t_R: Retention time of compound,
$W_{0.5\,h}$: Width of the peak at half peak height,

where t_R and $W_{0.5\,h}$ have the same unit.

Note: Avoid the use of authentic specimens, internal standards, reagents or solvents containing substances that may interfere with the determination.

Among the operating conditions specified in the individual monograph, inside diameter and length of the column, particle size of the column packing material, column temperature, composition ratio of the mobile phase, composition of buffer solutions in the mobile phase, pH of the mobile phase, concentration of ion pair-forming agents in the mobile phase, ionic strength of the mobile phase, numbers of condition changes, timing of such changes, gradient program, composition and flow rate of derivative-producing reagents, reaction time and temperature of reaction chamber and flow rate of mobile phase may be modified within limits which allow the required elution order, resolution, symmetry factor, and relative standard deviation to be obtained.

28. Loss on Drying Test

The Loss on Drying Test is a method to measure the loss in mass of the sample, when dried under the conditions specified in each monograph. This method is applied to determine the amount of water, all or a part of water of crystallization, or volatile matter in the sample, which is removed during the drying.

The description, for example, "not more than 1.0% (1 g, 105°C, 4 hours)" in a monograph, indicates that the loss in mass is not more than 10 mg per 1 g of the substance in the test in which about 1 g of the substance is accurately weighed and dried at 105°C for 4 hours, and "not more than 0.5% (1 g, in vacuum, phosphorus (V) oxide, 4 hours)," indicates that the loss in mass is not more than 5 mg per 1 g of the substance in the test in which about 1 g of the substance is accurately weighed, transferred into a desiccator (phosphorus (V) oxide), and dried in vacuum for 4 hours.

Procedure

Weigh assurately a weighing bottle that has been dried for 30 minutes according to the method specified in the monograph. Take the sample within the range of ±10% of the amount directed in the monograph, transfer into the weighing bottle, and, unless otherwise specified, spread the sample so that the layer is not thicker than 5 mm, then weigh it accurately. Place the loaded bottle in a drying chamber, and dry under the conditions specified in the monograph. When the size of the sample is large, convert it to small particles having a size not larger than 2 mm in diameter by quick crushing, and use the crushed sample for the test. After drying, remove from the drying chamber, and reweigh accurately. When the sample is dried by heating, the temperature is within the range of ±2°C of that directed in the monograph, and, after drying the bottle, the sample is allowed to cool in a desiccator (silica gel) before weighing.

If the sample melts at a temperature lower than that specified in the monograph, expose the sample for 1 to 2 hours to a temperature between 5°C and 10°C below the melting temperature, dry under the conditions specified in the monograph. Use a desiccant specified in the monograph, and renew frequently.

29. Loss on Ignition Test

The Loss on Ignition Test is a method to measure the loss in mass when the sample is ignited under the conditions specified in each monograph. This method is usually applied to inorganic drugs which lose a part of the components or impurities during ignition.

The description, for example, "40.0 – 52.0% (1 g, 450 – 550°C, 3 hours)" in a monograph, indicates that the loss in mass is 400 to 520 mg per g of the substance in the test in which about 1 g of the substance is weighed accurately and ignited between 450°C and 550°C for 3 hours.

Procedure

Previously ignite a crucible or a dish of platinum, quartz or porcelain to constant mass, at the temperature directed in the monograph, and weigh accurately after cooling.

Take the sample within the range of ±10% of the amount directed in the monograph, transfer into the above ignited container, and weigh it accurately. Ignite under the conditions directed in the monograph, and, after cooling, reweigh accurately. Use a desiccator (silica gel) for the cooling.

30. Mass Variation Test

Mass Variation Test is the test to determine the uniformity of dosage units by mass variation. This test is not applied to the dosage forms to which *Content Uniformity Test* is applied. Apply the following test unless otherwise specified in the individual monograph. The *Content Uniformity Test* can be employed for this test when the method directed in the *Assay* is used for determination.

Select 30 units, weigh the first 10 units individually and calculate the acceptance value. The requirements are met if the acceptance value is less than or equal to 15.0%. When the acceptance value is greater than 15.0%, test the next 20 units. The requirements are met if the final acceptance value of the 30 dosage units does not exceed 15.0% and no unit shows a deviation that exceeds 25.0% of the label claim.

$$\text{Acceptance value} = |M - A| + ks$$

M: Label claim (100%), unless otherwise specified in the individual monograph.
A: Content of active ingredient (% of label claim) determined under Assay.

$$x_i = w_i \times A/\overline{W}$$

$x_1, x_2 \cdots x_i \cdots x_n$: Individual estimated contents of the units tested.
$w_1, w_2 \cdots w_i \cdots w_n$: Individual masses of the units tested.
$\overline{W}$: Mean of individual masses ($w_1, w_2 \cdots w_i \cdots w_n$).
n: Sample size (number of units in a sample).
k: Acceptability constant, $k = 2.2$ when the sample size is 10, and $k = 1.9$ when the sample size is 30.
s: Standard deviation of the sample.