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Effects of Vessel Geometric Irregularity on Dissolution Test Results

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ABSTRACT: Dissolution testing of pharmaceutical products is an important technique used extensively for both product development and quality control, but there are many variables that can affect dissolution results. In this study, the effect of the inner shape of standard 1-L dissolution vessels on drug dissolution results was investigated. The geometric dimensions and irregularities of commercially available vessels (obtained from four different manufacturers) were examined using a three-dimensional video-based measuring machine (VMM). The same analyst, dissolution test assembly, and experimental conditions were used for dissolution testing involving 10 mg of prednisone tablets (NCDA #2) with dissolution apparatus 2 (paddle). Mechanical calibration of the dissolution apparatus was performed prior to dissolution testing with each set of vessels. Geometric characteristics varied within and among the sets of vessels, but the overall averages and standard deviations of dissolution results (six vessels) showed no statistical significant differences among the vessel sets. However, some dissolution differences were noted when comparing individual vessels. With these types of comparisons, the vessel concentricity, sphericity, and radius of sphere were found to possibly influence the amount of prednisone dissolved, but flatness of vessel flange, cylindricity, and circularity showed no effect on dissolution results. The study shows that VMM is a technique that could be used to qualify dissolution vessels. © 2010 Wiley-Liss, Inc. and the American Pharmacists Association J Pharm Sci 100:1093–1101, 2011

Keywords: dissolution; analysis; physical characterization; solid dosage form; apparatus 2; in vitro method; geometric irregularity; VMM

INTRODUCTION

Dissolution testing is widely used as an analytical technique for evaluating the drug release characteristics of a pharmaceutical product. It is necessary to minimize the variance due to the dissolution apparatus in order to obtain results that distinguish changes between different dosage forms or the same dosage form from different lots.[1–5]

Dissolution testing involves many variables, which can be grouped into four main categories: (1) analyst, (2) dissolution apparatus, (3) testing environment, and (4) sample. The variables in the second category include vessel geometric irregularities, alignment of the instrument, and agitation speed. Variables of the testing environment include deaeration of dissolution media, media temperature, and vibration. To obtain reliable dissolution results, the variables from the first three categories must be minimized. Many reports have been published concerning the effects of alignment of the instrument, vibration, deaeration, and analyst.[6–11] Some of these discussions have led to tightened specifications in the mechanical calibration of dissolution apparatus.

The United States Pharmacopeia (USP) specifications for a dissolution vessel currently specify the inner diameter of the cylindrical part and the height of vessel and assume that the inner surface of cylinder and hemisphere of the vessel are uniform.[12] A few discussions have focused on vessel geometric irregularities.[13–17] According to Scott,[14] each vessel should be treated as an individual handcrafted product, with flaws and imperfections on the inner surface that produce unique flow dynamics. The USP also conducted studies to examine vessels from different manufacturers, using a three-dimensional (3D) coordinate

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Table 1. The Definitions of Geometric Dimensions and Irregularities

Terms	Definitions
Geometric dimensions	
Sphere radius	The measured value of the radius of the hemispheric region
Vessel height	The measured value from the base of the vessel to the top of the flange.
Angle of the cylinder relative to the flange	The angle measured between the flange plane (horizontal) and the axis (vertical) of the cylinder.
Diameter of cylinder	The measured value of the perpendicular cross-section diameter across the cylinder.
Geometric irregularities	
Sphericity	All points on a 3D surface share a common center point. The value will be zero for perfect shape.
Circularity	The condition on a 2D surface such as a sphere, cone, or cylinder where all the points along that surface are of equal distance to the center point of that feature. In the case of a circle, the points would be of equal distance to the center of the circle. For the perfect shape, the value will be zero.
Cylindricity	All points on a surface are of equal distance from a common axis.
Concentricity of two features (sphere part and cylinder part for dissolution vessel)	Both features share a common axis or center point. The measured sphere and cylinder share a common axis.
The perpendicularity of the cylinder to the flange	The condition of the center axis of the cylinder as related to the 90° axis of the plane formed by the flange. For the perfect shape, the value will be zero.
The flatness of the flange	All points measured are in the same plane. The plane is formed by all points measured on the flange surface. The flatness measurement is the sum of two distances from the plane. Distance 1 is the distance from the plane to the point farthest away from the plane in a positive direction. Distance 2 is the distance from the plane to the point farthest away from the plane in a negative direction. For the perfect shape, the value will be zero.

