Application Note

Validation of Automated Online Dissolution with the ADS 100 and the Agilent 1260 HPLC-System

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Introduction

Prednisone is commonly used in laboratories as a dissolution bath calibrator. Manual dissolution is a very time intensive process; because of that automation of this technique is highly desirable. In this study, the ADS 100 (Figure 1) is used as a tool to automate the dissolution sampling process at the appropriate intervals and initiating the analysis with HPLC. In addition to the reduc- tion of the hands-on time involved in dissolution, ADS Control Software provides the documentation of the automated dissolution process. The objective of this study is to determine the equivalency between manual and automated dissolution sampling and analysis using the prednisone calibrator tablet.

Material and Methods

The study was run using USP Prednisone tablets Lot P1I300 containing 10 mg Prednisone. HPLC grade degassed water was used for the dissolution media according to the USP specifications. The samples were taken 30 minutes after the start of the dissolution experiment manually with syringes and automatically. The samples automatically taken by the ADS 100 were filtered under pressure. Both the manual and automated samples were analyzed according to the procedure contained in the USP method

manual on the same UV-spectrophotometer (HPLC-DAD).

Figure 1: AnaTox ADS 100

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Table 1: Devices

Device	Description
Dissolution-Bath	SR8 PLUS Dissolution Test Station, Hanson Research, USA
Dissolution-Sampler	ADS 100, AnaTox, Germany
Degasser	1260 µ-Degasser, Agilent Technologies, Germany
Pump	1260 Binary Pump, Agilent Technologies, Germany
Injector	1260 WellPlate-ALS, Agilent Technologies, Germany
Colum oven	1290 Infinity TCC, Agilent Technologies, Germany
Detector	1260 DAD, Agilent Technologies
Vacuum pump	Alcatel, Germany
Restriction capillary	2m * 0,12mm stainless steel capillary

The modules used in this application note are described in Table 1. The samples were analyzed using a restriction capillary (see Table 1) at 40°C in a thermostated column compartment. The flow rate of the binary HPLC pump was set isocratic (100% water) to 1ml/min, the detection wavelength of the DAD to 242nm (absorption maximum of prednisone). The injection of the samples (50µl) was carried out by using the same HPLC autosampler already used for sample collecting (wellplate sampler, G1367C). The ADS 100 configuration consists of 6 circulating pumps, one flushing pump, a 8-position valve and a flow sensor. The ADS 100 settings for transferring samples are described in Table 2. The samples (250µl) were collected in a 96-position wellplate and analyzed by HPLC after collection of all samples (asynchron).

Table 2: ADS 100 Settings

Setting	Description
Flow rate	5 ml/min
Sampling volume	250 µl
Analysis	asynchron
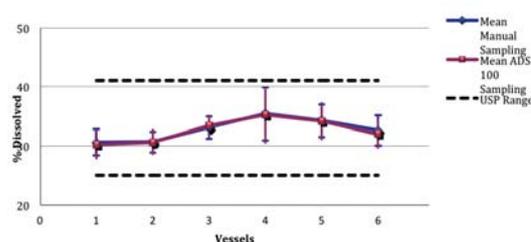
Figure 2: Dissolution rates depending on manual or automatic taken samples

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Results of Testing

Table 1: Autosampler Precision

Sample_Name	Area	Amount	Unit
P2-A-1: Precision Sample 1	33683025.00	2.03	mg/l
P2-A-1: Precision Sample 2	33500261.00	2.02	mg/l
P2-A-1: Precision Sample 3	33359026.00	2.01	mg/l
P2-A-1: Precision Sample 4	33168254.00	2.00	mg/l
P2-A-1: Precision Sample 5	32778532.00	1.98	mg/l
P2-A-1: Precision Sample 6	32574443.00	1.96	mg/l
	Average	2.00	
	Standard Deviation	0.03	
	RSD	1.30	
Autosampler precision [RSD, %]	1.30		
Result ALS Precision [RSD < 2%]	PASS		

Figure 3: Example of the qualification reporting: Autosampler precision

Result Summary

1. Autosampler Precision	PASS
2. Automatic Dissolution	
USP Range [2-Stage], GM (%)	PASS
USP Range [2-Stage], CV (%)	PASS
3. Comparision of automatic to manual sampling	PASS
4. Identification of connected vessels	PASS
5. Carry over of the Autosampler	PASS
6. Carry over of the AnaTox Dissolution Sampler	PASS
7. Linearity of the Autosampler	PASS

Figure 4: Example of the qualification reporting: Result Summary

Results

With the qualification procedure proceeded with the AnaTox AIQ-Software the ADS 100 as well as the HPLC autosampler and the dissolution bath can be qualified. Figures 3 and 4 show examples of the qualification report automatically created with the AIQ-software in conjunction with EZ-Chrom from Agilent Technologies.

At the 30-minute time event, the mean results of the samples taken with the ADS 100 and of the manually taken samples for 6 vessels are essentially identical. The dissolved prednisone concentration was in the USP range (see Figure 2). USP prednisone tablets can be used for qualification not only to qualify the dissolution bath but also the ADS 100 and the HPLC autosampler.

Conclusion

Equivalency between manual sampling and automated dissolution sampling with the ADS 100 and analysis by HPLC using the prednisone calibrator tablets has been demonstrated. The AIQ-software from AnaTox allows the qualification of the whole dissolution system with bath, dissolution sampler and HPLC autosampler.

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