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# The Preferred Method of Gas Permeability Test for Drug Packaging Materials

## -Differential Pressure Method

**Abstract:** based on YBB00082003 *Test Methods of Gas Permeability,* this article presents a detailed introduction to the methods of gas permeability test. It also deals with the latest developments of each method as well as how specific drug packaging material standard influence the application of permeability test methods.
**Key words:** drug, drug packaging materials, and oxygen permeability

The application of packaging materials with excellent barrier property can efficiently prolong quality guarantee period, expand storage environment of products, thus providing more conveniences to transportation and storage. For the above-mentioned reason, the application of barrier materials witnessed a very rapid development. Test methods of gas permeability can be divided into differential-pressure method and equal-pressure method. The influence of different test methods on test data cannot be completely eliminated. Because the methods of barrier property test are not well understood, current drug packaging enterprises do not pay much attention during the purchasing of permeability testers. To establish a uniform test method for barrier property test of domestic drug packaging materials and to improve the comparability of test data, the State Food and Drug Administration of the People's Republic of China issued YBB00082003 Test *methods of Gas Permeability,* which becomes the directory in selecting gas permeability testers.

YBB00082003 Gas Permeance Measurement provides two methods: differential pressure method and coulometric method, which will be dealt with in detail below.

### 1. Differential Pressure Method

Differential pressure method is formulated in accordance with ISO 15105-1, ISO 2556, GB 1038-2000. In differential pressure method, higher-pressure chamber and low-pressure chamber are separated by drug packaging film or sheets. There is one pressure gauge in each chamber. The high-pressure chamber is filled with test gas of about 0.1MPa and the low-pressure chamber has known volume. Vacuumize the low chamber to about zero after the sealing of test finishes and then measure the pressure increment of low-pressure chamber with pressure gauge. In this way, gas permeance- function of time, from high-pressure chamber into low-pressure chamber can be determined. However, the initial period of transmission rate with time should be excluded. When the pressure variation rate of low-pressure chamber becomes stable, that is to say the gas permeance becomes stable, users can calculate gas permeance and gas permeability coefficient according to the formula offered in the standard. The unit is $cm^3/m^2 \cdot 24h \cdot 0.1Mpa$. It should be specially noted that in the initial period of test, the whole permeable chamber should be vacuumized to below 27kPa with additional continuous outgassing. Differential pressure method can also test gas permeability coefficient to materials, diffusion coefficient of gases within materials and solubility coefficient of materials to gases. It can also be used to test common inorganic gases such as oxygen gas, nitrogen gas, carbon dioxide and air.

In the draft of YBB00082003, it is stated that the differential pressure method is formulated referring to GB/T 1038-2000 *test method of gas permeance for plastic films and foils-differential pressure method.* After comparing the methods in these two standards we can see that the requirements are basically the same while the content of GB/T 1038-2000 is more complete than that of YBB00082003. Therefore, GB/T 1038-2000 can completely meet what required in the first method of YBB00082003. note that comparing with current international test standards of film permeability test with differential pressure method such as ASTM D1434、ISO 15105-1、ISO 2556：2001,

GB/T 1038-2000 is less complete in terms of detailed operation rules. But its demand on various parameters during test is uniform with that of these international standards. For instance, it is specified in ASTM D 1434-82（2003）that the vacuum degree of low-pressure side of test chamber should be lower than 26Pa, while that is required to be no high than 27 Pa in standards ISO 2556:2001and GB/T 1038-2000.

## 2. Coulometric Method

YYB00082003 formulate the coulometric method (the second method in the standard) While reserving the differential pressure method.

The coulometric method, or the sensor method, belongs to equal pressure test method. In this method, the permeable chamber is divided into two independent airflow systems by drug packaging film or sheet, with one side being the flowing testing gas (pure oxygen or mixed gas of oxygen) and the other side being the flowing dry nitrogen gas. The pressure of the two sides is equal but oxygen partial pressure is different. Under the function of oxygen concentration difference, oxygen transmits through the film and is diverted into the sensor by nitrogen carrier gas. Oxygen permeability of the package can be calculated with the oxygen quantity in nitrogen carrier gas is accurately measured by the sensor. The unit of oxygen permeance, tested in coulometric method without calibration, is $cm^3/m^2 \cdot d$. Instruments of coulometric method should be calibrated with standard film before test. Calibration coefficient of instrument should also be determined. For differential pressure method and equal pressure method, the test principle and test conditions are different. The units of their results are also different. Therefore, there is no comparability of the non-calibrated data obtained from the two methods. But the comparison becomes possible after calibrating the instrument with standard film. In addition, the data of coulometric method can be traced back to differential pressure method, which is clearly specified in ASTM D3985-05：“Limited statistical data on correlations with Test Method D1434 methods are available; however, the oxygen transmission rate of a standard reference material as determined manometrically by NIST, is in good agreement with the values obtained in the coulometric interlaboratory test using material from the same manufacturing lot.”。Among it, ASTM D 1434 is the test standard of differential pressure method.