measuring machine to measure dimensions and irregularities in dissolution vessels.[16,17] Although the USP examined nearly three times as many vessels as were employed in the present study, the geometric variability across all vessels used in their study was substantially less than what we observed. The USP concluded that differences in vessel dimensions and shape irregularities could influence the amount and variability of dissolution results. They further pointed out that the thickness and angle of the vessel flange may affect extent of drug dissolution, whereas the cylinder inner diameter, flange diameter, and standard deviation of concentricity may affect the variability of drug dissolution data. Variation in the hemisphere radius has also been shown to result in as much as an 18% change in the volume of dissolution media surrounding the paddle.[13,15] Although these parameters are not specified by the USP, they may be significant under certain conditions of rotation speed, medium, and volume and are expected to be API specific.

In this study, the geometric dimensions and irregularities of commercially available vessels from four different manufacturers were examined using a Seebrez 241212 (Quality Control Solutions, Inc., Temecula, California) 3D video-based measuring machine (VMM) with a Renishaw touch probe (Renishaw, Inc., Hoffman Estates, Illinois). The Seebrez uses a touch probe to record the location of points on the inner surface of the vessel. The points are plotted in 3D space, and the resulting numerical description of the vessel is compared with a modeled ideal shape (i.e., how well these points matched the characteristics of an ideal shape). The vessel dimensions measured were the height, the inner diameter of the cylindrical portion of the vessel, the radius of the hemispheric region, and the angle of the flange relative to the wall of the cylinder. These dimensional measurements were used to calculate the flatness of the vessel flange, sphericity of the vessel hemisphere, circularity of the cylinder at multiple heights, cylindricity, perpendicularity of the cylinder to the flange, and concentricity between the hemisphere and the cylinder. A glossary of geometric measurement terms is summarized in Table 1.[13–15,18]

The effect of the inner shape of a standard 1-L dissolution vessel on drug dissolution results was investigated. Vessel irregularities were correlated with changes in dissolution results to determine which geometric parameters effect dissolution testing. The results showed that the vessel concentricity, sphericity, and radius of sphere may influence the amount of prednisone dissolved. Vessel flange flatness, cylindricity, and circularity in studied ranges showed no correlation with dissolution results.

Experimental

Equipment for Vessel Inner Shape Measurement

A Seebrez 241212 3D VMM (Quality Control Solutions, Inc.) equipped with a Renishaw touch probe was used. It was controlled by Metronics (QC 5300, Heidenhain Corporation, Schaumburg, Illinois) software (Version 2.94).

Determination of Geometric Dimension and Irregularity

Dissolution vessels from four different manufacturers were labeled as **A**, **B**, **C**, and **D**. Six vessels from each manufacturer were numbered 1 to 6. All dissolution vessels were sent to Metrology Solutions Inc. (Romeoville, Illinois) for geometric dimensional and irregularity measurements. The resolution of the Seebrez system is 0.0005 mm, and it was calibrated before the tests. The Seebrez VMM was operated according to the 3D Metronics software (QC 5300). Vessels were placed individually in a work holding fixture, and measurement began on the top surface of the flange. From this measurement, the flatness of the flange was calculated and recorded. The Seebrez VMM then traveled to the bottom of the vessel and probed the hemisphere (200 points). From that result, the radius of the sphere and the sphericity were calculated. The diameters (100 points each) were then measured along the central portion of the vessel (cylinder) at five locations from the top of the vessel (at 20, 40, 60, 80, and 100 mm down from the top of the flange). From these features, the software reported the diameters and circularity of each feature at the given depths. The Seebrez VMM then inspected the cylinder by using 300 probed points. The software recorded the cylindricity of the feature along with the angle of the cylinder relative to the top of the flange. The perpendicularity of the cylinder to the top of the flange was then calculated along with the concentricity of the cylinder to the sphere. The bottom of the flange was probed, and the remaining two distances were calculated: heights from the bottom of the hemisphere to both the top and the bottom of the flange.

