the individual monograph. Fix the testing assembly to the shaft bearing so that a distance between the lower end of the basket or paddle and the inside bottom of the vessel is maintained at 25 ± 2 mm, and the axis of the rotatory shaft is not more than 2 mm from the vertical axis of the vessel. During the operation, remove the thermometer, cover the vessels in order to prevent evaporation of the dissolution medium, and ensure that the stirring element rotates smoothly without significant agitation or vibration. When Method 1 is performed, unless otherwise specified, place one sample in the dry basket, fit the basket to the coupling disk, lower the basket to a specified position, and immediately start rotation. When Method 2 is performed, unless otherwise specified, allow one sample to sink to the center of the vessel, and immediately start rotation of the paddle at a specified position. If the use of the sinker is specified in the individual monograph, place the sample in the sinker and allow to sink to the center of the vessel.

(2) Method 3

In a cell, specified in the individual monograph, place one glass bead 5 mm in diameter and a specified amount of glass beads 1 mm in diameter, and, unless otherwise specified, place one sample on the layer of glass beads, or on a holder in the case where the use of a holder is specified in the individual monograph. After assembling a specified filter, introduce the dissolution medium warmed to 37 ± 0.5°C through the bottom of the cell to obtain a suitable flow rate within ± 5% of the prescribed rate by using a pump. Use a pump with suitable pulse flow characteristics, if specified in the monograph.

Sampling of the dissolution medium

When only a lower limit of the dissolution rate is specified at a point of time in the individual monograph, collect the dissolution medium at a prescribed time. However, in the case where the sample meets the requirement of the dissolution test, the dissolution medium may be collected at a time before the prescribed time, and the test may be halted. When two or more points of withdrawal time or both upper and lower limits of the dissolution rate are specified in the monograph, collect the dissolution medium at the prescribed time within a tolerance of ±2%.

In Method 1 and Method 2, collect a volume of the dissolution medium from a position midway between the surface of the dissolution medium and the top of the basket or blade and not less than 10 mm from the vessel wall, filter immediately by a suitable method, and use the filtrate as the sample solution. For the filtration, an inert filter must be used that does not adsorb the active ingredient from the solution and does not contain substances extractable by the dissolution medium that would interfere with the prescribed analytical method. In Method 3, the dissolution medium that emerges from the cell and collected in the receptacles or the medium in the reservoir is used as the sample solution.

The active ingredient in the sample solution is assayed by a method described in the individual monograph, and the quantity dissolved in a specified time is expressed as a percentage of the labeled amount.

Determination

Unless otherwise specified, perform the test on 6 samples: if the individual dissolution rate obtained from each sample meets the requirements specified in the individual monograph, the samples conform to the test. When individual dissolution rates of 1 or 2 samples fail to meet the requirements, repeat the test on 6 additional samples: if individual dissolution rates of not less than 10 samples out of 12 meet the requirements, the samples conform to the test.

16. Endpoint Detection Methods in Titrimetry

Titrimetry is a method or a procedure for volumetric analysis, which is usually classified into acid-base titration (neutralization titration or pH titration), precipitation titration, complexation titration, oxidation-reduction titration, etc., according to the kind of reaction or the nature of the phenomenon occurring between the titrate and the titrant (standard solution for volumetric analysis). Furthermore, titration performed in a nonaqueous solvent is generally called nonaqueous titration, which is frequently used for volumetric analysis of weak acids, weak bases, and their salts. The endpoint in titrimetry can be detected by color changes of indicators and/or by changes of electrical signals such as electrical potential or electrical current.

The indicator method is one of the endpoint detection methods in titrimetry. In this method the color of an indicator dye, dissolved in the titrate, changes dramatically in the vicinity of the equivalence point due to its physico-chemical character, and this property is used for visual endpoint detection. Selection of an indicator and specification of the color change induced in the respective titration system, should be described in the individual monograph. An appropriate indicator should change color clearly, in response to a slight change in physico-chemical properties of the titrate, such as pH, etc., in the vicinity of the equivalence point.

