The determination of drug tablet concentration in pharmaceutical applications for drug development using the Agilent Cary 60 UV-Vis with fiber optics

Application Note

Pharma

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Note: All of this work was conducted under controlled conditions in a GMP laboratory within a leading global pharmaceutical manufacturing company.

Summary

The Agilent Cary 60 UV-Vis spectrophotometer is the new, improved successor to the award-winning Cary 50. This instrument platform is used in a plethora of applications, including the online dissolution and analysis of pharmaceutical dosage forms. This document highlights some key benefits of using the Cary 60 in pharmaceutical applications for drug development and production in terms of time and cost savings. Specifically, the approach described in this application note may be of significant benefit for pharmaceutical applications where an *in situ* measurement system, with essentially real-time results could improve productivity and dissolution profile information.

Introduction

In the pharmaceutical industry, dissolution is an essential tool to determine the biopharmaceutical quality of solid dosage forms. Essentially, the process involves placing the dosage form (i.e., tablets or capsules) in a set of vessels and agitation components contained within the dissolution apparatus. This simulates conditions within the gastro-intestinal tract and, as samples are pulled at specific timepoints, the charting of the release of the active pharmaceutical ingredient (API) from the dosage form is determined by UV-Vis spectroscopic measurement.

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In this short review, the benefits that taking *in situ* measurements using fiber optics can have for drug development are explored and potential cost savings are discussed. In this instance, concentration measurements of manufactured tablets of anti-malarial API were taken. This antimalarial compound belongs to the chemical class of naphthalenes.

Apparatus and materials

Part Number	Description
G6860AA	Cary 60 UV-VIS Spectrophotometer, PC & Software
7910029900	Torlon fiber optic probe
G6866A	Torlon fiber optic probe coupler

Methods and results

Methods were adapted in-house from those described in British Pharmacopoeia 2011[1].

The Cary 60 instrument was fitted with the fiber optics coupler and Torlon probe. A blank reading was taken using 10 mL of isopropanol. Six standard solutions of anti-malarial API were prepared from zero to 300 mg/mL in isopropanol. Using the Concentration module in the WinUV software, the standards were sequentially read using the fiber optic probe, resulting in a linear concentration curve as shown in Figure 1. Finally, the concentration of the anti-malarial API sample in the dissolution bath was determined using the WinUV software, as shown in report in Figure 2. The WinUV software contained the 21 CFR part 11 module that assists with meeting regulatory requirements.

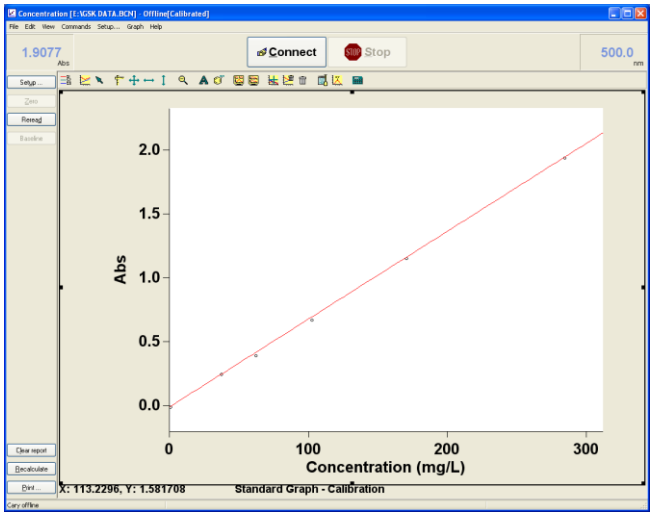

Figure 1. Concentration curve for anti-malarial API standards. Calibration equation: Abs = 0.00688*Conc -0.01056; correlation coefficient= 0.99976. The dissolution bath was used to facilitate the dissolution to completion, and the sample was analysed for total dissolved active ingredient after time, The concentration measurement of the unknown sample was made at the end of the dissolution reaction.

Analysis

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Sample	Concentration mg/L	Readings (Abs)
Original anti-malarial API	282.3	1.9312
Duplicate	280.7	1.9200
Triplicate	281.2	1.9238
Mean	281.4	1.9250
	SD =0.0057; %RSD = 0.29583	

Figure 2. Concentration curve parameters transcribed directly from the WinUV Conc software for the concentration curve shown in Figure 1. Data show three independent replicates of an unknown sample of anti-malarial API following being analyzed for total dissolved active ingredient in an Agilent dissolution bath. The data demonstrates the excellent reproducibility of the Cary 60 fiber optics instrument platform,

Discussion

Data given in Figures 1 and 2 demonstrate that the performance of the Cary 60 instrument fitted with fiber optics was almost perfectly linear (correlation coefficient = 0.99976) over the absorbance range 0–2 Absorbance units. Moreover, results also showed excellent reproducibility in determining the concentration of the three unknown anti-malarial API samples. This level of performance is critical in pharmaceutical applications such as this, since the data is ultimately used to determine the precise concentration of active drug in manufactured tablets.

Conclusions

1. The instrument platform can save time by streamlining dissolution processes in drug development by virtue of fiber optics. This permits sample measurement *in situ* and alleviates the need for external UV-Vis analysis away from the dissolution work station, with no compromise in the quality of data generated. Because the sample is read *in situ*, the sampling time points can be faster than can be achieved with conventional sample transfer systems.

   As evidenced in the data presented in this document, this *in situ* approach may be of significant fiscal benefit to pharmaceutical organizations where a comparatively low number of samples are analyzed that do not perhaps justify purchase and validation of fully automated systems. For those applications that require the handling of larger numbers of samples, Agilent manufactures an automated fiber optic dissolution system. This is an extension of the application discussed in this document and provides users with the options for not just increased sample throughput, but also the opportunity to take measurements unattended over the course of analyses.

2. Versatile, 21 CFR part 11 capable software assists in compliance with regulatory requirements at all times for pharmaceutical manufacture.

[1] British Pharmacopoeia 2011 online; British Pharmacopoeia Volume III; *Formulated Preparations: Specific Monographs.*

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