21 Ružička days
TODAY SCIENCE – TOMORROW INDUSTRY
September 9–11, 2026 • Vukovar • Croatia

A DESIGN-OF-EXPERIMENTS APPROACH TO STUDYING THE "COFFEE RING" EFFECT IN ACTIVE PHARMACEUTICAL INGREDIENTS

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Introduction

When a droplet of a drug solution dries on a surface, outward capillary flow carries dissolved material to the pinned contact line in the well-known coffee-ring effect. The final morphology of the dried deposit, which can be a pronounced edge ring, a uniform film, a central deposit or a multi-ring pattern, depends on many coupled nonlinear factors.

Aim of this research was to replace one-factor-at-a-time experimentation with a structured Design-of-Experiments (DoE) plan that maps how process factors shape deposit morphology in active pharmaceutical ingredients (APIs) [1].

The DoE approach

FACTORS
- initial concentration c_0
- saturation ratio Σ (c_0 / solubility)
- evaporation rate (T, RH)
- droplet volume
- substrate wettability

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MORPHOLOGY RESPONSES
- rim-to-centre intensity ratio
- number and position of internal rings
- overall deposit width

Instead of varying one factor at a time, a structured experimental plan simultaneously explores the key drivers of deposit formation: initial concentration, the concentration-to-solubility (saturation) ratio, evaporation rate (set by temperature and relative humidity), droplet volume and substrate wettability, as well as their interactions, and quantifies their influence on measurable morphology responses such as the rim-to-centre intensity ratio, the number and position of internal rings and the overall deposit width (*Fig. 1*).

Two-stage strategy

1 SCREENING
A fractional-factorial or Plackett–Burman design identifies the dominant factors and their interactions from a minimal number of experiments.

2 RESPONSE SURFACE
A central-composite or Box–Behnken design builds a predictive model Y = f(x) and locates the conditions giving a target morphology.

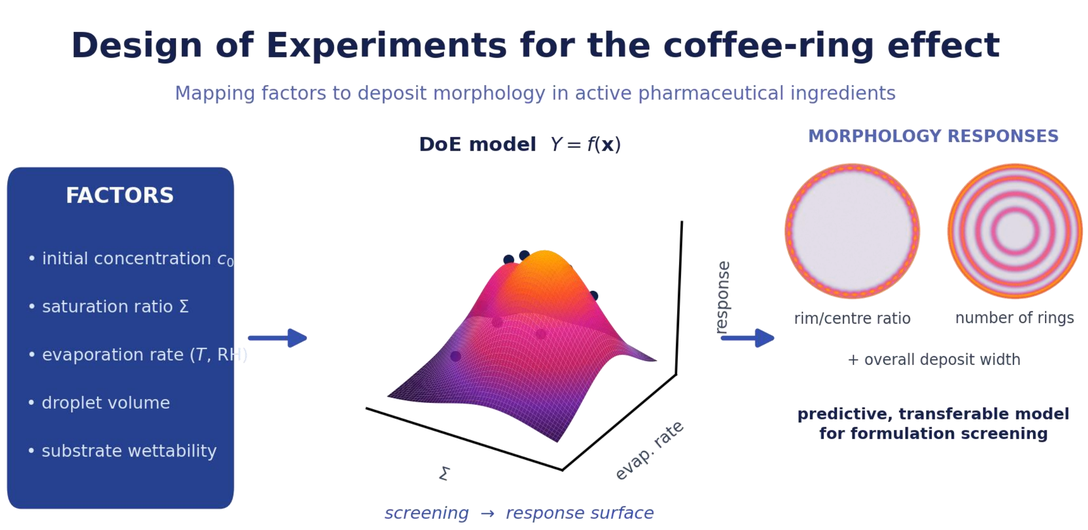

Fig. 1 DoE workflow: factors → empirical response-surface model → morphology responses.

References [1] E. Meštrović, K. Čemerin, T. Mlinarić, I. Rezić, Coffee ring effect in synergy with copper nanoparticles for sustainable future of industrial processing, in: Book of Proceedings of the 17th Scientific–Professional Symposium and 7th International Scientific–Professional Symposium Textile Science & Economy, University of Zagreb Faculty of Textile Technology, Zagreb, 2025, pp. 48–55.

