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Application News

No. i267

Material Testing Machine

Evaluation of Structural Strength of Semisolids Conforming to USP 915 and USP 1912 by Penetration Method

Introduction

Methods for characterization of the structural strength or consistency of semisolid materials which are scheduled for inclusion in the United States Pharmacopeia USP 915 and USP 1912, are useful for understanding the performance and quality stability of various pharmaceutical products. These USP chapters have shown that comparative evaluations of characteristics between semisolid materials are possible through evaluation of structural strength. As representative characteristics of pharmaceutical products related to structural strength, the ease of application and quality of spreading of ointments and lotions, resistance to dripping of liquid preparations for external use, and ease of application of adhesives for transdermal patches can be mentioned.

In the past, majority of evaluations of the structural strength of pharmaceutical products were conducted by sensory evaluation. However, the need for quantitative evaluation of the structural strength of pharmaceuticals in order to ensure a stable supply of products with appropriate viscosity has become apparent in recent years, but until now, there had been no officially recognized method for quantitative evaluations of structural strength in the pharmaceutical industry. By providing measurement methods related to the characterization of pharmaceutical products in USP 915 and USP 1912, it is hoped that techniques which enable quantitative evaluation of the viscoelasticity of pharmaceutical products will gain official recognition, and a stable supply of products and more accurate comparative evaluations of products under development will be possible.

Four evaluation methods for pharmaceutical products, namely, Strain ramp measurement, Shear rate ramp measurement, Oscillation amplitude sweep measurement, and Penetrometry measurement, are scheduled for inclusion in USP 915. Of these four methods, this article introduces the constant-speed measurement method as one evaluation method by penetrometry measurement. Because a predetermined conical test jig geometry is used with this method, it is not necessary to select a jig, and since the test is to measure the cone penetration by the penetration depth of the conical test jig, the test analyst can evaluate the data by a simply, easy-to-understand method.

In connection with penetration depth, details are provided in USP 1912, and the various characteristic values, including penetration depth, are explained from the theoretical viewpoint referring to the standard test methods ASTM D217 and ASTM D937, which were established for the semisolid substances such as industrial grease and petrolatum, respectively.

This article introduces examples of application of the penetration method in tests of a medical hand cream, which is sold commercially as a medicine, and a toothpaste known for displaying test speed-dependency of viscosity as the pharmaceutical products.

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Evaluation by Constant-Speed Measurement Method

Table 1 shows the sample information. A homogenous medical hand cream and a toothpaste containing a polishing powder were used as the samples.

Table 1 Sample Information

Samples
Medical hand cream
Toothpaste (for comparison)

Fig. 1 shows the appearance view of the conical test jig provided in USP 915. The jig consists of two parts having respective taper angles of 30° and 90° ±0.25°. The total length, surface condition, and other specifications of these parts are given in detail in the standard document. The shape of the container in which the medical agent is placed is not clearly specified, allowing room for the discretion of the person performing the test. For the test performed here, a container with an inner diameter of φ76.4 mm and a height of 63.5 mm was used (referring to the container dimensions specified in ASTM D217 and ASTM D937), and the container was set on a platform jig, which was developed as a compact table-top tester (Fig. 2). Simple jig exchange is possible by one touch.

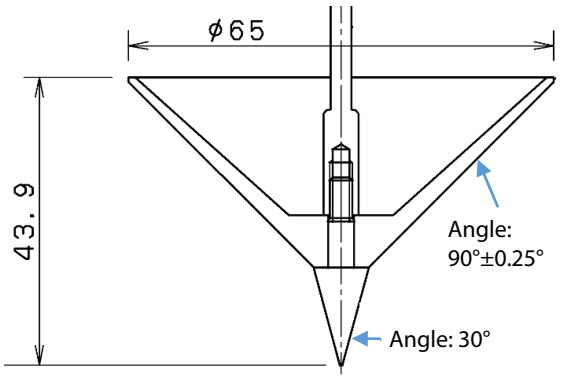

Fig. 1 Geometry of Conical Test Jig

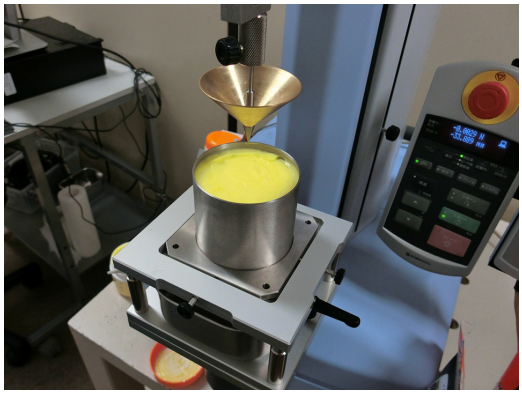

Fig. 2 Photograph of Test

USP 915 and USP 1912 provide Method I, a gravity-driven method in which a conical test jig with a total mass of 150 g is penetrated into the sample, and Method II, in which the conical test jig is penetrated under a constant speed by using a material testing machine. Of these two methods, the test described here was performed in accordance with Method II. In preparing the samples, care was taken to prevent bubbles from entering the container, and the condition was adjusted so as to obtain a flat sample surface after introduction into the container. The room temperature in the test laboratory was set to 25 °C, and the samples were allowed to stand for a certain time before the test so that the temperature of the conical test jig used to penetrate the sample was the same as room temperature. The allowable test speed range in Method II is 1 to 20 mm/s. USP 915 and USP 1912 assume application mainly to liquid and semisolid medical agents. Since the rheological properties of some samples in these states depend on the strain rate, the samples were evaluated at two test speeds of 1 mm/s and 10 mm/s in this test.

