophytes* complex were tested for terbinafine susceptibility using broth microdilution, following the CLSI M38-A2 protocol. Isolates with minimum inhibitory concentrations above 0.25 µg/mL were classified as resistant. These resistant isolates, along with a standard sensitive strain (PFCC 5809), were exposed to a helium-based CAP jet, which was applied directly to fungal suspensions in 96-well microtiter plates. The expression levels of *Hsp90* before and after CAP exposure were quantified by real-time PCR using the $\Delta\Delta Ct$ method.

Results and Discussion: The baseline expression of *Hsp90* was 124.7-fold higher in resistant isolates compared to the sensitive strain. CAP treatment reduced *Hsp90* expression to 13.3-fold, which was significantly lower than baseline levels ($p < 0.005$).

Conclusion: CAP significantly downregulated *Hsp90* expression in terbinafine-resistant fungal strains. These findings suggest that CAP may serve as a promising adjunct antifungal strategy to enhance the management of resistant dermatophytosis.



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Keywords: Antifungal therapy, Cold atmospheric plasma, *Hsp90*, Terbinafine resistance, *Trichophyton mentagrophytes*

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