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The Analysis on Infusion Bag Testing Requirements and Introduction to Relevant Testing Methods

Abstract: Infusion bag (or IV bag) is the future trend for the packaging of injection liquid. This article analyses the testing requirements for infusion bags, and introduces the testing methods for specific indexes based on the testing standards for pharmaceutical packaging material.

Key Words: infusion bag, oxygen transmission rate (OTR), nitrogen transmission rate, suspension force, piercing force

Compared with traditional glass packaging, infusion bag is more environmental-friendly, cost-saving, safe, healthy and convenient. In USA and many European countries, plastic infusion package/container has taken up a great market share. Though fierce competition exists between infusion bag and plastic infusion bottle, the trend of flexible plastic packaging for injection liquid is irresistible. Differing from the traditional glass infusion bottle testing, more specific and appropriate performance testing for infusion bags should be applied so as to guarantee the safety of injection liquid.

1. The Analysis on the Testing Requirements for Infusion Bag

Infusion bag is inferior to the glass bottle in the barrier property, sealing property and transparency; among which, barrier property is greatly influenced by material change. Oxygen is the main cause for deterioration of injection liquid. In order to lower the oxygen content inside the infusion bag and postpone/stop the oxidization of the injection liquid, anti-oxidants, metal chelate agents or inert gases are adopted. As to inert gases for this purpose, the most commonly applied inert gas is nitrogen. Water vapor would transmit into the bag and result in concentration change of the injection liquid, whose medicinal safety would be endangered. Therefore, barrier property testing is very important for infusion bag.

Besides, the mechanical indexes of film materials and glass materials are fundamentally different. The mechanical testing for infusion bag is, therefore, very important. Meanwhile, the combinational closure used in the infusion bag should also be tested so as to meet the standards and actual application.

2. Barrier Property Testing for Infusion Bag

The testing requirements for water vapor transmission rate (WVTR), oxygen transmission rate (OTR) and nitrogen transmission rate are stated in YBB00102005, *3-layer Co-extrusion Films and Bags Used for Infusion,* and YBB00112005, *5-layer Co-extrusion Film (I) and Bags Used for Infusion.* At present, the technology for whole infusion bag barrier property testing has become mature. Since there is no support from the national standards, the above-stated YBB standards don't mention barrier property testing. Actually, owing to the evenness of the material, sealing property of the mouth and other factors, the actual gas transmission rate of the whole infusion bag is higher than the calculated value of the film. Thus, gas transmission rate testing of the whole infusion bag is of great need.

Oxygen transmission rate (OTR) testing is mainly used for oxygen transmission rate measurement of infusion bag film materials, infusion bags or the whole infusion bottles. Equal pressure method and differential pressure method, the two methods for oxygen transmission rate testing can both test the oxygen transmission rate of films and of the whole infusion bags and bottles. Those two methods have their respective advantages: differential pressure method has no requirements for testing gas, and can be used to test the transmission rate of any gas. Thus, this method can be used to test nitrogen transmission rate without further costs. However, this method is still at the initial stage in package testing. On the other hand, equal pressure method has become mature both for

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film testing and package testing. Yet, there exist limitations for testing gas.

Water vapor transmission rate (WVTR) testing is used for water vapor transmission rate measurement of infusion bag film materials, infusion bags or the whole infusion bottles. At present, weighing method and sensor method (including moisture sensor method, IR sensor method and electrolytic sensor method) can both be used to test water vapor transmission rate for films as well as for whole infusion bags and bottles. As to testing efficiency, sensor method, especially electrolytic sensor method, has a better perspective in the water vapor transmission rate testing of the whole infusion bags or the whole bottles.

Nitrogen transmission rate testing for infusion bag film material has always been a hotspot. At present, the testing can only be done with differential pressure testing instruments. However, some holds that both nitrogen and oxygen belong to the normal inorganic gases, and there would be some kind of 'interior' combination for oxygen transmission rate and nitrogen transmission of the same specimen; thus, nitrogen transmission rate can be estimated and assumed from the oxygen transmission rate with simple proportional relationship. However, great amount of testing data has proved this estimation is low in accuracy, and would bring hidden danger to the material selection.

