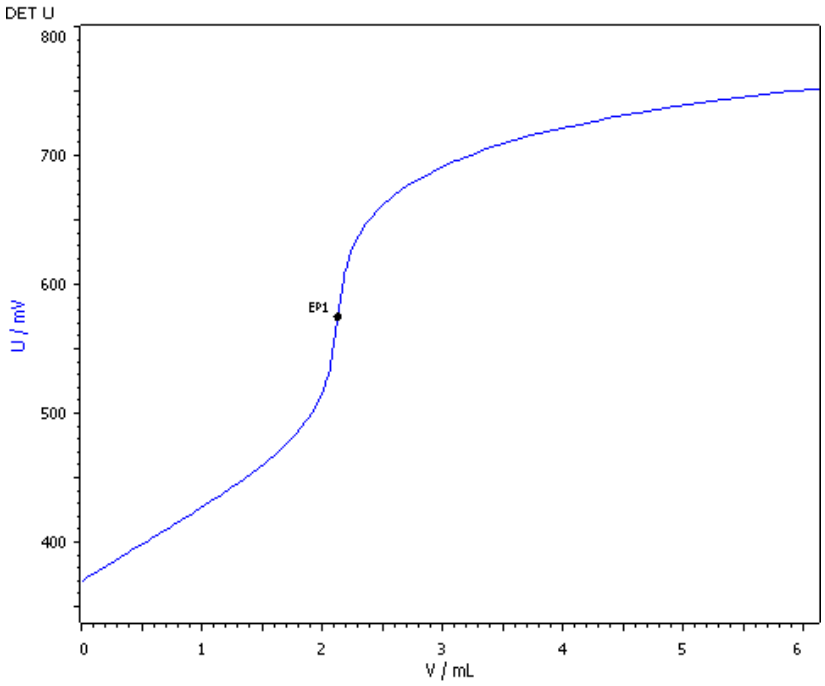
Titration Application Note T–151

Titration of ketoconazole according to Ph. Eur.



The concentration of ketoconazole was determined by nonaqueous acid-base titration using the Solvotrode easyClean according to the European Pharmacopoeia.

Metrohm

Method description

Sample

Ketoconazole, Sigma-Aldrich, (Purity ≥ 99.3 ± 0.2%)

Preparations

The Solvotrode easyClean has to be conditioned in acetic acid for 24 hours before use.

75 mL acetic acid is mixed with 175 mL ethyl methyl ketone; therein 0.57 g ketoconazole is dissolved.

Configuration

907 Titrando	2.907.0010
801 Stirrer	2.801.0040
800 Dosino, 2×	2.800.0010
50 mL Dosing unit	6.3032.250
10 mL Dosing unit	6.3032.210
Titration vessel with thermostat jacket, 5–70 mL	6.1418.150
Thermostat	Third-party device

Solutions

Titrant	Perchloric acid, c(HClO4) = 0.1 mol/L If possible this solution should be bought from a supplier.

Analysis

20 mL sample solution is pipetted into the titration vessel. Afterwards, the sample is titrated with $c(HClO_4)$ = 0.1 mol/L until after the first equivalence point. A thermostat is used during the titration, which cools the solution to 20 °C.

Additionally, before each titration, the electrode has to be conditioned in acetic acid for 5–10 min. After the conditioning, the diaphragm is rinsed by releasing 5–6 drops of electrolyte. Then, the electrode is dipped in acetic acid for about 2 seconds again.

Parameters

Measuring mode	DET U
Titration rate	Optimal
Stop volume	10 mL
EP criterion	5
EP recognition	All

Results

Mean result (n = 3)

Ketoconazole	s(rel), n = 3
99.28%	0.26%