

Investigation of the Profile and Kinetics of Degradation of Fenticonazole Nitrate using Stability-indicating HPLC Assay in Presence of Methyl and Propyl Parabens: Application to Preformulation Studies

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Abstract

Fenticonazole (FEN), an imidazole group containing antifungal was subjected to stress conditions; acid and base hydrolysis, photodegradation, thermal decomposition and oxidation. The structure of one major oxidative degradation product was elucidated using LC-MS/MS. A stability-indicating HPLC assay was developed and validated according to ICH guidelines which enabled the determination of FEN in presence of its degradation product and paraben preservatives (methyl and propyl parabens). Determination was carried out using Zorbax RP-C18-column (5 μ m, 15 cm x 4.6 mm i.d.) and gradient elution mode over a concentration range of 10.00-200.00 μ g mL⁻¹, 3.50-35.00 μ g mL⁻¹ and 1.75-7.50 μ g mL⁻¹ for FEN, methyl paraben and propyl paraben, respectively. Column temperature was maintained at 25°C and detection was carried out at 254 nm. As confirmed by the results of HPLC-PDA, FNTI formulations were susceptible to autooxidation. Different anti-oxidants were tested and results were evaluated following accelerated stability studies (40°C \pm 2°C and 75 \pm 5% relative humidity). Results indicated that using a combination of water soluble and fat soluble antioxidants provided the optimum protection against autooxidation. The reaction was found to follow the zero order reaction kinetics and the K_{Obs} and t₉₀% were calculated for each formula.

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