AVANTES
MEMBER OF THE NYNOMIC GROUP

RUTGERS UNIVERSITY CASE STUDY

EVALUATING AVANTES SPECTROMETER PERFORMANCE FOR MONITORING API DISSOLUTION IN CONTINUOUS PHARMACEUTICAL MANUFACTURING

INTRO

API DISSOLUTION MONITORING WITH AVANTES SPECTROSCOPY INSTRUMENTS

Significant technological advancements mark the current state of dissolution testing in pharmaceutical manufacturing to improve efficiency, precision, and reliability. Traditional methods, which involve manual sampling and offline analysis, are significantly enhanced by advanced real-time monitoring techniques. Fiber-optic probes and real-time data acquisition systems have become crucial tools, providing continuous and accurate results without needing or requiring sample extraction. These innovations allow for rapid and automated measurements, essential for capturing fast and small changes significant in pharmaceutical manufacturing.

One significant study evaluated the performance of an in-situ UV fiber optic system for monitoring the dissolution of efavirenz tablets in various biorelevant media. This study demonstrated that the in-situ method provided precise and continuous drug release profiles, reducing labor intensity and the potential for human error compared to traditional manual sampling methods.[1]

Signal saturation at high absorbance levels can impede real-time assessment and lead to inaccurate dissolution profiles. However, linear PLS and PCR models could effectively overcome UV signal saturation.[2] In cases where suspensions are small enough, second-derivative UV spectroscopy has been shown to be an effective tool for characterizing the dissolution behavior of nanocrystal formulations in real-time. Additionally, in-situ monitoring has proven feasible for dissolution processes occurring within seconds, which cannot be easily tested by current methodologies.[3]

The integration of fiber-optic probes and improvements in optical sampling into dissolution testing show significant potential to enhance the precision, efficiency, and reliability of drug release monitoring. These innovative approaches modernize dissolution testing and improve pharmaceutical manufacturing quality control and validation processes.

NIR CALIBRATION DOE – CAFFEINE LD IR FORMULATION

FEEDERS

CONTINUOUS BLENDER

TABLE PRESS

TABLES PREPARED IN A CONTINUOUS MANUFACTURING LINE AT RUTGERS UNIVERSITY

TEST RUNS:

- 3 Factor
- 3 Level (API, Surfactant, Compaction Force)
  1. API: 3, 5, and 7 %w/w
  2. Surfactant: 2.5, 5.0, and 7.5 %w/w
  3. Comp force: 5, 10, and 15 kN

ID	Caffeine	PLX 188	M200	CCS	MgSt
1	1.00	9.00	87.30	2.30	0.37
2	3.66	1.00	90.30	3.30	1.70
3	6.33	9.00	80.20	3.06	1.38
4	9.00	1.00	87.40	2.26	0.30

AVANTES INSTRUMENTS USED

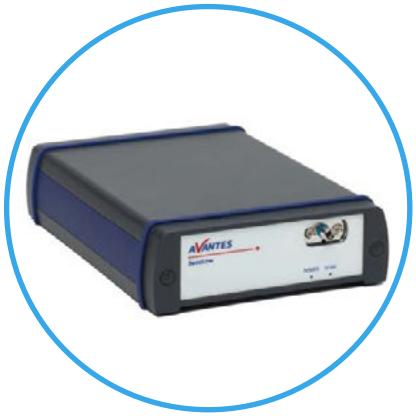
Transmission Dip Probe

- Uses 2x 600um fibers (1 to illuminate, 1 to read).
- 600 micron core fibers
- Stainless steel 316 tip , 121 mm long x 6.4 mm diameter.
- Replaceable tip with various optical pathlengths 1, 2, 5, 10 mm.
- Suitable for dissolution testing, absorbance measurements.
- For use with AvaLight-DHS, Avalight-DHc or AvaLight-HAL-S-Mini light sources.
- Can be used with VIS or NIR spectrometer(200-2500 nm).

