Comparison of CD14 Comparative Dissolution Testers with Vision® G2 Elite™ 8 Dissolution Systems using AutoPlus Autosamplers

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Introduction

Dissolution is a well-known process in which a solid substance gets dissolved into solute and forms a solution. As described by the United States Pharmacopeia (USP), "dissolution testing measures the extent and rate of solution formation from a dosage form such as a tablet, capsule, ointment, etc. The dissolution of a drug is important for its bioavailability and therapeutic effectiveness. Dissolution and drug release are terms used interchangeably."[1]

According to the United States Food and Drug Administration (FDA), "the objective of in vitro dissolution testing is to evaluate the variables that affect the rate and extent of release of a drug substance from the finished dosage form, which affects the in vivo performance of the drug product. When this objective is met, a comparison of product in vitro dissolution profiles or adherence to the product release specification ensures that the product or batch being evaluated will have consistent quality and performance."[2] Hence, dissolution testing is one of the most important product performance tests.

Teledyne Hanson manufactures and sells the highest quality dissolution testers to meet all the regulatory requirements from the USP, U.S. FDA, ASTM, EP, JP, CE, CSA, and RoHS, as well as having 21 CFR part 11 compliance. Dissolution products sold by Teledyne Hanson include the Vision Classic 6, Vision G2 Elite 8, and the Comparative Dissolution (CD14) system. In this paper, two dissolution tester configurations are compared: the CD14 with two CD AutoPlus autosamplers, and two Vision G2 Elite 8 system with one AutoPlus autosampler.

Background

It is very important to develop a discriminating, non-interfering, robust, accurate, and precise method for dissolution[3]. The 14-vessel CD14 Comparative Dissolution Tester runs two methods simultaneously or independently, which is ideal for bioequivalence studies. This apparatus allows automated sampling under five minutes if an AutoPlus is connected. This tester is compatible with USP apparatus 1, 2, 5, and 6. Bioequivalence studies are required for all regulatory agencies to compare the dissolution profile between a reference listed drug (RLD) and the generic drug product. After conducting this study on n=12 units, the similarity factor (f2) and dissimilarity factor (f1) are calculated as required by the

Figure 1: CD14 Comparative Dissolution Tester with two CD AutoPlus Autosamplers

Figure 2: Two Vision G2 Elite 8 Dissolution Systems with a single AutoPlus Autosampler

U.S. Food and Drug Administration[4]. The CD14 tester provides the same environment to compare the results of dissolution tests for both the innovator and the generic drug product. A 14-vessel system allows for 6+1 or 12+2 configurations to enhance the efficiency of any laboratory performing multiple dissolution tests in any given day. This tester can be connected to a CD14 AutoPlus automated sampling system that can work independently or simultaneously per a method running on the CD14 dissolution tester.

The Vision G2 Elite 8 dissolution tester is a well-proven, high-quality dissolution tester with eight vessels. It is known for its ergonomic design and robust performance. This is ideal for automated and manual sampling techniques chosen at the user's convenience. Up to three of these testers can be connected to an AutoPlus auto sampling system. All testers can be programmed to run individual tests by giving the appropriate tester an offset time for collecting the samples using AutoPlus software.

Comparative Testing Procedure

Two tests were run to compare the two systems. The Performance Verification Test (PVT) using prednisone tablets, USP is a gold standard method adopted worldwide to qualify dissolution testers. The study objective is to compare data obtained by both dissolution system configurations using prednisone tablets, USP from the same lot. The test was performed using the procedure mentioned for PVT in the USP. Sampling was done using cannula manually and, in a separate test, using the AutoPlus attached to the instruments. All samples were filtered using a PVDF 0.45 µm syringe filter immediately after withdrawal. The absorption was measured on a UV spectrophotometer for all samples and standard solutions on the day of the test. In addition to this, the manual sampling and automated sampling on both systems produces comparatively similar results. Another study was performed using acetaminophen tablets, USP sold at retail pharmacies in the United States. This test is simple to run, as acetaminophen is readily available. The purpose of acetaminophen tablet dissolution testing is just to evaluate the differences between manual and automated sampling techniques. These results are obtained for research purposes only. The results obtained on a CD14 system for manual against automated sampling is presented in Table 3, and the graphical presentation of the same data is shown in Figure 3 below. The results of a similar test using a Vision G2 Elite dissolution system from other sources of acetaminophen tablets is presented in Table 4 below, and the graphical presentation of the same data is shown in Figure 4 below.

