Evaluation of In-situ UV Fibre Optic Arch Probe vs. traditional offline LC-UV analysis for 'real-world' dissolution studies

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Background

In-situ UV fibre optic arch probes (see Figure 1) are designed to enable the generation of real-time dissolution profiles. Claimed advantages over traditional manual sampling and LC-UV analysis method: *1)* produce more frequent data points; *2)* less labour intensive (1). These advantages could potentially increase work productivity and improve data quality in formulation screening and dissolution testing. However, in-situ UV measurement without filtration can be challenging due to light scattering effects of particulates and background absorbance of dissolution media. Mathematical "filters" including baseline correction can be used to overcome these challenges (1). Recent software advances have enabled multicomponent analysis (MCA) of samples containing multiple interfering components within the same UV spectral region (2). Majority of published examples have been conducted in simple buffers or water. Here, we evaluate the suitability of the fibre optic arch probes for dissolution testing in complex media and in the presence of insoluble excipients. Testing the method with 'real world' examples is of value to those working in the field.

Figure 1: *Arch probe, 10mm pathlength*

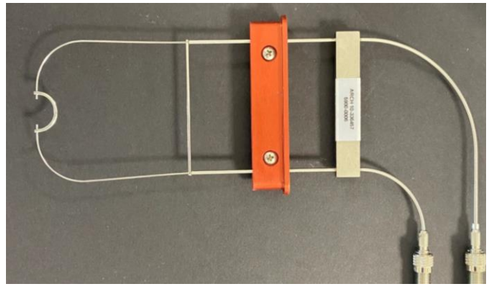


Figure 2: *Arch probe in a vessel*

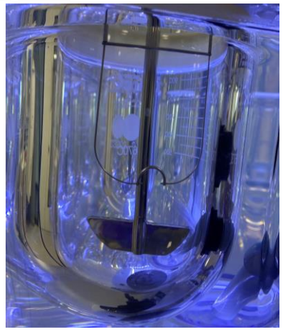


Figure 3: *Overall image of 6 arch probes in each vessel with fibre optic cables connected to a PC*

Objective

1. To examine suitability of in-situ UV fibre optic arch probe analysis for measurement of API dissolution under the following conditions:
   - In commonly used **complex media** i.e., FaSSIF, Triton X100, FeSSGF.
   - In the presence of commonly used **excipients** i.e., D-α-Tocopheryl polyethylene glycol (TPGS) and Gelucire 44/14.
   - From an API blend containing **particulates** i.e., calcium phosphate (CP), microcrystalline cellulose (MCC).
   - **Complex experimental method**: pH shift dissolution with the addition of FaSSIF to 0.1M HCl during dissolution run.
2. To understand **data quality** and **labour-saving** potential of using UV arch probe vs. the traditional method.

Method

Dissolution runs were conducted in Distek 2500 RTD, USP 2 (Figure 2,3). Caffeine Pro Plus (50 mg) were used in complex media dissolutions. Caffeine powder (99.7%) was used to produce API blend/mixture, with CP, MCC, TPGS or Gelucire, filled in Quali-G Capsules Size 1 and dissolution was conducted in pH 6.5 media. Opt-Diss 410 (Distek) was used with 10 mm (Figure 1) or 2 mm (Triton only) pathlength. 36 readings were taken across 60 minutes with 4 scans each (n=3). For comparison, manual samples (1mL) were taken at 5 timepoints for offline LC-UV analysis following centrifugation. Caffeine standards were prepared in respective media to match sample composition. Data analysis was conducted with suitable baseline correction applied to UV arch probe data and compared against data generated from LC-UV.

