4007 Determination of Gas Permeance of packaging materials and containers for pharmaceutical use

This method, which is applicable to determining the gas permeance of the packaging materials or containers for pharmaceutical use, consists of differential-pressure method and coulometric method. The differential-pressure method is only suitable for testing of the films or sheeting, and the coulometric method is only suitable for determining the oxygen gas permeance.

Gas transmission rate (GTR) is defined as the volume of the steady-state transmission of a gas through a unit area of the test specimen or a container in unit time, under specified conditions of temperature and humidity. It is generally expressed as the volume at a standard temperature and under standard atmospheric pressure, in the unit of cm^3/ (m^2·24h) for films or sheeting, and in the unit of cm^3/ (container·24h) for containers.

Gas permeance is defined as the volume of the steady-state transmission of a gas, under unit pressure difference, through a unit area of the test specimen or a container in unit time, under specified conditions of temperature and humidity. It is generally expressed as the volume at a standard temperature and under standard atmospheric pressure, in the unit of cm^3/ (m^2·24h·0.1Mpa) for film or sheeting, and in the unit of cm^3/ (container·24h·0.1Mpa) for containers.

Gas permeability coefficient is defined as the volume of the steady-state transmission of a gas, under unit pressure difference, through the test specimen of unit thickness, per unit area and unit time, under specified conditions of temperature and humidity. It is generally expressed as the volume at a standard temperature and under standard atmospheric pressure, in the unit of cm^3·cm/ (m^2·24h·0.1Mpa).

Test environment should be at a temperature of 23℃±2℃.

Method1 Differential-pressure method

The high-pressure chamber filled with about 0.1MPa of the test gas and the low-pressure chamber of known volume are separated by the film or sheeting for pharmaceutical use. After being sealed by the test specimen, the low-pressure chamber is evacuated of all air by a vacuum pump. Then the pressure increment (ΔP) of the low-pressure chamber is measured by a manometer to determine the amount of gas passing through the test specimen from the high-pressure chamber to the low-pressure chamber as a function of time, but the initial period during which the gas transmission rate changes with the time should be excluded.

Apparatus and materials An apparatus for determining gas permeance by differential-pressure method mainly consists of the following parts:

Transmission cell The cell consists of an upper part and a lower part. When the test specimen is mounted, the upper part equipped with a gas inlet tube is the high-pressure chamber for containing the test gas, and the lower part is the low-pressure chamber for containing the permeated gas and determining the difference in pressure before and after the gas permeation.

Manometric device The high-pressure chamber and the low-pressure chamber should be respectively equipped with a manometer. The manometer in the high-pressure chamber should be with a minimum sensitivity of 100 Pa, and that in the low-pressure chamber should be with a minimum sensitivity of 5 Pa.

Vacuum pump The pump should be capable of producing a pressure lower than 10 Pa in the lower-pressure chamber.

Test gas The purity of the test gas should not be less than 99.5%.

Procedure Choose three pieces of the test specimens, which should be of uniform thickness and suitable size, and should be free from wrinkles, creases, pinholes and other defects. Mark the side of each specimen facing the test gas, and condition the specimens at 23°C±2°C in a desiccator for more than 48 hours. Measure the thickness at least five points of each specimen to the nearest 0.001 mm with a suitable gage, and take the arithmetic mean of the measurements. Mount the specimen, and carry out the test. Perform a pre-permeation experiment for 10 minutes to reject the nonlinear phase in the initial period of the test, and continue the test until the steady permeation to be attained as the changes of pressure difference in the equal intervals of timeremain constant.

The gas permeance (P_g) could be calculated according to the followingequation:

$$P_g = \frac{\Delta P}{\Delta t} \times \frac{V}{S} \times \frac{T_0}{P_0 T} \times \frac{24}{(P_1 - P_2)}$$

Where: P_g is the gas permeance of the test specimen, $cm^3/(m^2 \cdot 24h \cdot 0.1Mpa)$;

$\Delta P/\Delta t$ is the arithmetic average of pressure changes of the low-pressure chamber per unit time, under steady permeation, Pa/h;

V is the volume of the low-pressure chamber, cm^3;

S is thetestarea of the test specimen, m^2;

T is the test temperature, K;

P_1-P_2 is the pressure difference between the two sides of the specimen, Pa;

T_0 is the standard temperature (273.15K);

P_0 is the standard atmospheric pressure (0.1Mpa).