Regarding the electrical endpoint detection methods, there are an electrical potential method and an electrical current method, which are called potentiometric and amperometric titration methods, respectively. They are generically named electrometric titration. In the potentiometric titration method, the endpoint of a titration is usually determined to be the point at which the differential potential change becomes maximum or minimum as a function of the quantity of titrant added. In the amperometric titration method, unless otherwise specified, a bi-amperometric titration method is used, and the endpoint is determined by following the change of microcurrent during the course of a titration. Furthermore, the quantity of electricity (electrical current × time) is often used as another electrochemical signal to follow a chemical reaction, as described in "*Water Determination 2. Coulometric Titration*".

The composition of a titration system, such as amount of specimen, solvent, standard solution for volumetric analysis, endpoint detection method, equivalent amount of substance to be examined (mg)/standard solution (mL), should be specified in the individual monograph. Standardization of the standard solution and titration of a specimen are recommended to be done at the same temperature. When there is a marked difference in the temperatures at which the former and the latter are performed, it is necessary to make an appropriate correction for the volume change of the standard solution due to the temperature difference.

Indicator Method

Weigh an amount of a specimen in a flask or a suitable vessel as directed in the monograph or in "*Standard Solutions*

for Volumetric Analysis", and add a specified quantity of solvent to dissolve the specimen. After adding a defined indicator to the solution to prepare the titrate, titrate by adding a standard solution for volumetric analysis by using a buret. In the vicinity of the endpoint, observe the color change induced by the cautious addition of 0.1 mL or less of the titrant. Calculate the quantity of titrant added from the readings on the scale of the buret used for the titration at the starting point and at the endpoint at which the specified color change appears, as directed in the individual monograph or in the "*Standard Solutions for Volumetric Analysis*". Although addition of the volumetric standard solution by buret is usually done manually, an automatic buret can also be used.

Unless otherwise specified, perform a blank determination according to the following method, and make any necessary correction.

Measure a specified quantity of solvent, as directed in the monograph or in the "*Standard Solutions for Volumetric Analysis*", and titrate as directed. The required quantity of the standard solution added to reach a specified color change, is assumed to be the blank quantity for the titration system. However, when the blank quantity is too small to evaluate accurately, the quantity can be assumed to be zero.

Electrical Endpoint Detection Methods

1. Potentiometric titration

(1) Apparatus

The apparatus consists of a beaker to contain the specimen, a buret for adding a standard solution, an indicator electrode and a reference electrode, a potentiometer for measuring potential difference between the electrodes or an adequate pH meter, a recorder, and a stirrer for gentle stirring of the solution to be examined. Separately, an automatic titration apparatus assembled from suitable units and/or parts, including a data processing system, can also be used.

In this titration method, unless otherwise specified, indicator electrodes designated in Table 1 are used according to the kind of titration. As a reference electrode, usually a silver-silver chloride electrode is used. Besides the single indicator electrodes as seen in Table 1, a combined reference electrode and indicator electrode can also be used.

Table 1 Kinds of Titration and Indicator Electrodes

Kind of titration	Indicator electrode
Acid-base titration (Neutralization titration, pH titration)	Glass electrode
Precipitation titration (Titration of halogen ion by silver nitrate)	Silver electrode. A silver-silver chloride electrode is used as a reference electrode, which is connected with the titrate by a salt bridge of saturated potassium nitrate solution.
Oxidation-reduction titration (Diazo titration, etc.)	Platinum electrode
Complexation titration (Chelometric titration)	Mercury-mercury chloride (II) electrode
Nonaqueous titration (Perchloric acid titration, Tetramethylammonium titration)	Glass electrode

When the potentiometric titration is carried out by the pH measurement method, the pH meter should be adjusted according to the "*pH Determination*".