Because the sensor used belongs to the consumptive type, corrected factor of the instrument is not always valid and needs to be periodically calibrated as required. the sensor must be changed when it deteriorates to a certain extend. At the same time, the consumption of oxygen gas and nitrogen gas during test is rather big. Thus test cost of this method is much higher than that of the differential pressure method.

## 3. The Application of Test Methods

Based on specific executive standard of drug packaging materials, we will discuss the detailed application of the above-mentioned two methods:

Table 1: gas permeability measurement of drug packing materials

| Number of standard | Name of standard | YBB00082003 | |
|---|---|---|---|
| | | The first method differential pressure method | The second method coulometric method |
| YBB00132002 | General rules on laminated film and bag for drug packaging | √[1] | × |
| YBB00172002 | Laminated film and bag of | √[1] | × |

| | | | |
|---|---|---|---|
| | polyester/aluminum/polyethylene for drug packaging | | |
| YBB00182002 | Laminated film and bag of polyester/ low density polyethylene for drug packaging | √[1] | × |
| YBB00192002 | Laminated film and bag BOPP/ low density polyethylene for drug packaging | √[1] | × |
| YBB00242002 | Laminated sheet of polyamide/aluminum/pdythene film for cold forging moulded drug | √[1] | × |
| YBB00342002 | General rules on multi-layer co-extrusion | √[1, 2] | × |
| YBB00182004 | Laminated hard sheet of aluminum / pdythene for cold forging moulded solid drug | √ | √ |
| YBB00192004 | Laminated film and bag of BOPP/ Vacuum aluminum coated casting polypropylene for drug packaging | √ | × |
| YBB00202004 | Laminated film and bag of cellophane paper/aluminum/ polypropylene for drug packaging | √ | × |
| YBB00072005 | Low density polyethylene film and bag for drug use | √ | × |
| YBB00102005 | three-layer co-extrusion film（Ⅰ）,bag for transfusion | √[2] | × |
| YBB00112005 | five-layer co-extrusion film（Ⅰ）,bag for transfusion | √[2] | × |
| YBB00202005 | Polypropylene/polyethylene/polyvinylidene chloride for cold forging moulded solid drug | √[1] | × |
| YBB00212005 | Polypropylene hard sheet for solid drug | √[1] | × |
| YBB00222005 | Laminated hard sheet of polypropylene/polyvinylidene chloride for solid drug | √[1] | × |
| YBB00232005 | Laminated hard sheet of polypropylene/low density polyethylene for solid drug | √[1] | × |
| YBB00252005 | Laminated flexible ointment tube of drug polyethylene/aluminum/ polyethylene | √ | √ |

Note: 1. if YBB00082003 has not been formulated at the time when current standard is being formulated or when the original standard of this modified standard is being formulated, the standard GB/T 1038-2000 would be executed.

2. oxygen permeance and nitrogen gas permeance of materials should be tested.

From table 1 we can see that almost all the gas permeability tests of drug packaging materials are based on differential pressure method except. The coulometric method is applicable for gas permeability test of only two materials as the alternative method. Therefore, permeability testers differential pressure method can completely meet the requirements of barrier property test. However, currently speaking, the coulometric method is unable to satisfy the test requirements of most of the materials.

## 4. Conclusion

The standard of gas permeability test for drug packaging materials is in accordance with international test methods. Moreover, new test methods based on new industry characteristics of drug packaging industry are proposed. However, we can see from the above-mentioned analysis that although differential-pressure method can completely meet test requirements of drug packaging materials, the application of coulometric method is

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rather narrow. Therefore, selecting gas permeability testers of differential pressure method can better meet the requirements of drug packaging test standards. It can also efficiently avoid the possible influence resulting from the adopting of different test methods, thus reducing test and improving productivity.