The sample properties were evaluated by the cone penetration when force of 1470 mN was applied to the sample in the container.

Table 2 Test Conditions

Instrument	:	Compact table-top tester EZ-SX
Load cell	:	50 N
Jig	:	Shimadzu Autograph consistency test jig for semisolids Container inner diameter φ76.4 mm × height 63.5 mm (3.0 inches × 2.5 inches)
Test speed	:	10 mm/s, 1 mm/s
Software	:	TRAPEZIUM™ X (Single)

Fig. 3 and Fig. 4 show the relationship between the test force and penetration depth for the medical hand cream and the toothpaste, respectively. Table 3 shows the penetration depth at 1471 mN. In the test of the medical hand cream, there was no change in the penetration depth depending on the test speed, and the curves for the two speeds overlapped. With the toothpaste, in comparison with the low test speed condition, the penetration depth increased when the test speed was set to the high value. Although the reason is unknown, this result was the opposite of that with general toothpaste, which is classified as a pseudoplastic fluid.

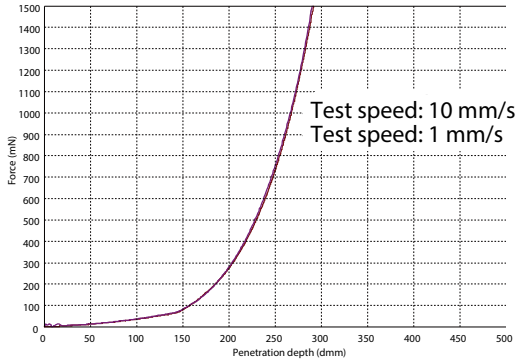

Fig. 3 Average Test Force- Penetration Depth Curves (n=3) (Medical Hand Cream)

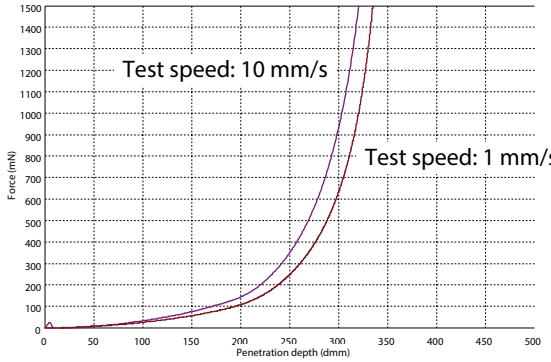

Fig. 4 Average Test Force- Penetration Depth Curves (n=3) (Toothpaste)

Table 3 Penetration Depth at 1471 mN (n=3)

Sample	Test speed (mm/s)	Penetration depth (dmm)
Medical hand cream	1	290.6
	10	293.5
Toothpaste	1	334.6
	10	320.0

Nonstandard Test Using Small Container

Although the test method specified in USP 915 does not indicate the size of the container in which the sample is introduced, the size of the conical test jig is specified. Considering the geometry of the jig, use of a container with large dimensions, like those of the containers specified in ASTM D217 and ASTM D937, is assumed. However, this is not a suitable method for simple evaluations of expensive samples, as it is necessary to use a large quantity of the sample in each test. This section describes a nonstandard test performed with a small container as a suitable method for evaluating small-quantity samples (Fig. 5). In the previous section, the container dimensions were an inner diameter of 76.4 mm × height of 63.5 mm. In contrast, the dimensions of the container used here were 25.4 mm × 24.5 mm (1 inch × 1 inch). Because the penetration of the conical test jig was limited due to the container size, the penetration depth at 400 mN was evaluated in this test. While this was not the evaluation method specified in the standard, the data acquired in the test were stable, demonstrating that this method also enables simple evaluations of samples (Fig. 6, Table 4).

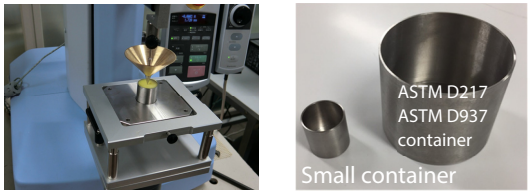

Fig. 5 Photograph of Test

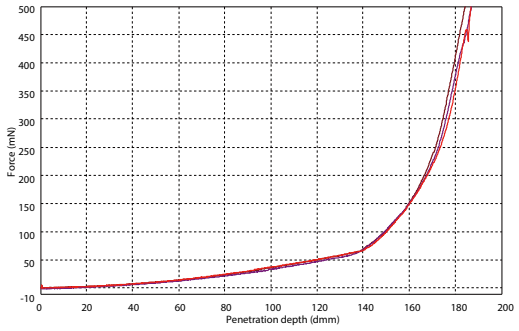

Fig. 6 Test Force- Penetration Depth Curves (Medical Hand Cream)

Table 4 Penetration Depth at 400 mN (n=3)

Sample	Penetration depth (dmm)
Medical hand cream	160.2
	159.8
	160.0

Conclusion

It was found that evaluations of the test speed dependency of the structural strength of semisolid materials are possible by using a material testing machine.

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