(2) Procedure

Weigh a defined amount of a specimen in a beaker, and add an indicated quantity of solvent to dissolve the specimen, as directed in the monograph. After the potential difference E (mV) or the pH value of the solvent to be used for titration has reached a stable value, immerse both reference and indicator electrodes, which have previously been washed with the solvent being used, in the solution to be examined, and titrate with a standard solution for volumetric analysis with gentle stirring of the solution. During the titration, the tip of the buret should be dipped into the solution, to be examined. The endpoint of titration is determined by following the variation of the potential difference between two electrodes as a function of the quantity of titrant added. In the vicinity of the endpoint, the amounts of a titrant added should be 0.1 mL or less for adequate titrimetry. Plot the obtained potential values along the ordinate and the quantity of a titrant added V (mL) along the abscissa to draw a titration curve, and obtain the endpoint from the maximum or the minimum value of $\Delta E/\Delta V$ or from the value of electromotive force or pH corresponding to the equivalence point.

Unless otherwise specified, the decision of the endpoint in this method is usually made by either of the following methods.

(i) Drawing method

Usually, draw two parallel tangent lines with a slope of about 45° to the obtained titration curve. Next, draw a 3rd parallel line at the same distance from the previously drawn two parallel lines, and decide the intersection point of this line with the titration curve. Further, from the intersection point, draw a vertical line to the abscissa, and read the quantity of titrant added as the endpoint of the titration.

Separately, the endpoint of the titration can also be otained from the maximum or the minimum of the differential titration curve ($\Delta E/\Delta V$ vs. V).

(ii) Automatic detection method

In the case of potentiometric titration using an automatic titiration system, the endpoint can be determined by following the respective instrumental indications. The endpoint is decided either by following the variation of the differential potential change or the absolute potential difference as a function of the quantity of titrant added: in the former case the quantity given by the maximum or the minimum of the differential values, and in the latter the quantity given by the indicator reaching the endpoint potential previously set for the individual titration system, are assumed to be the endpoint volumes, respectively.

2. Amperometric titration

(1) Apparatus

The apparatus consists of a beaker for holding a specimen, a buret for adding a standard solution for volumetric analysis, two small platinum plates or wires of the same shape as the indicator electrode, a device to load direct current microvoltage between two electrodes, a microammeter to measure the indicator current between the two electrodes, a recorder, and a stirrer which can gently stir the solution in a beaker. Separately, an automatic titration apparatus assembled from suitable units and/or parts, including a data processing system, can also be used.

(2) Procedure

Weigh a defined amount of a specimen in a beaker, and add an indicated quantity of solvent to dissolve the specimen, as directed in the individual monograph. Next, after washing the two indicator electrodes with water, immerse both electrodes in the solution to be examined, apply a constant voltage suitable for measurement across two electrodes by using an appropriate device, and titrate the solution with a standard solution for volumetric analysis. During the titration, the tip of the buret should be dipped into the solution to be examined. The endpoint of titration is determined by following the changes of microcurrent between the two electrodes as a function of the quantity of titrant added. In the vicinity of the endpoint, the amounts of the titrant added should be 0.1 mL or less for adequate titrimetry. Plot the obtained current values along the ordinate and the quantity of the titrant added V (mL) along the abscissa to draw a titration curve, and usually take the inflection point of the titration curve (the point of intersection given by the extrapolation of two straight lines before and after the inflection) as the endpoint in amperometric titration.

The blank test in this titration is usually performed as follows: Take a volume of the solvent specified in the individual monograph or in the "Standard Solution for Volumetric Analysis", and use this as the sample solution. Determine the amount of the volumetric standard solution needed for giving the endpoint, and use this volume as the blank. If this volume is too small to determine accurately, the blank may be considered as 0 (mL).

Unless otherwise specified, the endpoint in this titration is decided by either of the following methods.