600 µm fiber

Light Source: AvaLight-DH-C

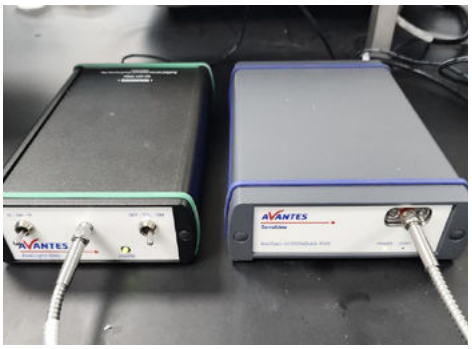
- Deuterium + Halogen source (200-2500 nm)
- 0.2 µW UV deuterium + 7µW VIS/NIR tungsten halogen; individually controllable sources TTL shutter
- Can be used with any UV/VIS or NIR spectrometer.
- Ideal for probe and cuvette absorbance measurements.

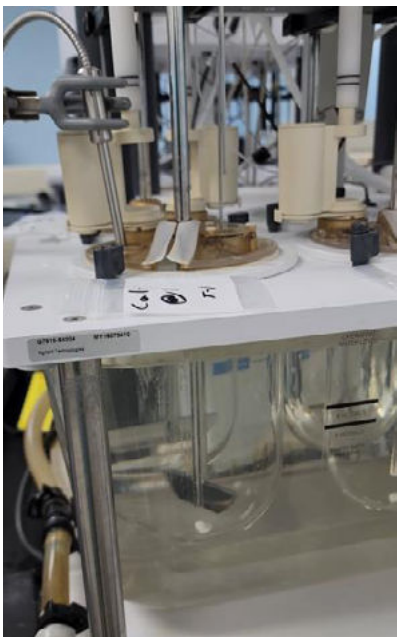


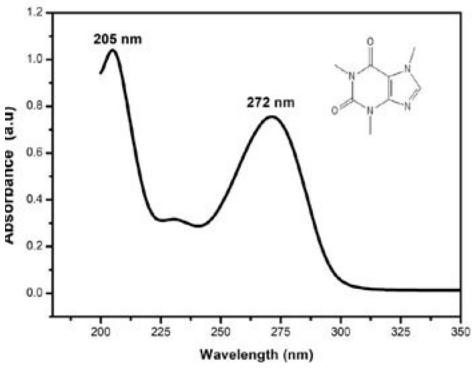
Spectrometer: Avaspec-ULS2048X64-EVO

- UV/VIS (200-1160nm)
- Linear variable order sorting filter
- Replaceable slit (10, 25, 50, 100, 200 micron)
- 2048 pixel ultra-high sensitivity back-thinned CCD detector
- USB3.0 or gigabit ethernet communication
- Digital/analog I/O

