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Short communication

Integration of sensor-based technologies and PAT-oriented analysis for real-time assessment of curing processes in pharmaceutical manufacturing

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Introduction

Modern pharmaceutical manufacturing increasingly relies on digitalization, Quality by Design (QbD), and Process Analytical Technology (PAT) to improve process understanding, quality assurance, and continuous process verification. Sensor-based technologies provide real-time process data and support implementation of PAT principles through continuous evaluation of process behavior and quality-related outcomes (Kim et al., 2021).

Environmental conditions during curing may significantly influence moisture content, microbiological quality, overall product stability, and water activity, which represents an important quality indicator associated with product stability and microbial control (Prada-Ramirez et al., 2024). Unlike conventional end-product testing, PAT-oriented approaches facilitate process understanding through continuous monitoring of process variables and their relationship with Critical Quality Attributes (CQAs) (USFDA, 2004).

This study presents the integration of sensor-based monitoring technology for real-time assessment of curing operations in pharmaceutical manufacturing.

Materials and methods

Dried cannabis inflorescences for medical use obtained from an EU-GACP and EU-GMP compliant production system were used in this study.

A sensor-based monitoring technology was integrated into the curing process. Dedicated sensors installed within the headspace of individual curing units continuously monitored headspace temperature, relative humidity (RH), and CO_2 concentration in the immediate environment surrounding of the product as process variables.

PAT-oriented analysis was applied to evaluate process behavior and assess the influence of monitored process variables on CQAs, including water activity (aw), loss on drying (LOD), total aerobic microbial count (TAMC), total yeast and mold count (TYMC), and absence of specified microorganisms.

Pharmaceutical process validation was performed on three consecutive batches of the same potency class. Microbiological testing and LOD determination were conducted according to European Pharmacopoeia requirements (EDQM, 2023).

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Results and discussion

Continuous sensor-based monitoring generated high-resolution datasets for headspace CO_2 concentration, relative humidity, temperature and water activity throughout the curing process.

Trend analysis demonstrated a gradual reduction in headspace CO_2 concentrations from approximately 900-1050 ppm at the beginning of curing to 400-700 ppm at the end of the process, indicating progressive stabilization of the curing but environment within individual curing units.

Water activity remained stable throughout the curing process, ranging from 0.53-0.62, thereby maintaining conditions indicative of adequate product stability. LOD values showed limited variability (6.6–7.8%) and consistently complied with the European Pharmacopoeia specification (NMT 12.0%), demonstrating effective moisture control and reproducible process performance across all validation batches. Furthermore, consistent results between sampling locations (top, middle and bottom) confirm uniform moisture distribution throughout the curing units.

The results of microbial testing demonstrated compliance with the applicable Ph.Eur requirements throughout the validation. Total aerobic counts (TAMC) and total combined yeasts and molds count (TYMC) remained substantially bellow the established acceptance limits, while Escherichia Coli and Salmonella spp. were absent in all analyzed samples. The maintained environmental conditions, together with controlled water activity and consistent LOD values, were associated with sustained microbiological compliance throughout the curing process.

Collectively, the observed CO_2 trends, controlled water activity profile, consistent LOD values and microbiological compliance provided enhanced process understanding and supported verification of CPPs associated with consistent product quality.

Furthermore, the implementation of continuous sensor-based monitoring enabled data-driven assessment of curing performance and demonstrated the applicability of PAT principles for improved in-process control in pharmaceutical manufacturing.

Conclusion

Integration of sensor-based technologies and PAT-oriented analysis represents an innovative approach for real-time assessment of curing processes in pharmaceutical manufacturing.

Continuous monitoring of headspace conditions enerated a high-resolution process data enabling better process characterization and supporting verification of CPPs relevant to product quality.

The presented approach highlights the value of integrating sensor-based monitoring and PAT oriented evaluation into pharmaceutical technologies as means of supporting process robustness, digital transformation and science-based decision making. To the best of our knowledge, this represents one of the first applications of integrated headspace continuous monitoring of temperature, relative humidity and CO_2 combined with PAT-oriented process evaluation for curing operations in pharmaceutical manufacturing in Republic of North Macedonia.

References

European Directorate for the Quality of Medicines & HealthCare, 2023. European Pharmacopoeia, 11th ed. Council of Europe, Strasbourg. https://www.edqm.eu/en/

Kim, E.J. et al., 2021. Process analytical technology tools for monitoring pharmaceutical unit operations: a control strategy for continuous process verification. Pharmaceutics 13, 919. https://doi.org/10.3390/pharmaceutics13060919

Prada-Ramírez, H.A. et al., 2024. Stability study through water activity measurements for pharmaceutical and biological materials. AAPS PharmSciTech 25, 52. https://doi.org/10.1208/s12249-023-02719-2

United States Food and Drug Administration, 2004. PAT — A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance. Guidance for Industry. United States Food and Drug Administration, Silver Spring. https://www.fda.gov/media/71012/download