Results

Results obtained in this study using CD14 and two Vision G2 Elite 8 systems with Apparatus II (paddles) are

Vessel Number	Apparatus II Paddles (Manual)		
	CD14	Vision G2 System 1	Vision G2 System 2
1	34.77	32.57	35.40
2	36.25	32.93	36.38
2	35.97	36.36	35.25
4	35.35	33.68	35.32
5	34.66	34.63	36.93
6	35.58	35.37	33.92
7	31.90	N/A	N/A
8	36.10		
9	34.30		
10	33.22		
11	35.42		
12	35.27		
Average	34.90	34.26	35.53
%RSD	3.5	3.9	2.7

Vessel Number	Apparatus II Paddles (AutoPlus)		
	CD14	Vision G2 System 1	Vision G2 System 2
1	34.32	33.66	29.67
2	32.28	33.98	34.84
2	35.99	32.71	33.55
4	33.89	35.36	34.34
5	34.13	33.45	34.79
6	34.22	32.64	35.27
7	34.80	N/A	N/A
8	34.05		
9	34.71		
10	35.81		
11	32.32		
12	32.24		
Average	34.06	33.63	33.74
%RSD	3.5	2.7	5.6

Table 1: % Dissolved of Prednisone Tablets UPS using Apparatus II (Paddles)

Results obtained in this study using CD14 and two Vision G2 Elite 8 systems with Apparatus I (Baskets) are summarized in Table 2 below.

Vessel Number	Apparatus I Baskets (Manual)		
	CD14	Vision G2 System 1	Vision G2 System 2
1	66.60	72.07	68.52
2	74.46	72.59	66.66
2	75.88	72.82	68.74
4	71.10	63.19	68.62
5	74.42	69.06	59.32
6	71.21	69.67	71.00
7	69.10	N/A	N/A
8	74.56		
9	75.05		
10	66.05		
11	73.94		
12	66.18		
Average	71.55	69.90	67.14
%RSD	5.7	4.8	5.5

Vessel Number	Apparatus I Baskets (Automated)		
	CD14	Vision G2 System 1	Vision G2 System 2
1	70.71	69.58	66.60
2	74.99	67.36	63.17
2	75.31	64.01	64.59
4	66.23	69.62	69.93
5	74.07	67.29	63.12
6	65.82	65.82	71.21
7	66.26	N/A	N/A
8	73.75		
9	73.87		
10	74.66		
11	74.01		
12	71.20		
Average	71.74	67.28	66.44
%RSD	5.1	2.9	4.8

Table 2: % Dissolved of Prednisone Tablets UPS using Apparatus I (Baskets)

Time Minutes	Manual Sampling CD14 % Dissolved												
	V-1	V-2	V-3	V-4	V-5	V-6	V-7	V-8	V-9	V-10	V-11	V-12	Average
0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	78.5	79.2	68.4	88.6	73.5	68.0	80.1	80.5	75.4	78.5	82.1	67.6	76.7
10	98.4	97.6	98.2	100.6	98.0	94.0	94.5	98.7	99.3	97.2	96.5	95.2	97.3
15	101	100.4	99.7	103.5	102.2	99.2	96.8	102.5	100.1	98.5	100.6	102.6	100.6
20	101	102.2	101.2	96.1	103.9	103.4	97.3	101.0	102.0	100.4	101.7	102.1	101.0
30	103	101.5	100.7	101.0	101.4	101.3	97.3	100.7	100.5	98.3	98.8	98.8	100.3

Time Minutes	Automated Sampling CD14 % Dissolved												
	V-1	V-2	V-3	V-4	V-5	V-6	V-7	V-8	V-9	V-10	V-11	V-12	Average
0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	59.3	61.5	67.8	68.1	73.6	72.8	72.6	64.6	79.4	62.7	64.4	64.1	67.6
10	93.5	89.4	93.5	91.7	103.1	94.2	96.9	96.3	97.7	92.0	83.5	91.3	93.6
15	100.1	95.3	100.8	97.0	102.9	100.2	103.6	102.8	100.8	98.9	98.4	96.1	99.7
20	100.7	96.0	100.0	100.3	102.8	100.7	102.6	100.9	98.8	97.0	101.5	95.8	99.7
30	100.7	99.5	100.6	102.7	99.0	100.7	102.2	100.8	98.2	96.0	102.7	96.4	99.9

Table 3: % Time for Dissolved Acetaminophen obtained on CD14; manual vs automated sampling