Dissolution Testing

- Apparatus: USP apparatus 2 (Distek model 2100A, Serial # D12547192, North Brunswick, New Jersey)—mechanically calibrated.[19]

(i) Media: 500 mL of deionized water at 37°C, degassed according to the method of Gao et al.[8].
(ii) Paddle speed: 50 rpm.

- Dissolution vessels: These were obtained from four manufacturers (**A**, **B**, **C**, and **D**) and labeled as such, and the six vessels from each manufacturer were labeled 1 to 6. During the runs of the same set of vessels, each individual vessel was kept in the same position on the vessel plate and in the same orientation.
- Analyst: One chemist conducted all the dissolution runs over a period of 2 months.
- Samples: NCDA #2, 10 mg of prednisone tablets used in this study have been well characterized in a Gauge R&R study. From that study,[9] the mean and standard deviation of percentage release of at 30 min were 31.4% ± 1.38%, respectively.
- Sampling: Automated ultraviolet (UV) sampling system with monitoring at 242 nm by using a 0.5-cm path length cell.
- Time points: All dissolution runs were 60 min in length. UV absorbance measurements were obtained at 2, 4, 6, 8, 10, 15, 20, 25, 30, 35, 40, 45, 50, and 60 min with an online system (Agilent 8453).
- All media samples were filtered through Distek 45-μm ultrahigh-molecular-weight polyethylene filter tips attached to the top of the Distek sampling probes. Filters were not immersed in the dissolution medium. The thin metal sampling probes (1.7-mm OD) were left in the media throughout the run.
- To eliminate operational variables during the period of this study, eight dissolution runs were performed with vessel set **B**, followed by vessel sets **A**, **C,** and **D**, and then eight additional runs were again performed with vessel set **B**.

RESULTS AND DISCUSSION

Vessel Geometric Dimensions and Irregularities

The geometric shape of dissolution vessels has been described in detail in two reports.[14,17] For this study, sets of six dissolution vessels from each of four manufacturers were selected and measured by the VMM. The geometric dimensions and irregularities of each individual vessel are listed in Table 2. These measurements are summarized in Table 3, which also includes a summary of the USP results[17] as well as parameters describing the "ideal shape" and appropriate USP specifications. Dependent upon which parameter was used for comparison, the range in measured values for vessels used in the present study was 2 to 10 times larger than that observed in the USP study. For five of the nine metrics, the vessel set measurement standard deviations were substantially larger for the vessels used in the present study.

Comparing geometric irregularities in each set of vessels with the ideal shape, vessel set **B** shows the best overall inner surface with regard to sphericity, circularity of cylinder part, cylindricity, and concentricity of sphere and cylinder (data in Table 3). In contrast, vessel set **A** shows the worst cylindricity with an average of 0.78 mm, vessel set **C** shows the worst concentricity (average of 1.07 mm) and sphericity (average of 1.31 mm), and vessel set **D** has an inner shape in between the best and the worst, but they show the worst vessel flange flatness (average of 0.62 mm). The ideal shape for all of these parameters would be 0 mm.