3. Infusion Bag Sealing Performance Testing

Sealing performance of infusion bag mainly refers to the existence of leakage in the infusion bag, including the combinational closure. Leakage is defined as the transmission of gas going into or out of the bag through the chinks, pinholes or the minor gaps between the materials. Leakage happens, with higher probabilities, in the positions like heat seal area, combinational closure and the conjunction place between the bag and the closure. Sealing performance testing is a must to solve leakage.

The commonly adopted leakage testing methods include positive pressure method and negative pressure method. Positive pressure method is to determine the existence of leakage by filling the specimen with gas to achieve inner pressure change. This method should be especially emphasized, since it can be used to test the sealing performance of the infusion bag and other testing objects with the help of fixtures. Negative pressure method is to place the specimen into the water of the specialized testing chamber for vacuum pumping, so that pressure differences occur between the inside and outside of the immersed specimen. Observe the gas leakage or water steep to determine sealing performance of the specimen.

4. Mechanical Performance Testing for Infusion Bags

4.1 Heat Seal Strength Testing

YBB00122003, *Tests for Welding Strength* is the guideline for infusion bag heat seal strength testing. Auto tensile tester can do this test by measuring the ratio between the maximum tensile strength and the length of the heat sealed place after pulling the material to be fully separated. According to YBB00102005, *3-layer Co-extrusion Films and Bags Used for Infusion,* and YBB00112005, *5-layer Co-extrusion Film (I) and Bags Used for Infusion,* the heat seal strength should be no less than 20N/15mm.

4.2 Suspension Force Testing

The hanger at the bottom of the infusion bag is to hang the infusion bag onto the IV pole. When the injection liquid is still in the infusion bag, whether the hanger can withstand the suspension force without being pulled to split will affect the actual operation results. When testing, several infusion bag specimens should be prepared. Required tensile forces are exerted upon those bags: 7N for bags less than 250ml; and 15N for bags bigger than 250ml. It's required that the bag should not be pulled to split in 60 minutes.

4.3 Pull Open Force Testing

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The open easiness of the pull open cap ring would directly influence the operational convenience of the infusion bag and the safety of the injection liquid. This force should be within a specific force range so as to avoid open difficulty, low tensile force and the corresponding leakage caused by decreased sealing performance of the infusion bag.

The pull open force can be tested in the following way: sterilize the specimen with wet heating treatment. Then, fix the specimen onto the fixture of the auto tensile tester, and the pull open ring onto the other fixture. Pull the ring at a speed of 200mm/min±20mm/min in a 23℃ oblique angle against the vertical direction. Record the force value at which the ring is pulled to open. According to YBB00242004, *Combinational Closures for Plastic Infusion Containers (with pull open cap),* the pull open force of the ring should not exceed 80N, and no split should occur around the piercing area.

4.4 Piercing Force Testing

Prepare several specimens, and pierce into the piercing area of the infusion bag at a speed of 200mm/min±20mm/min with the required piercing device mentioned in GB 8368-2005, *Infusion Sets for Single Use, Gravity Feed*. Record the force values onto the combinational cap. Piercing force testing should be done with the auto tensile tester. Chart 1 below is a set of piercing data obtained in the test of Labthink Lab.

Chart 1. Piecing Force Testing Data

	Specimen 1	Specimen 2	Specimen 3	Average Value
Data/N	38.42	41.12	43.04	40.86

As regulated in YBB00242004, *Combinational Closures for Plastic Infusion Containers (with pull open cap)*, the average value of piercing force should not exceed 75N, and the maximum value should not exceed 80N. According to YBB00102005, *3-layer Co-extrusion Films and Bags Used for Infusion,* and YBB00112005, *5-layer Co-extrusion Film (I) and Bags Used for Infusion,* the piercing force of the metal piercing device should not exceed 80N.

5. Conclusions

Compared with glass infusion bottle, plastic infusion bag has more testing items in the testing of its barrier property, sealing performances and mechanical properties, etc. Those testing items are closely related to the safety of the injection liquid as well as the storage and convenience of the infusion bag. Therefore, every testing item is very important for safe operation of the infusion bag. Though the testing items for infusion bag seem to be numerous, there exists universality of the testing instruments. The auto tensile tester produced by Labthink can accomplish many mechanical testing items of the infusion bags with varied testing accessories, which provides a better instrument choice for pharmaceutical packaging manufacturers and infusion bag manufacturers, so that instrument investment can be greatly reduced, and the testing demands can be satisfied with only the addition of certain fixtures.