Contribution ID: **39** Type: **not specified**

Quality by Design (QbD) and Analytical Quality by Design (AQbD): A Holistic Approach to Pharmaceutical Quality

Thursday, 29 May 2025 11:30 (20 minutes)

The Quality by Design (QbD) approach has been widely adopted in the development of both novel and generic pharmaceutical formulations1. Extending these principles to the analytical domain, Analytical Quality by Design (AQbD) has emerged as a structured framework for optimizing analytical methodologies2. The aim of the present work was to outline a comprehensive framework for development of a texture analyzer-based mucoadhesion method integrated with rheological analysis for the evaluation of ointment formulations3. The ATP was carefully defined for the mucoadhesion method, taking into account both preliminary studies and method requirements. The AQbD approach facilitated the identification of key sources of variability affecting Critical Method Variables (CMVs). Using this methodological framework, critical analytical attributes (CAAs) such as peak force (adhesiveness), work of adhesion (the area under the force/distance curve), and debonding distance were systematically investigated. Optimal conditions were determined using response surface methodology within the Method Operable Design Region (MODR). The study implemented a three-factor, three-level Box-Behnken design (BBD), a widely accepted design of experiments (DoE) approach for exploring quadratic response surfaces and developing second-order polynomial models. The determination coefficients showed that the quadratic model effectively represented these response variables, confirming its predictive power. The root mean square error values for peak force (0.25) and work of adhesion (1.54) indicate minimal deviation between observed and predicted values. However, the model showed less robustness for the debonding distance response, with an R^2 of 0.24, explaining only 24% of variability. The RMSE of 44.63 indicates high variability, but remains within an acceptable range for this response parameter. The final optimized conditions—2 N applied force, 60 seconds contact time, and 0.05 N trigger force—were established to ensure compliance with the predefined ATP. The incorporation of mucin dispersion into the method showed significant rheological synergism, validating the robustness of the optimized method. Furthermore, compliance with ICH guidelines confirmed the method's reproducibility and reliability4. Overall, this study demonstrates the successful application of AQbD principles in the development of a mucoadhesion assessment method that integrates texture analysis and rheology to optimize the evaluation of ointment formulations. The use of a Box-Behnken design allowed for systematic optimization, ensuring robust, reproducible, and analytically sound results, thereby strengthening the credibility of AQbD-driven analytical methods.

Acknowledgements

Lucas Chiarentin acknowledges the research grants PD/BDE/150717/2020 and COVID/BDE/153661/2024 assigned by FCT (Fundação para a Ciência e a Tecnologia) and Laboratórios Basi, from Drugs R&D Doctoral Program. The authors also thank UCQFarma for making available the Haake MARS 60 Rheometers (Thermo Scientific, Karlsruhe, Germany). Moreover, we also acknowledged Coimbra Chemistry Center (CQC), supported by FCT, through the project UID/QUI/00313/2020.

References

1.Thorsten, V. et al. Analytical Quality by Design, Life Cycle Management, and Method Control. AAPS PharmSciTech 24, 1–21 (2022).

2.Chiarentin, L. et al. Drilling into "Quality by Design"Approach for Analytical Methods. Crit. Rev. Anal. Chem. 0, 1–42 (2023).

3.Chiarentin, L., Moura, V. & Vitorino, C. Mucoadhesion and rheology characterization in topical semisolid formulations: An AQbD-driven case study. Int. J. Pharm. 673, 125389 (2025).

4.Analytical procedure development - ICH (Q14). at https://database.ich.org/sites/default/files/ICH_Q14_Document_Step2_Guideline_202 (2024).

Type of presentation

Contributed Talk

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Session Classification: Session

Track Classification: Spring Meeting