(i) Drawing method

Usually, extrapolate the two straight lines before and after the inflection, and obtain the inflection point of the titration curve. Next, read the quantity of titrant added at the inflection point, and assume this point to be the endpoint.

(ii) Automatic detection method

In the case of amperometric titration using an automatic titration system, the endpoint can be determined by following the instrumental indications. The endpoint is decided by following the variation of the indicator current during the course of a titration, and the quantity of titrant added is assumed to be that at which the current has reached the endpoint current set previously for the individual titration system.

When atmospheric carbon dioxide or oxygen is expected to influence the titration, a beaker with a lid should be used, and the procedure should be carried out in a stream of an inert gas, such as nitrogen gas. Further, when a specimen is expected to be influenced by light, use a light-resistant container to avoid exposure of the specimen to direct sunlight.

17. Fats and Fatty Oils Test

The Fats and Fatty Oils Test is a method applied to fats, fatty oils, waxes, fatty acids, higher alcohols, and related substances.

Preparation of test sample

For a solid sample, melt with care, and, if necessary, filter the melted sample with a dry filter paper by warming. For a turbid liquid sample, heat at about 50°C. If it is still turbid, filter it with a dry filter paper while warm. In either case, mix the sample to make it homogeneous.

Melting point

Proceed by the method described in Method 2 of the test for Melting Point.

Congealing point of fatty acids

(1) Preparation of fatty acids—Dissolve 25 g of potassium hydroxide in 100 g of glycerin. Transfer 75 g of this solution into a 1-L beaker, and heat at 150°C. Add 50 g of the sample to this solution, and heat at a temperature not higher than 150°C for 15 minutes under frequent stirring to saponify completely. Cool the solution to 100°C, dissolve by addition of 500 mL of hot water, and add slowly 50 mL of diluted sulfuric acid (1 in 4). Heat the solution under frequent stirring until the clear layer of fatty acid is separated distinctly. Separate the fatty acid layer, and wash the fatty acid with hot water until the washing shows no acidity to methyl orange TS. Transfer the fatty acid phase to a small beaker, and heat on a water bath until the fatty acid becomes clear owing to the separation of water. Filter the warm solution, and complete the evaporation of water by carefully heating the filtered solution to 130°C.

(2) Measurement of congealing point—Proceed by the method described in the test for Congealing Point.

Specific gravity

(1) Liquid sample at ordinary temperature

Proceed by the method described in the test for Specific Gravity and Density.

(2) Solid sample at ordinary temperature

Unless otherwise specified, fill a pycnometer with water at 20°C. Weigh accurately the pycnometer, and, after discarding the water and drying, weigh accurately the empty pycnometer. Then, fill the pycnometer with the melted sample to about three-fourths of the depth, and allow to stand at a temperature a little higher than the melting temperature of the sample for 1 hour to drive off the air in the sample. After keeping at the specified temperature, weigh accurately the pycnometer. Fill up the pycnometer with water over the sample at 20°C, and weigh accurately again.

The other procedure is the same as described in Method 1 of the test for Specific Gravity and Density.

$$d = \frac{W_1 - W}{(W_2 - W) - (W_3 - W_1)}$$

W : Mass (g) of the empty pycnometer.
W_1: Mass (g) of the pycnometer filled with the sample.
W_2: Mass (g) of the pycnometer filled with water.
W_3: Mass (g) of the pycnometer filled with the sample and water.

Acid value

The acid value is the number of milligrams of potassium hydroxide (KOH) required to neutralize the free acids in 1 g of sample.

Procedure: Unless otherwise specified, weigh accurately the amount of sample shown in Table 1, according to the expected acid value of the sample, in a glass-stoppered, 250-mL flask, add 100 mL of a mixture of diethyl ether and ethanol (95) (1:1 or 2:1) as the solvent, and dissolve the sample by warming, if necessary. Then, add a few drops of phenolphthalein TS, and titrate with 0.1 mol/L potassium hydroxide-ethanol VS until the solution develops a light red