Table 2. The Vessel Geometric Dimensions and Irregularities Results

Vessel	Sphere Radius (mm)	Vessel Height (mm)	Angle of the Cylinder Relative to the Flange (°)	Diameter of the Cylindical Part at Different Heights (mm)					Perpendi cularity of the Cylinder to the Flange (°)	Sphericity (mm)	Circularity of cylinder part at different heights (mm)					Cylindri city (mm)	Concentri city of Sphere and Cylinder (mm)	Flatness of Flange (mm)
				At 100 mm	At 80 mm	At 60 mm	At 40 mm	At 20 mm			At 20 mm	At 40 mm	At 60 mm	At 80 mm	At 100 mm			
A1	50.32	162.52	90.05	101.39	101.73	102.09	102.39	102.70	0.19	0.05	0.08	0.07	0.03	0.05	0.04	0.77	0.20	0.03
A2	50.32	162.55	90.06	101.40	101.73	102.05	102.40	102.69	0.24	0.09	0.02	0.07	0.02	0.01	0.03	0.79	0.15	0.00
A3	50.30	162.56	90.09	101.39	101.72	102.07	102.40	102.70	0.27	0.07	0.04	0.07	0.06	0.01	0.04	0.78	0.16	0.00
A4	50.36	162.52	90.05	101.40	101.76	102.09	102.40	102.71	0.20	0.05	0.07	0.07	0.03	0.03	0.04	0.78	0.18	0.03
A5	50.37	162.52	90.07	101.40	101.76	102.09	102.40	102.72	0.20	0.05	0.04	0.05	0.02	0.02	0.02	0.77	0.17	0.01
A6	50.33	162.54	90.07	101.39	101.73	102.04	102.37	102.69	0.23	0.09	0.02	0.02	0.03	0.02	0.04	0.78	0.15	0.00
B1	50.57	163.18	90.26	101.19	101.18	101.18	101.17	101.09	0.51	0.06	0.05	0.04	0.04	0.04	0.02	0.04	0.07	0.02
B2	50.55	161.62	89.80	101.10	101.10	101.09	101.06	100.95	0.48	0.04	0.04	0.06	0.02	0.04	0.03	0.06	0.08	0.41
B3	50.51	161.79	90.00	101.07	101.07	101.09	101.08	101.03	0.56	0.03	0.03	0.04	0.03	0.03	0.03	0.02	0.10	0.12
B4	50.56	159.63	89.99	101.15	101.16	101.15	101.14	101.02	0.28	0.05	0.03	0.06	0.04	0.03	0.03	0.05	0.11	0.02
B5	50.59	162.51	90.28	101.16	101.15	101.15	101.14	101.08	0.39	0.04	0.02	0.02	0.01	0.01	0.01	0.02	0.08	0.26
B6	50.46	162.27	90.28	101.10	101.10	101.11	101.11	101.06	0.42	0.03	0.02	0.01	0.02	0.01	0.02	0.02	0.10	0.26
C1	52.03	167.40	89.87	101.08	100.94	100.94	100.87	100.73	0.38	1.20	0.42	0.46	0.41	0.37	0.32	0.26	0.35	0.04
C2	50.82	168.01	90.62	100.52	100.60	100.69	100.69	100.67	0.89	0.74	0.06	0.11	0.15	0.20	0.22	0.14	3.58	0.14
C3	51.90	166.87	89.98	100.79	100.77	100.83	100.84	100.84	0.46	1.89	0.65	0.61	0.60	0.59	0.60	0.59	1.70	0.05
C4	52.06	167.64	90.09	100.34	100.34	100.38	100.38	100.38	0.53	1.43	0.47	0.45	0.44	0.37	0.40	0.47	0.39	0.03
C5	52.26	167.69	90.05	101.72	101.79	101.82	101.84	101.81	0.23	1.46	0.30	0.29	0.30	0.34	0.35	0.33	0.19	0.06
C6	51.34	167.12	89.77	100.74	100.73	100.75	100.79	100.81	0.52	1.17	0.32	0.29	0.27	0.30	0.33	0.26	0.21	0.06
D1	52.56	162.98	89.84	102.05	101.76	101.76	101.81	101.78	0.67	1.02	0.53	0.51	0.49	0.49	0.50	0.56	0.78	0.08
D2	54.41	162.75	89.43	101.06	100.96	100.94	100.90	100.76	0.81	0.58	0.62	0.58	0.56	0.53	0.54	0.68	0.47	0.07
D3	52.40	165.65	89.84	101.59	101.39	101.39	101.37	101.26	0.50	0.87	0.10	0.07	0.05	0.08	0.15	0.13	0.11	0.12
D4	52.23	165.08	89.96	101.23	101.13	101.21	101.25	101.18	0.36	1.40	0.12	0.12	0.11	0.09	0.03	0.13	0.15	3.43
D5	52.01	–	89.92	101.82	101.64	101.67	101.67	101.63	0.17	0.99	0.11	0.11	0.12	0.12	0.06	0.12	0.14	0.00
D6	50.81	–	89.81	101.42	101.17	101.08	101.09	101.05	0.14	0.24	0.25	0.24	0.26	0.08	0.12	0.22	0.31	0.01