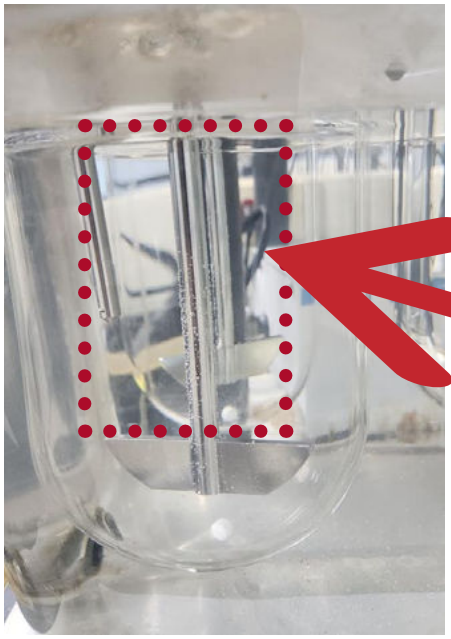
SETUP FOR MONITORING DISSOLUTION OF CAFFEINE TABLETS

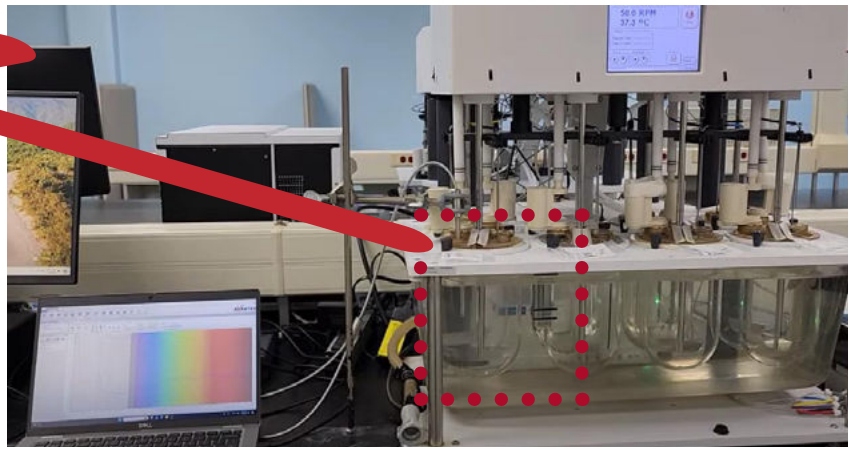


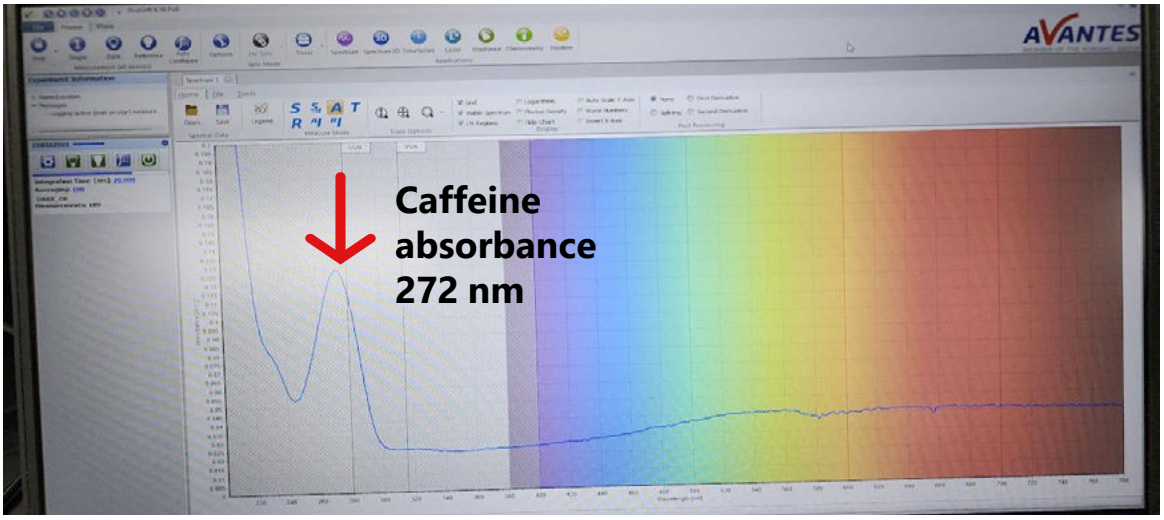




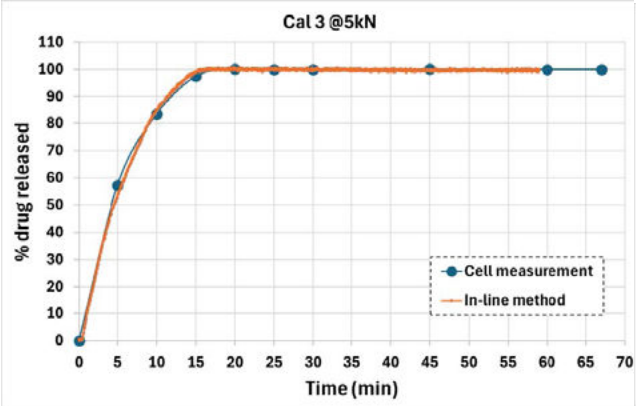
Published caffeine spectrum: D'Souza, Joyce Q., and Nalini G. Sundaram. "UV induced photocatalytic degradation of caffeine using TiO2–H-beta zeolite composite." Minerals 13, NO. 4 (2023): 465.

