Determination of ketoconazole in pharmaceutical formulations

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Ketoconazole is used to treat fungal infections. Ketoconazole is most often used to treat fungal infections that can spread to different parts of the body through the bloodstream such as yeast infections of the mouth, skin, urinary tract, and blood, and certain fungal infections that begin on the skin or in the lungs and can spread through the body. Ketoconazole is also used to treat fungal infections of the skin or nails that cannot be treated with other medications. Ketoconazole is in a class of antifungals called imidazoles. It works by slowing the growth of fungi that cause infection. Branded as Nizoral^{R} ketoconazole is formulated as tablets, cream and over-the-counter ketoconazole shampoo.

The aim of this research was to study and to standardize an ultraviolet spectrophotometric (UVS) method, potentiometric and a high performance liquid chromatographic (HPLC) method for the determination of ketoconazole in commercially available pharmaceutical preparations (tablets and creams). These three methods were compared and discussed with respect to their sensitivity and ready-applicability in routine analytical work.

Absorption spectra and spectrophotometric determination were carried out on a UVS spectrophotometer, in 1 cm cuvettes. The concentration of ketoconazole stock solutions was 10^{-4} mol·dm^{-3} in 0.1 mol·dm^{-3} HCl. Solutions in range of investigated concentrations were obtained by diluting of stock in range from 0.003 to 0.02 mg·dm^{-3}. The absorbance was measured at 224 nm.

Potentiometric titrations were made using glass and saturated (KCl) calomel electrode. The determined ketoconazole is dissolved in acetic acid. A solution of $HClO_4$ (0.1 mol·dm^{-3}) in acetic acid was used for titrations. Each cm^3 of $HClO_4$ (0.1 mol·dm^{-3}) is equivalent to 0.02657 g of ketoconazole.

HPLC analysis of ketoconazole, in the presence of econazole as internal standard, was performed using Ultrapac LiChrosorb RP 18 (5 μm) column, with the mobile phase consisting of 0.2% diethilamin in methanole/0.5% ammonium acetate solution (78:22); flow rate = 0.9 cm^3/min and UV detection at 224 nm.

The described methods for quantitative determination of ketoconazole in pharmaceutical preparations are simple and accurate. They can be performed directly without removing the ingredients. The differences in assay values in all methods were not statistically significant. The spectrophotometric method is recommended for quantitative determination in routine analysis. It is not only satisfactorily reproducible, but also selective with respect to the ingredients. Although, the potentiometric method cannot be considered as selective, it is rapid and reproducible enough to be used as an alternative routine method. The HPLC method is useful especially for determination of impurities and degradation products in stability studies.