Results and Discussion

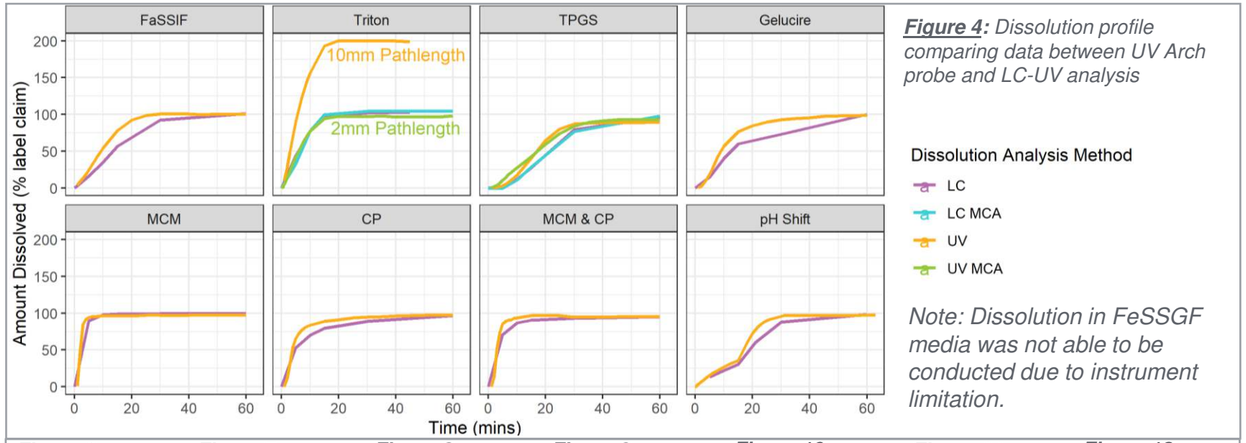


Figure 4: *Dissolution profile comparing data between UV Arch probe and LC-UV analysis*

Note: Dissolution in FeSSGF media was not able to be conducted due to instrument limitation.

Figure 6: *Triton UV (10mm)*

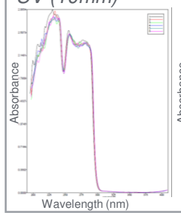


Figure 7: *Triton UV (2mm)*

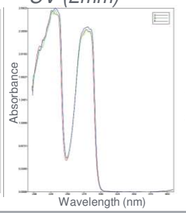


Figure 8: *Triton & caffeine UV (10mm)*

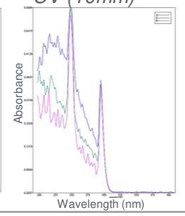


Figure 9: *Triton & caffeine UV (2mm)*

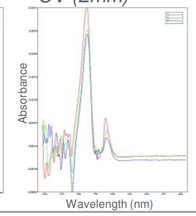


Figure 10: *TPGS UV (10mm)*

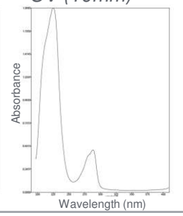


Figure 11: *FeSSGF UV (2mm)*

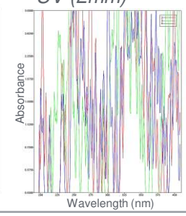
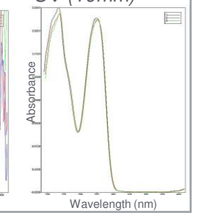


Figure 12: *Caffeine UV (10mm)*



- Similar dissolution profiles in UV arch probe and LC-UV for all media except Triton and FeSSGF (Figure 4).
- Overlapping absorbance spectra seen in Triton media (Figure 6) and TPGS (Figure 10) with caffeine (Figure 8, 12). MCA and/or use of a shorter pathlength have successfully circumvent these issues (Figure 7 and 9).
- MCA involves lengthy preparation and UV scanning of 5 different standard mixtures of components with different ratios.
- UV arch probe is unsuitable for opaque media e.g. FeSSGF (1:1 ratio of buffer with whole milk) (Figure 11).

Conclusions

We have demonstrated suitability of in-situ UV fibre optic arch probes for early formulation screening applications including those with insoluble excipients, and generated data of appropriate quality in a less labour-intensive manner compared with offline LC-UV analysis. In addition, where more complex media or interfering excipients are used, there are innovative ways of using MCA with careful experimental design to circumvent these issues without the need for chromatographic separation (with the exception of opaque media for which UV arch probe is not suitable). However, due to the preparation of multiple standards and data processing required for MCA, the time/labour efficiencies are less pronounced in early development/screening applications but may be of value in a more routine analysis/QC environment.

References

1. http://dx.doi.org/10.14227/DT250318P70
2. Kielt, A., et al. (2016) 'Analysis of Two Active Pharmaceutical Ingredients (API) Products Using UV Spectrophotometry with Multi-Component Analysis and a Fiber Optic Dissolution Analyzer' *American Pharmaceutical Review*, pp.67-69.