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Table 3. Statistical Summary of the Vessel Geometric Dimensions and Irregularities Results, and Comparisons with Data from Ideal Shape and Other Report

Vessel Set		Sphere Radius (mm)	Vessel Height (mm)	Angle of the Cylinder Relative to the Flange (°)	Diameter of the Cylinder Part (mm)	Perpendicularity of the Cylinder to the Flange (°)	Sphericity (mm)	Circularity of the Cylinder Part (mm)	Cylindricity (mm)	Concentricity of the Sphere and the Cylinder (mm)	Flatness of the Flange (mm)
A	Mean	50.33	162.53	90.07	102.06	0.22	0.07	0.04	0.78	0.17	0.01
	SD	0.03	0.02	0.02	0.47	0.03	0.02	0.02	0.01	0.02	0.01
	Range	50.30–50.37	162.52–162.56	90.05–90.09	101.39–102.72	0.19–0.27	0.05–0.09	0.01–0.08	0.77–0.79	0.15–0.20	0–0.03
B	Mean	50.54	161.84	90.10	101.11	0.44	0.04	0.03	0.04	0.09	0.18
	SD	0.05	1.21	0.20	0.05	0.10	0.01	0.01	0.02	0.01	0.16
	Range	50.46–50.59	159.63–163.18	89.80–90.28	100.95–101.19	0.28–0.56	0.03–0.06	0.01–0.06	0.02–0.06	0.07–0.11	0.02–0.41
C	Mean	51.73	167.46	90.06	100.88	0.50	1.31	0.37	0.34	1.07	0.06
	SD	0.55	0.42	0.30	0.46	0.22	0.38	0.15	0.16	1.35	0.04
	Range	50.82–52.26	166.87–168.01	89.77–90.62	100.34–101.84	0.23–0.89	0.74–1.89	0.06–0.65	0.14–0.59	0.19–3.58	0.03–0.14
D	Mean	52.40	164.11	89.80	101.37	0.44	0.85	0.26	0.31	0.32	0.62
	SD	1.16	1.46	0.19	0.33	0.27	0.40	0.21	0.25	0.26	1.38
	Range	50.81–54.41	162.75–165.65	89.43–89.96	100.76–102.05	0.14–0.81	0.24–1.40	0.03–0.62	0.12–0.68	0.11–0.78	0–3.43
Data from USP (Ref 17)	Mean	–	160.8	90.0	102.3	0.22	0.82	0.16	0.34	0.9	0.19
	SD	–	1.2	0.1	1.9	0.12	0.63	0.09	0.17	0.4	0.11
	Range	–	158.8–162.6	89.8–90.3	99.9–104.7	0.04–0.43	0.04–1.98	0.01–0.32	0.08–0.75	0.5–1.6	0.04–0.48
Ideal shape		–	–	90	–	0	0	0	0	0	0
USP specifications		–	160–210	–	98–106	–	–	–	–	–	–

USP, United States Pharmacopeia.

The USP specifications require that the height of a vessel be between 160 and 210 mm and the inside diameter be between 98 and 106 mm.[12] The measured dimensions shown in Table 2 indicate that all 24 of the vessels meet USP requirements except vessel **D**2. The vessel height and cylinder diameter for vessel **D**2 are within USP specification; however, the hemispherical portion of the vessel shows a larger diameter (108.8 mm). Observed differences in the hemisphere radius have been shown to result in as much as an 18% change in the volume of dissolution media surrounding the paddle.[16]

Although there are many ways to characterize vessels based on geometric dimensions, considering the dissolution process, and apparatus' mechanical calibration procedure, some parameters are not expected to have an effect on dissolution and can be disregarded. For example, because the distance between the bottom of dissolution paddle blade and vessel bottom must be 25 mm, the height of the vessel may not affect dissolution testing. In addition, according to the ASTM standard for the mechanical calibration procedure, each vessel must be centered on the paddle shaft at two levels, which ensures that the vessel is not only centered but also vertical.[19] Because of this, we expect the flatness of the vessel flange and the perpendicularity of the cylinder to the flange should have no effect on dissolution results. Given these considerations, the following vessel geometric dimension and irregularities were examined to assess possible correlation to dissolution results: sphere radius, flatness of flange, sphericity, cylindricity, and concentricity of sphere and cylinder.