Indomethacin: effect of pH

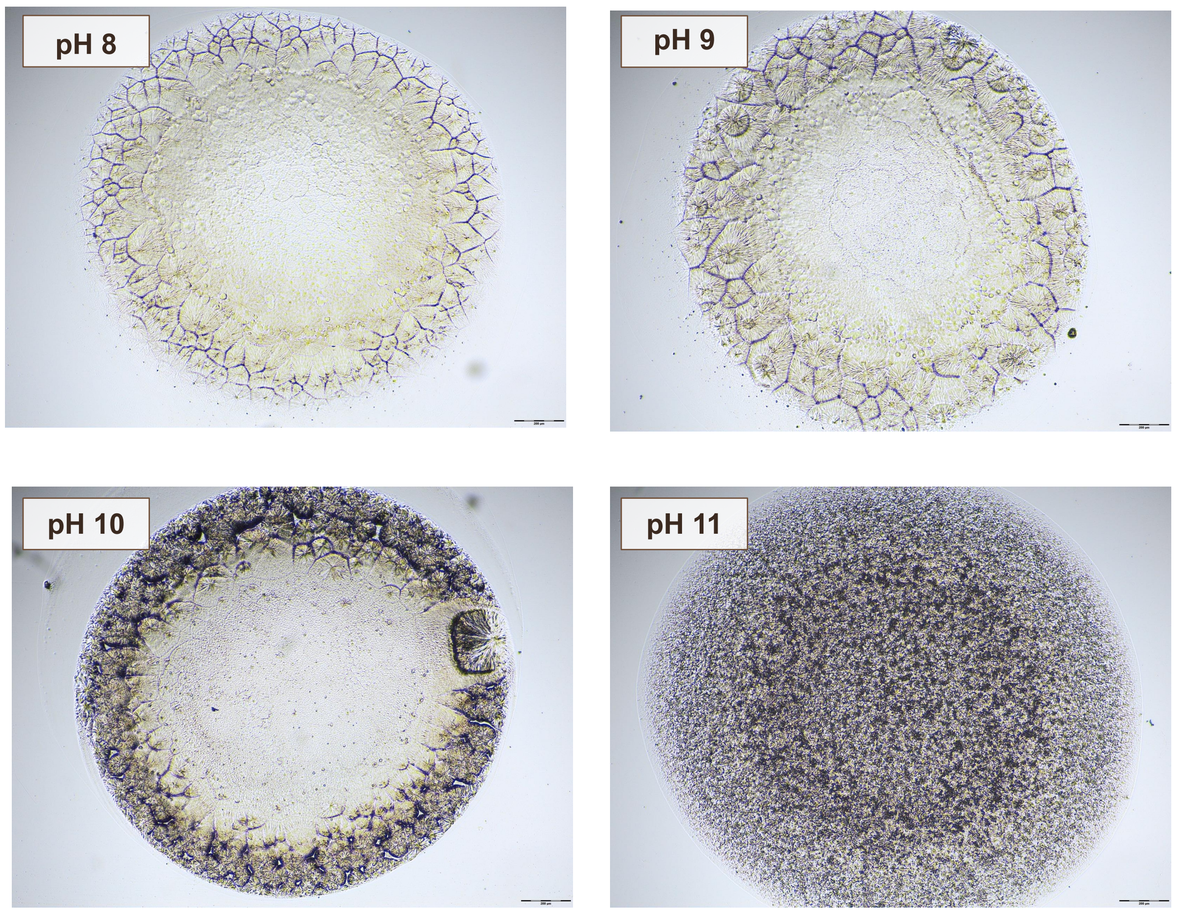

Fig. 2 Dried indomethacin droplet deposits at pH 8–11: from a cracked, gel-like ring network (pH 8–9) to a pronounced edge ring (pH 10) and an almost uniform dense deposit (pH 11).

Sugammadex: effect of concentration

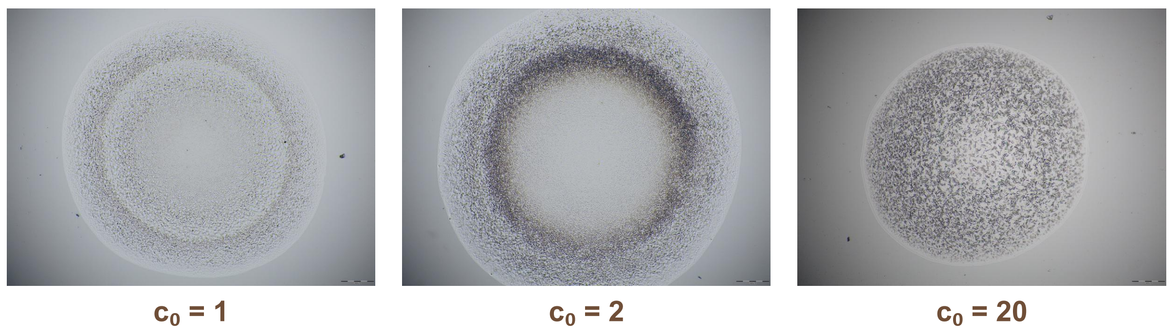

Fig. 3 Sugammadex deposits at increasing relative initial concentration (1 : 2 : 20): a faint double ring evolves into a pronounced coffee ring and finally a dense, nearly uniform deposit.

A two-stage strategy is outlined: an initial screening design (fractional-factorial or Plackett–Burman) identifies the dominant factors and interactions, followed by a response-surface design (central-composite or Box–Behnken) that builds a predictive model and locates the conditions giving a target morphology. This approach extracts maximum information from a minimal number of experiments (*Fig. 2)*, makes factor interactions explicit and yields a statistically grounded, transferable model, offering an efficient route to the rational control of evaporation-driven deposition in pharmaceutical formulation screening (*Fig. 3)*.

Conclusions

- Deposit morphology of APIs responds strongly to solution conditions such are pH value (Indomethacin) and initial concentration $c_{0.}$ (Sugammadex) already span the whole ring-to-uniform spectrum.
- A two-stage DoE (screening → response surface) enables extracting maximum information from a minimal number of experiments and makes factor interactions explicit.
- The outcome is a statistically grounded, transferable predictive model of evaporation-driven deposition.
- An efficient route to rational morphology control in "Lab-on-a-Chip" pharmaceutical formulation screening.

Acknowledgments

This work was supported by the Croatian Science Foundation (HRZZ) through the project IP-2024-05-4339 "'Coffee ring' effect in 'Lab on a Chip' environments in the development of new drug formulations" (Core4Pharm).