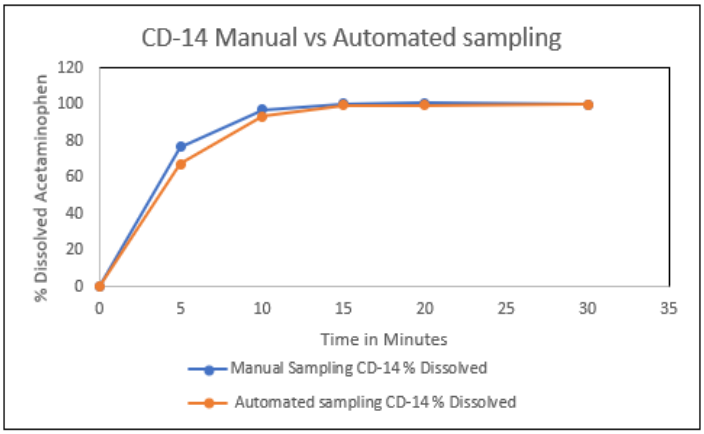

Figure 3: CD14 Manual vs Automated Sampling

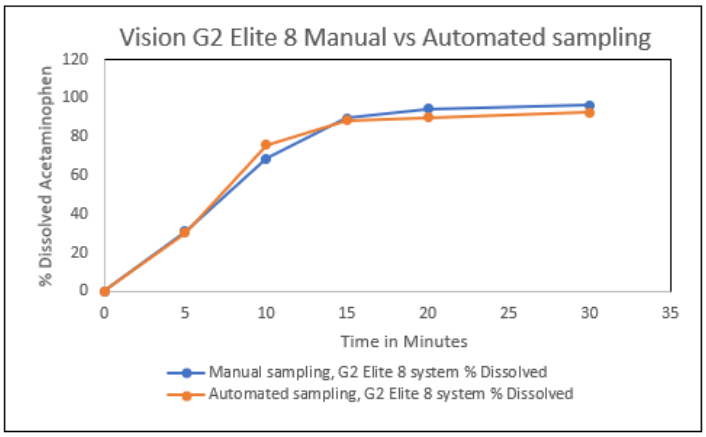

Figure 4: Vision G2 Elite 8 Manual vs Automated Sampling

Time Minutes	Manual Sampling G2 Elite 8 System % Dissolved						
	V-1	V-2	V-3	V-4	V-5	V-6	Average
0	0	0	0	0	0	0	0
5	31.9	31.5	30.1	31.7	31.1	29.4	31.0
10	69.9	68.2	70.3	67.7	69.0	68.0	68.8
15	89.3	90.9	90.7	89.8	97.3	90.1	89.7
20	95.1	94.2	93.0	94.2	94.6	95.8	94.5
30	97.0	96.0	95.3	96.2	96.1	97.2	96.3

Time Minutes	Automated Sampling G2 Elite 8 System % Dissolved						
	V-1	V-2	V-3	V-4	V-5	V-6	Average
0	0	0	0	0	0	0	0
5	29.9	30.7	33.2	27.1	30.6	30.1	30.3
10	77.7	77.2	75.7	70.9	74.0	79.2	75.8
15	89.0	87.7	87.2	87.1	87.9	91.8	88.3
20	91.3	90.5	89.1	87.9	88.6	92.0	89.9
30	92.5	91.5	90.3	93.8	90.3	98.0	92.7

Table 4: % Data for Dissolved Acetaminophen obtained on Vision G2 Elite 8 System by Manual vs Automated Sampling

summarized in Table 1 below.

Conclusion

The CD14 with two AutoPlus and Two Vision G2 Elite 8 dissolution systems with a single autosampler show comparable results. With this configuration, users have options to either procure a new CD14 system or to add two AutoPlus samplers to an existing CD14. This option will allow users to perform comparative dissolution testing in the most compliant and time efficient manner. Vision G2 Elite 8 users may install the AutoPlus unit and connect two dissolution systems to it and obtain the same test results on either configuration. Regarding the compliance to 21 CFR part 11, there is no difference in using the CD14 and Vision G2 Elite 8 systems. The CD14 is a more compact unit which requires less lab bench space. An advantage of using a single dissolution instrument is that there is less down time for periodic qualification compared to using two systems.

Resources

1. United States Pharmacopeia. Dissolution Testing and Drug Release Tests [Internet]. www.usp.org. Available from: https://www.usp.org/small-molecules/dissolution
2. U.S. Food and Drug Administration. Compilation of FDA Guidance and Resources for in vitro Dissolution Testing of Immediate Release Solid Oral Dosage Forms. https://www.fda.gov/animal-veterinary/new-animal-drug-applications/compilation-fda-guidance-and-resources-in-vitro-dissolution-testing-immediate-release-solid-oral-dosage. Accessed 06/07/2022.
3. United States Pharmacopeia (2022). *General Chapter, <1092> The Dissolution Procedure*: Development and Validation. USP-NF. Rockville, MD: United States Pharmacopeia.
4. U.S. Food and Drug Administration. Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances Guidance for Industry. August 2018.

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