DEVELOPMENT AND VALIDATION OF ANALYTICAL METHOD FOR MICROBIOLOGICAL QUALITY CONTROL OF KETOCONAZOLE CREAM 2%

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INTRODUCTION

Ketoconazole is a well-established antifungal active substance widely used in topical formulations, particularly 2% creams and shampoos (Franchesca D Choi et al, 2019). As a lipophilic imidazole derivative with weak basic properties (Beggs WH, 1991), it may present challenges during microbiological examination due to its intrinsic antimicrobial activity.

VALIDATED METHOD

1. ***10 g cream + 90 mL PDN***
   Primary suspension = 1:10
2. ***PDN neutralizers***
   3% Polysorbate 80 • 0.3% Lecithin
   0.1% Histidine • pH 7.0 diluent
3. ***Challenge inoculum***
   10–100 CFU/mL • duplicate tests • 3 batches
4. ***Ph. Eur. endpoints***
   TAMC / TYMC **S. aureus** **P. aeruginosa**
   2.6.12 quantitative • 2.6.13 specified microorganisms

EXPERIMENTAL DESIGN

PRIMARY SUSPENSION **1:10 IN PDN** → **INOCULATE** (P. aeruginosa, B. subtilis, S. aureus, C. albicans, A. brasiliensis) → **RECOVERY** (Compare to controls)

- **QUANTITATIVE COUNTS** — TSA 30–35°C / 3 d • SDA 20–25°C / 5 d
- **SPECIFIED ORGANISMS** — TSB 24 h → MSA / Cetrimide 24 h

VALIDATION PERFORMANCE

50-200% Accuracy — acceptable recovery	**≤ 2** Recovery factor — all microorganisms
<15% Precision — RSD repeatability	**2/2** Specified organisms — positive recovery

RESULTS & INTERPRETATION

- **SPECIFICITY** — Culture media and test conditions supported expected growth without product-matrix interference.
- **NEUTRALIZATION** — PDN effectively controlled the antimicrobial activity of Ketoconazole cream at the 1:10 dilution.
- **REPEATABILITY** — Repeated testing under the same conditions met the predefined precision criterion.

The method showed good specificity, with no interference from the product matrix and expected growth of all test microorganisms. Accuracy met acceptance criteria (recovery 50–200%; recovery factor ≤2), and precision was confirmed with repeatability RSD <15%.

CONCLUSION

METHOD SUITABLE FOR ROUTINE QC

The validated method showed no product matrix interference, and the antimicrobial activity of ketoconazole 2% cream was effectively neutralized. All challenge tests successfully recovered Staphylococcus aureus and Pseudomonas aeruginosa, confirming method suitability. The method complies with Ph. Eur. requirements and is suitable for routine microbiological quality control of the product.

Ph. Eur. 2.6.12 **Ph. Eur. 2.6.13** **Non-sterile topical product**

REFERENCE BASIS:

European Pharmacopoeia 12.0 (2025); Beggs WH (1991); Choi FD et al. (2019).

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