Average of Dissolution Results

Because vessel set **B** showed the best inner surface, the dissolution results obtained from vessel set **B** were used as a reference and compared with results from the other vessels. The overall average results of 16 runs with six vessels each obtained from vessel set **B** was compared with the overall average results of 8 runs with six vessels each obtained from the other sets of vessels (**A**, **C**, and **D**).

Figure 1 shows average dissolution profiles by using the four different sets of vessels. Although each set of vessels has different geometric characters, the dissolution results show that the average values, and the standard deviations, are very similar. The similarity of dissolution results at 30 min shown in Table 4 indicates that the mean vessel geometric irregularity, within the ranges observed in this study, is not a significant cause of dissolution variability. Results from a previous gauge R&R study[9] are also included in Table 4. The similarity of dissolution results indicates that when the dissolution apparatus is set up correctly and mechanically calibrated following the ASTM procedure, the variability can be minimized.

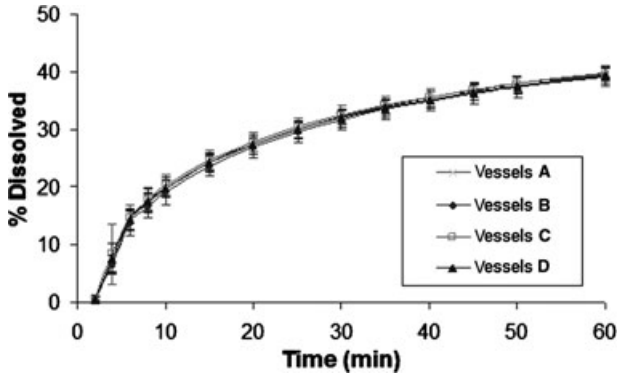

Figure 1. Dissolution profiles obtained from four sets of vessels.

Relationship Between Vessel Geometric Parameters and Dissolution Results

Examining the overall average dissolution results for all vessels, no vessel geometric effect on dissolution testing was observed. This could occur because the variation caused by random flaws and imperfections of the inner surface of the individual vessel (each of which is an individually handcrafted product[14]) is averaged out over six vessels. To better understand vessel geometric irregularity effects, average dissolution results from each individual vessel were compared.

As shown in Table 3, vessels from different manufacturers show differences in sphere radius, sphericity, cylindricity, concentricity of sphere and cylinder, and flatness of flange. To focus on these geometric differences, the average dissolution results at 30 min obtained from individual vessels were compared by applying Student's *t*-test. These statistical results (*p* values at 95% confidence interval), shown in Table 5, indicate that only for vessels **C**2, **C**3, and **D**2 are there significant differences when compared with vessels in the same positions for the **B** set. The dissolution profiles from these vessels are also shown in Figure 2. The vessel geometric parameters, which are different from set **B**, are also shown in Table 5. To assess whether there were correlations between

Table 4. Percentage Dissolution of 10 mg of Prednisone at 30 Min

	Vessel Set **A**	Vessel Set **B**	Vessel Set **C**	Vessel Set **D**	Data from Gauge R&R Study [ref 9]
Overall average	32.19	31.66	32.53	32.06	31.37
SD	1.09	1.77	1.64	1.56	1.38
RSD%	3.39	5.59	5.05	4.87	4.40

Table 5. Results of Statistical Comparisons (p Values per Student's t-Test) for Dissolution Values at 30 Min for Vessel Sets Versus Set B*

	Dissolution Vessels						
Pairs	1	2	3	4	5	6	Possible Vessel Geometric Sources for Observed Difference
A vs. **B**	0.264	0.114	0.169	0.318	0.479	0.134	Cylindricity
C vs. **B**	0.358	0.028	0.002	0.233	0.443	0.246	Concentricity of the sphere and cylinder sphericity
D vs. **B**	0.421	0.048	0.379	0.355	0.119	0.397	Flatness of flange radius of the sphere

*$p < 0.05$ is statistically significant.

