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Topic: Antifungal potential and mode of action of *Nigella sativa* seed essential oil and its major bioactive components

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Findings

Fungal infections, particularly candidiasis caused by *Candida albicans* and emerging non-*albicans* species, are increasing due to rising drug resistance and toxicity of conventional antifungals. This study evaluated the antifungal potential and mechanism of *Nigella sativa* seed essential oil (NSSEO) and its major constituents, thymoquinone and thymol, against *C. albicans*, *C. tropicalis*, and *C. glabrata*. NSSEO was extracted by hydro distillation and characterised by GC–MS, revealing thymoquinone (26.85%) and thymol (19.47%) as the dominant components. Broth microdilution, disc diffusion, and time-kill assays showed concentration-dependent fungicidal activity, with minimal toxicity compared to fluconazole. Mechanistic studies demonstrated reduced ergosterol biosynthesis and downregulation of *ERG11*, indicating interference with membrane integrity. Inhibition of H^+-ATPase activity, SEM imaging, and PI/CFW staining confirmed membrane disruption and cell death. NSSEO and its components also suppressed the secretion of hydrolytic enzymes, the yeast-to-hyphal transition, adhesion, and biofilm formation, accompanied by the downregulation of key virulence genes (SAP2, PLB1, ALS3, and *HWP1*). Among the tested strains, *C. albicans* was most susceptible. Overall, NSSEO, thymoquinone, and thymol exhibit potent, multi-targeted antifungal activity with low cytotoxicity, highlighting their promise as safe, mechanism-based alternatives to current antifungal agents and potential adjuncts in combating drug resistance.