The coefficient of gas permeability (P_g') could be calculated according to the following equation:

$$P_g' = \frac{\Delta P}{\Delta t} \times \frac{V}{S} \times \frac{T_0}{P_0 T} \times \frac{24 \times D}{(P_1 - P_2)} = P_g \times D$$

Where P'_g is the coefficient of gas permeability of the test specimen, $cm^3 \cdot cm/(m^2 \cdot 24h \cdot 0.1Mpa)$;

$\Delta P/\Delta t$ is the arithmetic average of pressure changes of the low-pressure chamber per unit time, under steady permeation, Pa/h;

T is the test temperature, K;

D is the thickness of the test specimen, cm.

Take the arithmetic mean of three specimens as the test result. Except for the specimen of high barrier property (the result of gas permeance is less than or equal to $0.5cm^3/(m^2 \cdot 24h \cdot 0.1MPa)$), the measurement of each specimen should not deviate from the mean value by more than ±10%. The measurement of each specimen of high barrier property should not be greater than $0.5cm^3/(m^2 \cdot 24h \cdot 0.1MPa)$.

Method 2 Coulometric analysis method (Coulometric method)

The transmission cell is divided into two parts by the test specimen. Oxygen is purged on one side, and the carrier gas of nitrogen is purged on the other side. The oxygen passing through the specimen is transported by the nitrogen carrier gas into the coulometric analyzer, where chemical reaction occurs to produce electric voltage, which is proportional to the amount of oxygen flowing into the coulometricanalyzer per unit time.

Apparatus and materials An apparatus for determining gas permeance by coulometric analysis method mainly consists of the following parts:

Transmission cell Consisting of two parts, the cell should be equipped with thermometric devices and assembled with suitable closures. The test area of the specimens, generally between1-150 cm^2, should be adapted according to the range of values to be determined.

Carrier gas It normally could be nitrogen gas or a nitrogen-hydrogen hybrid gas containing certain ratio of hydrogen.

Test gas The purity should not be less than 99.5%.

Coulometric detector (Coulometer) The detector, sensitive to oxygen, with a constant operation characteristic, could be used to measure the quantity of oxygen transmitted.

Procedure Choose three pieces of the test specimens, which should be of uniform thickness and suitable size, and should be free from wrinkles, creases, pinholes and other defects. Mark the side of each specimen facing the test gas, and condition the specimens at 23°C± 2°C in a desiccator for more than 48 hours. Measure the thickness at least five points of each specimen to the nearest 0.001 mm with a suitable gage, and take the arithmetic mean of the measurements. Place the specimen into the transmission cell, and then perform the test. End the test when the output signals of the apparatus are steady for a period of time.

The oxygen gas transmission rate (O_2GTR) could be calculated according to the following equation:

$$O_2GTR = \frac{(E_e - E_0) \times Q}{A \times R}$$

Where: O_2GTR is the oxygen transmission rate, $cm^3/(m^2 \cdot 24h)$;

E_e is the observed steady-state voltage, mV;

E_0 is the zero level voltage before the experiment, mV;

A is the area of the specimen, m^2;

Q is the calibration constant of the apparatus, $cm^3\Omega/(mV \cdot 24h)$;

R is the value of load resistance, Ω.

The oxygen gas permeance (P_{O_2}) could be calculated according to the following equation:

$$P_{O_2} = \frac{O_2GTR}{P}$$

Where: P_{O_2} is the oxygen permeance, $cm^3/(m^2 \cdot 24h \cdot 0.1MPa)$;

O_2GTR is the oxygen transmission rate, $cm^3/(m^2 \cdot 24h)$;

P is the partial pressure of oxygen on the test gas side of the transmission cell, MPa, which is the product of mol fraction of oxygen and total pressure (normally, one atmosphere). The partial pressure of oxygen on the carrier gas side is considered to be zero.

The oxygen permeability coefficient (P'_{O_2}) could be calculated according to the following equation:

$$P'_{O_2} = P_{O_2} \times D$$

Where: P'_{O_2} is the oxygen permeability coefficient, $cm^3/(m \cdot 24h \cdot 0.1Mpa)$;

P_{O_2} is the oxygen permeance, $cm^3/(m^2 \cdot 24h \cdot 0.1MPa)$;

D is the average thickness of the test specimen, m.

Take the arithmetic mean of three specimens as the test result. Except for the specimen of high barrier property (the gas permeance result is less than or equal to 0.5 $m^3/(m^2 \cdot 24h \cdot 0.1MPa)$), the measurement of each specimen should not deviate from the mean value by more than ±10%. The measurement of each specimen of high barrier property should not be greater than $0.5cm^3/(m^2 \cdot 24h \cdot 0.1MPa)$.

Note Under the controlled conditions of temperature and humidity, the tester equipped with suitable package test stations could be employed further to determine the oxygen permeance of containers. Perform the test according to the instrument operation manual.

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