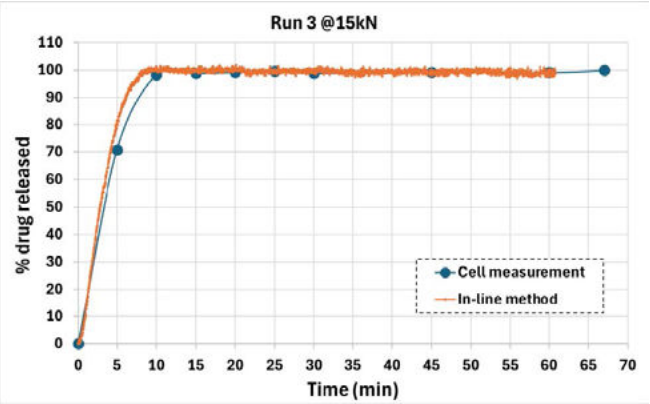


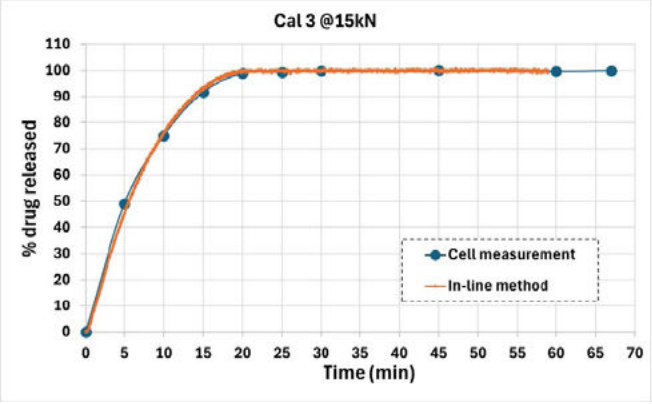


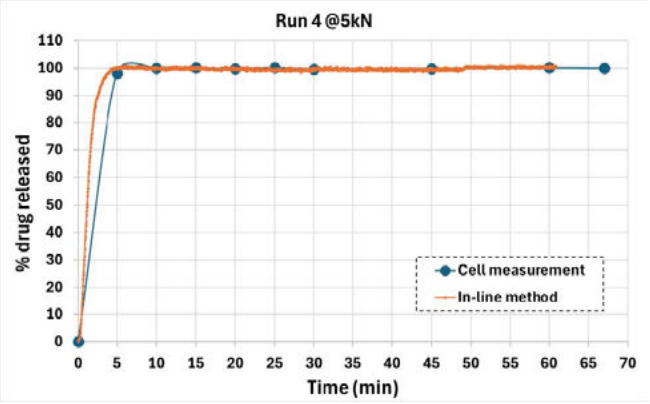


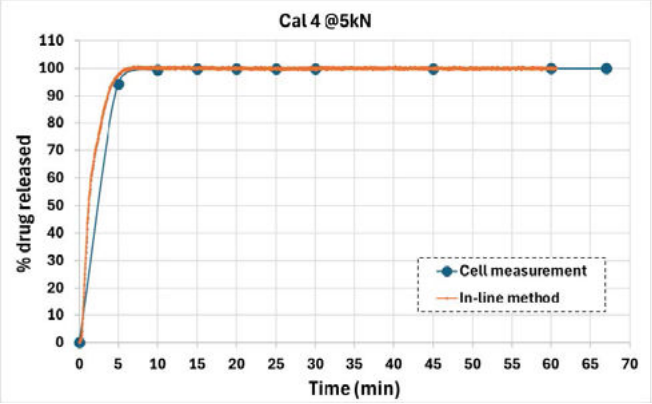
DISSOLUTION PROFILES OF CAFFEINE TABLETS