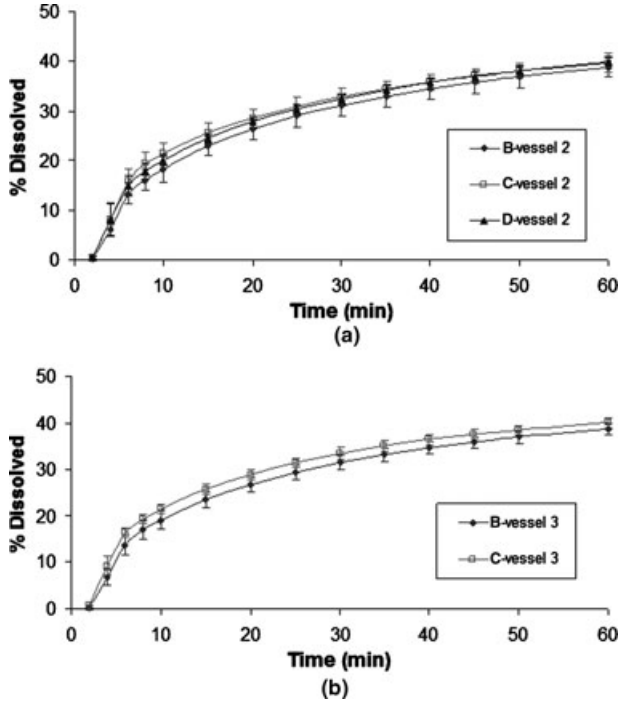

Figure 2. Comparisons of dissolution profiles obtained from vessels 2 and 3 for which t-test showed significant difference at 30-min dissolution time point. Results of (a) vessel 2 from sets **B**, **C**, and **D**; and (b) vessel 3 from sets **B** and **C**.

dissolution results and specific geometric irregularities of each individual vessel, the absolute difference of each geometric parameter between vessels from set **B** and other vessel sets (**A**, **C**, and **D**) was calculated and plotted in Figure 3. This difference for each of five parameters is plotted versus vessel number, and the probability (p value) that differences between the mean 30-min dissolution values for the specified vessel set and the vessel **B** set are statistically significant is indicated for each vessel. The USP reported that the flange thickness and flatness of vessel flange are the most important factors to affect dissolution testing.[17] Although both the range of individual vessel values for flange flatness and the maximum standard deviation for that metric within any given vessel set for the vessels used in the present study were many times that of the vessels used by the USP, there is no significant difference in dissolution results ($p > 0.05$) as seen in Figures 3a and 3c. The flange thickness

