Comparison of Deaerated vs Non-Deaerated Media for Dissolution Performance Verification Standard—Tablets

Ashvin Patel, PhD.

keywords: aerated media, baskets, dissolution testing, paddles

Figure 1. The Vision® G2 Elite 8 dissolution tester

Dissolution Test

A dissolution test is used to evaluate the rate at which and the amount of a compound that dissolves to form a solution under carefully controlled conditions. The dissolution test in a United States Pharmacopeia (USP) drug product monograph helps evaluate the performance of a drug product (article) and indicates when the drug product performs in a substandard fashion. Although passing the test does not definitively demonstrate bioavailability of the sample or bioequivalence to other products, failure is a cause for concern. Typically, for oral drug products, USP monographs call for the use of dissolution testing with apparatus described in General Chapter <711> Dissolution.[1]

USP Apparatus 1 (basket) and 2 (paddle) are widely used to perform dissolution tests of oral solid drug products. The Apparatus Suitability section in <711> describes the procedure and requirements for the qualification of dissolution apparatus.[2] Analytical instrument qualification/calibration is also required by FDA current Good Manufacturing Practices (cGMPs) and by ISO/IEC 17025, an international standard specifying general requirements for the competence of testing and calibration laboratories.[3,4]

Objective

The objective of this study is to evaluate the percentage difference in the amount of Prednisone dissolved by using either deaerated and non-deaerated dissolution media, i.e., purified water with Apparatus II (Paddles) and USP Apparatus I (Baskets) USP 40 mesh.

Test procedure and Results:

Prior to performing the dissolution test, the instrument was qualified for EMC and per the Dissolution Performance Verification Test (PVT) Standard - Prednisone tablets.

As mentioned in the USP, the dissolution test is performed using current Dissolution Performance Verification Standard - Tablets, lot number F161Y0, use by date: 14 November 2024.[5] Each tablet contains Prednisone 10 mg. In this study, the dissolution medium was deaerated for the test using the procedure described in USP General Chapter <711> Dissolution: "heat the medium while stirring gently, to about 41°, immediately filter under vacuum using a filter having a porosity of 0.45 µm or less, with vigorous stirring, and continue stirring under vacuum for about 5 minutes."[2] It was repeated using the same setup but with non-deaerated dissolution media. Two types of Apparatus II (Paddles), stainless steel or

PTFE, were used as the stirring device during the test. Additionally, Apparatus I Stainless Steel baskets of 40 mesh were also used to test for dissolution using either deaerated or non-deaerated dissolution media. A standard solution was prepared using Prednisone Reference Standard, current lot number R083A0. The UV absorption of samples and standards were measured concomitantly at 242 nm using 10 mm quartz cells on a Shimadzu Spectrophotometer, model UV 1800. The raw data were recorded per internal procedures. The results were calculated by tools provided by the USP and are reported in Table 1.

Table 1- Result of Dissolution Performance Verification Standard - Tablets using Apparatus II

Vessel/Tablet Number	Apparatus 2 S.S. (paddles)		Apparatus 2 PTFE (paddles)	
	deaerated medium	non-deaerated medium	deaerated medium	non-deaerated medium
1	52.8	54.0	53.2	61.9
2	51.6	51.6	50.0	59.1
3	51.7	53.3	52.4	56.3
4	51.6	59.0	56.2	52.2
5	54.1	58.0	50.7	56.1
6	55.5	55.5	53.3	59.4
Mean	52.9	55.2	52.6	57.1
Geometric Mean	52.8	55.1	52.6	57.0
% CV	2.8	4.7	3.8	5.4

Table 2 - Result of Dissolution Performance Verification Standard - Tablets using Apparatus I

Vessel/Tablet Number	Apparatus 1 (Baskets)	
	deaerated medium	non-deaerated medium
1	86.5	83.5
2	86.5	87.1
3	84.7	86.9
4	86.9	89.2
5	86.7	90.9
6	84.1	89.7
Mean	85.9	87.9
Geometric Mean	85.9	87.8
% CV	1.2	2.8

* Stainless Steel Paddles

Conclusion

All results obtained above met the acceptance criteria except when a non-deaerated medium with stainless steel paddles was used: the CV percentage failed by a margin of 0.1%, a variance that would have gone in either direction if additional tests were repeated under the same conditions. The percentage of dissolved Prednisone in a non-deaerated medium was also slightly higher than the deaerated dissolution medium results. The CV percentage also tended to be higher in non-deaerated medium. Due to the higher release obtained as expected with tests using Apparatus 1 (Baskets), the variation seems to be lesser when compared to the test results of Apparatus 2 (Paddles).

The purpose of this study was to evaluate the impact of a deaerated process on results, so additional tests were not performed. Based on the study data shown above, it is evident that there is only a marginal difference in the amount of dissolved drug product released using either PTFE or stainless steel paddles. Deaeration, performed as suggested by the USP, is recommended if Dissolution Performance Verification Standard tablets were used to qualify the dissolution tester.

References

1. United States Pharmacopeia, (USP) https://www.usp.org/small-molecules/dissolution-explained
2. United Sates Pharmacopeia, (USP) General Chapter <711> Dissolution, USP NF 2023
3. The Use of Mechanical Calibration of Dissolution Apparatus 1 and 2 – Current Good Manufacturing Practice (CGMP) U.S. Department of Health and Human Service Food and Drug Administration Center for Drug Evaluation and Research (CDER) January 2010 Current Good Manufacturing Practices (CGMP)
4. ASTM E2503-13(2020) Standard Practice for Qualification of Basket and Paddle Dissolution Apparatus
5. Dissolution Performance Verification Standard – Prednisone RS DEPTDOC-00276-01A