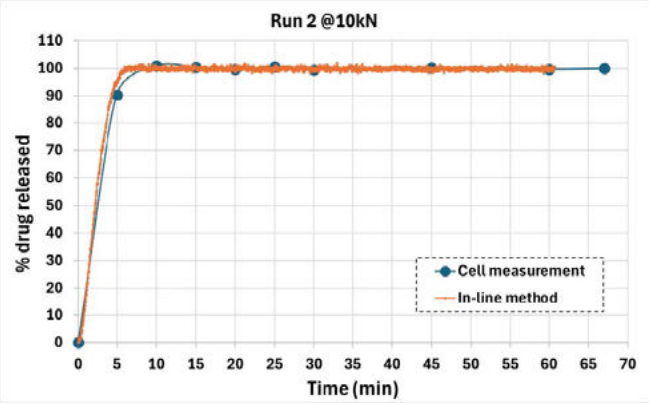


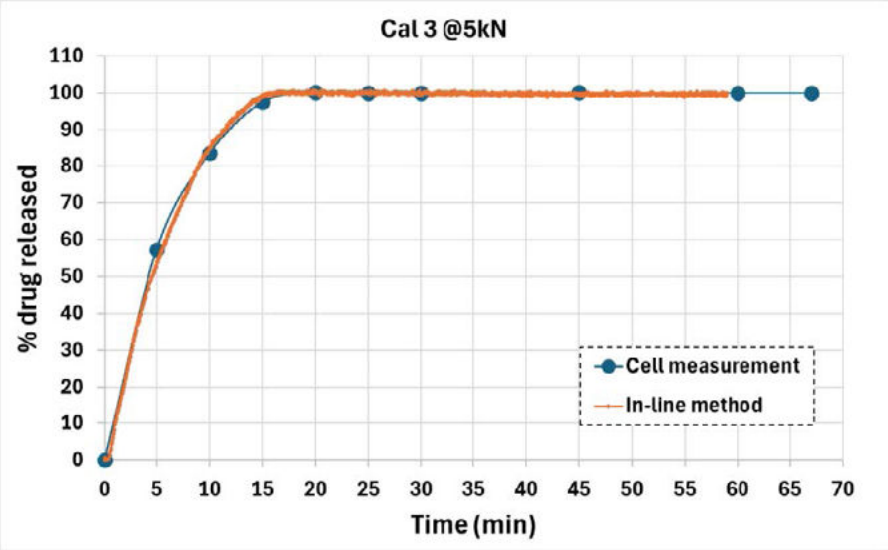












CONCLUSION

In conclusion, inline monitoring using Avantes instruments during the dissolution test proved to be effective, yielding results comparable to those obtained with conventional and more expensive methods. The initial minutes of the process could be monitored with high accuracy, showcasing the feasibility of detecting rapid changes. This capability suggests the potential for monitoring multiple vessels simultaneously using a multiplexer. Future studies will focus on extending this monitoring approach to non-clear samples.

REFERENCES AND FURTHER READING

1. Thalita Martins da Silva et al., "Comparison of Efavirenz Release in Biorelevant Dissolution Media Using Manual Sampling and In Situ UV Fiber Optic System," Dissolution Technologies, August 2021.

2. Sardhara, R., Chaturvedi, K., Shah, H. S., Vinjamuri, B. P., Al-Achi, A., Morris, K. R., & Haware, R. V. (2021). "Predictive performance comparison of computed linear and quadratic multivariate models for in-situ UV fiber optics tablet dissolution testing." European Journal of Pharmaceutical Sciences, 161, 10580).

3. Imono, M., Uchiyama, H., Ueda, H., Kadota, K., & Tozuka, Y. (2019). In-situ dissolution and permeation studies of nanocrystal formulations with second-derivative UV spectroscopy. International Journal of Pharmaceutics, 558, 242-249. https://doi.org/10.1016/j.ijpharm.2018.12.086)

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Curious how spectroscopy will help you reveal answers by measuring all kinds of material in-line, at your production facility, in a lab, or in the field? Visit our website or contact one of our technical experts.
We are happy to help you!

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