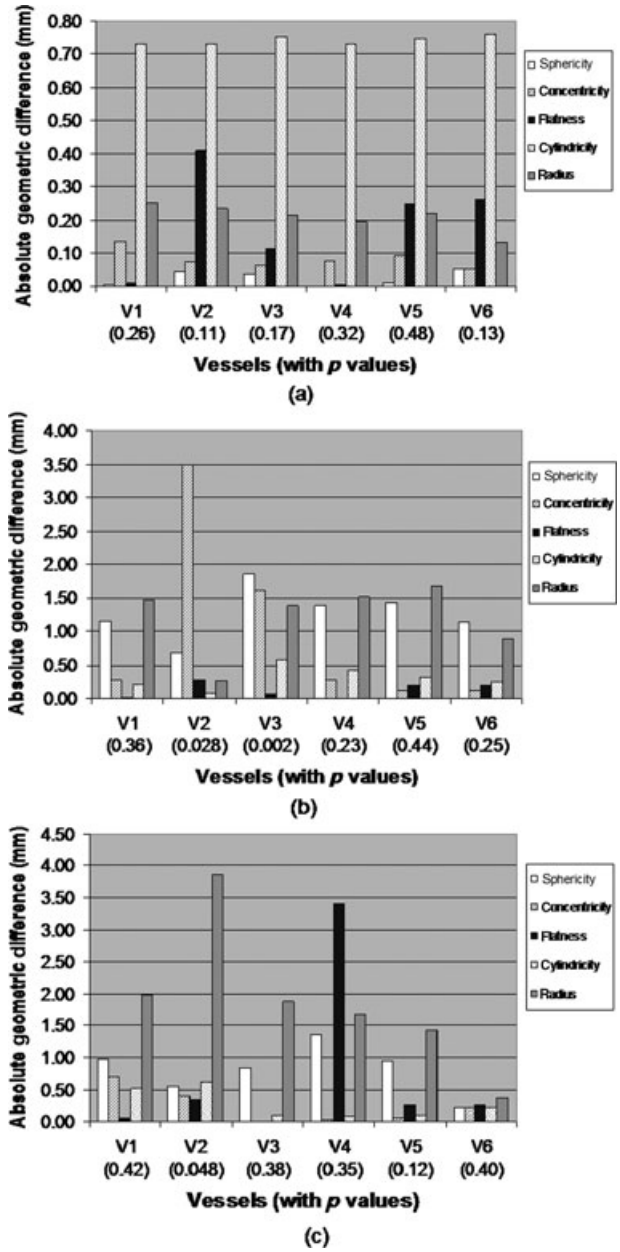

Figure 3. Correlations between vessel geometric irregularities with dissolution results. Comparison of (a) vessel sets **A** and **B**; (b) vessel sets **C** and **B**; and (c) vessel sets **D** and **B**. The x-axis of each plot shows the probability in parenthesis that differences between the mean 30-min dissolution values for the specified vessel set and vessel set **B** are statistically significant ($p < 0.05$).

should not have an impact on dissolution testing if the vessel is set up according to the ASTM procedure.[19] For the range of values studied here, neither is a significant difference observed for cylindricity. This means that the studied differences from ideality either in the cylindrical part of the vessel (~0.7 mm) or in flange flatness (~3.5 mm) observed in this study do not have a statistically significant effect on the dissolution of 10 mg of NCDA #2 prednisone tablets.

The *p* values for vessels 2 and 3 (V2 and V3, respectively, in Fig. 3b) are less than 0.05, indicating significant difference of dissolution results. From the geometric parameters of these two vessels, differences in the sphericity (1.89 mm), concentricity of sphere and cylinder (3.58 mm) stand out. These two geometric parameters characterize unevenness of the inner surface of the spherical part and distortion at the juncture of the sphere and the cylinder. The correlations indicate that these two geometric irregularities may affect dissolution results. Vessels with up to 1.46-mm sphericity showed no significant dissolution differences and for concentricity of the sphere and the cylinder, the next highest value was 1.70 mm. Restricting these two variables below these values should ensure that a given vessel is not affecting dissolution results.

Comparing the *p* values for vessel set **D** in Figure 3c shows that only vessel 2 (V2 in the graph) showed a significant difference in dissolution results. **D**2 vessel has the highest sphere radius (54.41 mm). This larger sphere radius may cause more volume of dissolution medium around the paddle, which may affect the hydrodynamics and thus the dissolution results. Restricting the sphere radius measurement below the next highest value (52.56 mm) may improve dissolution performance.

CONCLUSIONS

The geometric dimensions and irregularities of commercially available vessels obtained from four different manufacturers were characterized using a 3D VMM. The results indicate that vessels from different sources, and even from the same source, displayed differences in both geometric dimensions and inner surface irregularity measurements. However, no significant results were seen when comparing averages and standard deviations of the dissolution results of these four sets of vessels and the previous gauge R&R results. When comparing dissolution results on a vessel-by-vessel basis (amount dissolved at 30 min), a few statistically significant differences were seen. These comparisons showed that the vessel concentricity, sphericity, and the radius of sphere may influence the amount of prednisone dissolved. But the vessel flatness of flange, cylindricity, and circularity showed no effects on dissolution results in studied ranges. The VMM is a tool that could be used to qualify dissolution vessels with acceptance criteria within the limits discussed in this article as a starting point.

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