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POSTER COMMUNICATION · PHARMACEUTICAL INDUSTRY

# Development and optimization of an in vitro dissolution method for metronidazole and clotrimazole vaginal pessaries

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**KEY MESSAGES**

1. Surfactant-containing media are necessary for accurate in vitro dissolution testing of metronidazole and clotrimazole pessaries.
2. Phosphate buffer with Tween 80 at pH 4.5 is the most suitable dissolution medium for these combined vaginal pessaries.
3. The developed dissolution method showed comparable release profiles between test and reference products with f2 similarity values ≥ 50.

**ABSTRACT**

**Introduction.** Metronidazole is a nitroimidazole antimicrobial agent active against anaerobic bacteria and protozoa, acting through reduction under anaerobic conditions to damage microbial DNA leading to cell death. Clotrimazole is an imidazole antifungal agent with broad activity against dermatophytes, yeasts, and molds by inhibiting ergosterol synthesis and disrupting fungal cell membrane integrity and function. The combination provides broad antibacterial and antifungal coverage for mixed vaginal infections. Current pharmacopoeial quality control of pessaries includes uniformity of mass, content uniformity, disintegration, and microbiological quality but does not assess drug release behavior. In vitro dissolution testing can provide important information on formulation performance, especially for poorly water-soluble compounds such as clotrimazole. Limited information exists on suitable dissolution conditions for combined pessary formulations.

**Materials and methods.** Dissolution method development and comparative dissolution testing versus the reference product were performed according to USP <711> Dissolution. Test pessaries (metronidazole/clotrimazole 500 mg/200 mg) were manufactured by Replek Farm Ltd., Skopje, N. Macedonia; the reference product (Zifex Duo) was obtained from Antibiotice S.A., Romania. Four surfactant-containing media were evaluated to ensure appropriate sink conditions due to clotrimazole's poor aqueous solubility. Samples were analyzed using a validated analytical method for simultaneous quantification of both actives. Dissolution test conditions included USP Apparatus 2 (paddle), 75 rpm paddle speed, 900 mL medium volume, temperature 37 ± 0.5 °C, and sampling times at 15, 30, 60, 120, and 240 minutes. Dissolution media investigated were phosphate buffer pH 4.5 with 0.5% or 2.0% Tween 80, acetate buffer with 1.0% sodium lauryl sulfate (SLS), and phosphate buffer with 1.0% SLS.

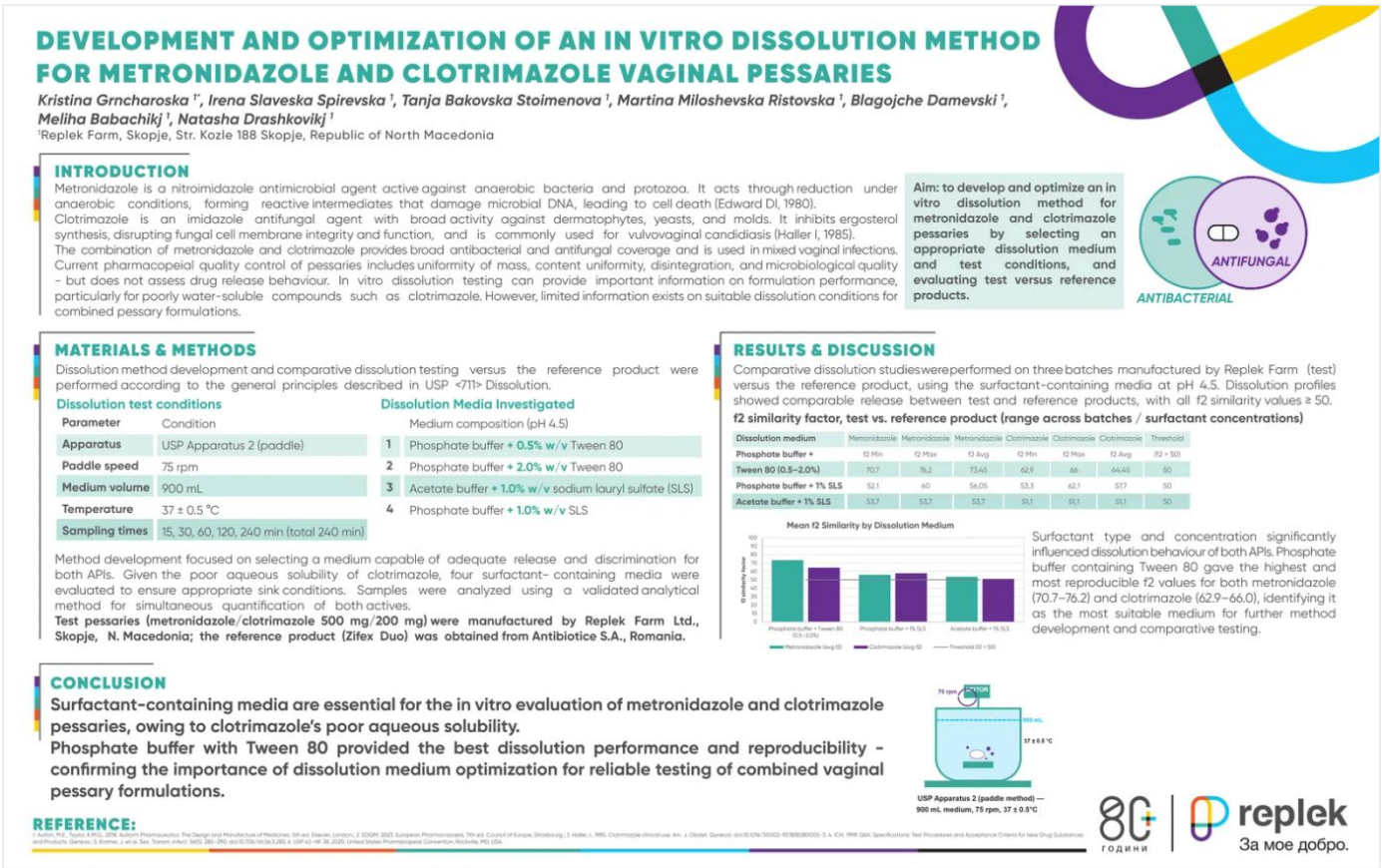
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## ABSTRACT (CONTINUED)

**Results.** Comparative dissolution studies were performed on three batches manufactured by Replek Farm (test) versus the reference product using surfactant-containing media at pH 4.5. Dissolution profiles showed comparable release between test and reference products, with all f2 similarity values ≥ 50. Phosphate buffer containing Tween 80 gave the highest and most reproducible f2 values for both metronidazole (70.7–76.2) and clotrimazole (62.9–66.0), identifying it as the most suitable medium for further method development and comparative testing. Surfactant type and concentration significantly influenced dissolution behavior of both APIs.

**Conclusion.** Surfactant-containing media are essential for the in vitro evaluation of metronidazole and clotrimazole pessaries due to clotrimazole's poor aqueous solubility. Phosphate buffer with Tween 80 provided the best dissolution performance and reproducibility, confirming the importance of dissolution medium optimization for reliable testing of combined vaginal pessary formulations.


## POSTER




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