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TITLE

Search for Novel Antifungal Agents by Monitoring Fungal Metabolites in Presence of Synthetically Designed Fluconazole Derivatives using NMR Technique

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The emergence of resistance to currently available antifungal drugs has created a need for new and effective antifungal agents against life-threatening systemic mycoses. This necessitates development of new antifungal drugs using methods which are rapid, robust and can be automated to test the activity of large number of newly synthesized drugs in comparatively less period of time.

We have compared the effect of antifungal agents ketoconazole and fluconazole on *Candida albicans* ATCC 10231. Based on the results the analogues of fluconazole (fluconazole benzoate, fluconazole p-nitrobenzoate, fluconazole p-methoxybenzoate, fluconazole toluate) have been synthesized. A metabolic profile of *Candida albicans* ATCC 10231 in presence of fluconazole and its analogues has been compared using ¹H NMR technique. Well resolved signals from metabolites such as ethanol, lactate and acetate, have been monitored at various time intervals. Minimum inhibitory concentration (MIC) determined for all the molecules using conventional methods has been compared with Metabolic End Point (MEP) obtained from NMR technique. Results indicate that the activity of the fluconazole derivatives is in the order fluconazole p-methoxybenzoate > fluconazole = fluconazole benzoate > fluconazole toluate > fluconazole p-nitrobenzoate.