

Automated Dissolution of Prednisone with the MultiDose G3

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Introduction

Prednisone is commonly used in laboratories as a dissolution bath calibrator. Manual dissolution is a very time intensive process; hence automation of this technique is highly desirable. In this study, the MultiDose G3 Workstation is used as a tool to automate the dissolution process by heating the media, filling vessels, dropping tablets, timing the dissolution process and sampling at the appropriate intervals. In addition to reducing the hands-on time involved in dissolution, the MultiDose G3 Workstation provides a 21CFR Part 11 compliant documentation of the automated dissolution process. The objective of this study is to determine the equivalency between manual dissolution sampling and analysis and automated dissolution sampling and analysis using the Prednisone calibrator tablet.

Materials and Methods

Instrumentation

All testing was performed using a MultiDose G3 Workstation (Caliper Life Sciences) and VK7000 dissolution bath (VanKel) with paddles and on-line MultiFill batch collection of samples in 16 x 100 test tubes. Off-line UV analysis was used to analyze the solutions with an 8453 UV/Vis Spectrophotometer (Agilent) with 1.0 cm cells.

Reagents and Standards

DI water was used for the dissolution media. The Prednisone standard Lot M was prepared according to the USP specification. The study was run using disintegrating USP Prednisone 10-mg tablets, Lot M.

The manually sampled solutions were filtered by drawing 10 mL of sample solution through a 35 mm VanKel Full Flow Filter. For the automated sampling, a Millipore Automation Certified 1.0 mm glass fiber filter is used.

MultiDose G3 Settings

The MultiDose G3 settings used to be consistent with the manual method are described in Table 1.

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MultiDose G3 Settings

Media Storage Temperature	37° C
Auxiliary Media	yes
Dissolution Media	DI water
Density of Dissolution Media	0.9982 g/mL
Media Tank Degas	15 minutes
Number of Sampling points	1
Sampling Pump Flush Volume	30 mL
Filtration Flow Rate	12 mL/min
Total Run Time	30 minutes
Hot Wash Stage 1 and 2	1 cycle of each
Line Clean Vessel Volume	550 mL
Line Wash Volume	100 mL, 1 cycle

Vankel 7000 Bath Parameters

Vessel Fill Volume	500 mL
Number of Vessels	6
Bath Type	VK 7000
Paddle Speed	50 rpm
Apparatus Type	USP II Paddles

Output Parameters

Output Device	MultiFill Collection Module
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Table 1. MultiDose G3 Automated Settings

MultiDose G3 with Concurrent Manual Sampling

The MultiDose G3 performs the dissolution run by pre-heating the media, washing the vessels, filling the vessels, equilibrating the vessels to temperature, dropping the calibrator tablets, and timing the sampling point. When the sampling point is reached, the MultiDose G3 and an analyst sample from each vessel at the same time. Manual sampling is done from each vessel according to the USP manual method. Both the manual and automated samples are analyzed according to the procedure contained in the USP manual method on the same spectrophotometer.

Results

The results are based on a UV standard reading before reading the dissolution samples. The results are shown in Table 2.

Vessel Number	Concurrent Manual Prednisone % Dissolved	MultiDose G3 Prednisone % Dissolved	Difference Manual - MultiDose
1	31	30	1
2	33	33	0
3	31	32	-1
4	32	32	0
5	31	31	0
6	30	29	-1
Mean	31	31	0
SD	1	1	
% RSD	3.2	3.2	

Table 2. Equivalency Study for Prednisone Lot M at 50 rpm

Discussion

The MultiDose G3 results for Prednisone did not vary from the concurrent manual results for any one vessel at the 30 minute time point by more than 1% dissolved. At the 30 minute time point, the mean results and manual mean results for 6 vessels are essentially identical.

The MultiDose G3 Prednisone passed the USP specification of 28-42% for percent dissolved at 30 minutes.

Conclusion

Equivalency between manual dissolution sampling and analysis and automated dissolution sampling and analysis using the Prednisone calibrator tablet has been demonstrated.