$$s = \sqrt{\frac{\sum_{i=1}^{n} (x_i - A)^2}{n - 1}}$$

Proceed by the following method for the dosage form designated.

Capsules and Solids (Granule, Powder, Syrup) in single-unit container

Assume the individual masses of intact units as the mass of the preparation and apply the above test. If the requirement was not met, measure the net mass by the following methods and apply the above test.

1. Hard Capsules and Solids (Granule, Powder, Syrup) in single-unit container

Weigh accurately individual units, taking care to preserve the identity of each unit. Remove the contents of each unit by a suitable means such as brushing. Weigh accurately the emptied shells individually, and calculate for each unit the net mass of its contents by subtracting the mass of the shell from the respective gross mass.

2. Soft Capsules

Weigh accurately individual units, taking care to preserve the identity of each unit. Cut open the capsules and remove the contents by washing with a suitable volatile solvent (e.g., diethyl ether). Allow the occluded solvent to evaporate from the shells at room temperature, taking precautions to avoid uptake or loss of moisture. Weigh accurately the emptied shells individually, and calculate for each unit the net mass of its contents by subtracting the mass of the shell from the respective gross mass.

Injections (to be dissolved or suspended before use)

Wash the containers of individual units after removal of paper labels, if these exist, and dry them completely. Open carefully the containers and weigh accurately all parts of the opened containers, taking care to preserve the identity of each unit. Remove the contents of each unit by washing sufficiently with water and ethanol (95), and dry them completely. Weigh accurately all parts of the cleaned containers individually, and calculate for each unit the net mass of its contents by subtracting the mass of the container from the respective gross mass.

31. Melting Point Determination

The Melting Point refers to the temperature determined by the following methods. When the melting point of a substance is given as a range, the substance should melt within that range of temperature.

Three procedures are provided for the determination depending upon the nature of the substance. Unless otherwise specified, proceed by Method 1.

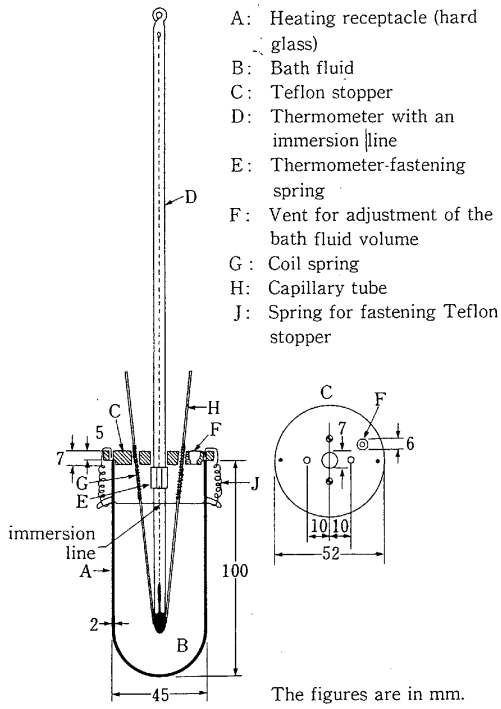
Method 1 This method is applied to those substances that can be readily reduced to fine powders.

(1) Apparatus

Use the apparatus illustrated in the figure.

Bath fluid: Use clear silicone oil having the viscosity of 50 to 100 mm^2/s at ordinary temperature.

Thermometer with an immersion line: For meltimg points



The figures are in mm.

lower than 50°C, use a thermometer Type 1; for 50°C to 100°C, Type 2; for 100°C to 150°C, Type 3; for 150°C to 200°C, Type 4; for 200°Cto 250°C, Type 5; for 250°C to 320°C, Type 6.

Capillary tube: Use a hard glass capillary tube 120 mm long, 0.8 to 1.2 mm in inner diameter and with walls 0.2 to 0.3 mm thick; one end is closed.

(2) Procedure

Reduce the sample to a fine powder, and, unless otherwise specified, dry in a desiccator (silica gel) for 24 hours. When it is specified to do the test after drying, dry the sample under the conditions in the test for Loss on Drying before the detemination. Place the sample in a dried capillary tube H, and pack the sample tightly in a layer about 3 mm in height by dropping it repeatedly, with the closed end of H down, through a glass tube, about 70 cm long, held vertically on a glass or porous plate.

Heat the bath fluid B until the temperature rises to about 10°C below the expected melting point, place the immersion line of the thermometer D at the same level as the meniscus of the bath fluid, and insert capillary tube H into coil spring G so that the sample is on a level with the middle of the mercury bulb of the thermometer D. Then continue the heating to raise the temperature at a rate of approximately 3°C per minute until the temperature rises to 5°C below the expected melting point, then carefully regulate the rate of increase to 1°C per minute.

Read the indication of the thermometer D at the point at which the sample liquefies throughout and no solid is visible in the capillary tube H, and designate the temperature as the melting point.

Method 2 This method is applied to such substances as fats, fatty acids, paraffins or waxes, that are insoluble in water and not readily reduced to powder.

Procedure

Carefully melt the sample at as low a temperature as possi-

ble, and, taking care to prevent bubbles, draw it into a capillary tube (one as used in Method 1 and which is left open at both ends) to a depth of about 10 mm. Allow the charged tube to stand for 24 hours at a temperature below 10°C, or for at least 1 hour in contact with ice, holding the tube so as not to allow loss of the sample from it. Then attach the tube to the thermometer by means of a rubber band so that the sample is on a level with the middle part of the mercury bulb. Adjust the tube in a water-containing beaker to such a position that the lower edge of the sample is 30 mm below the water surface. Heat the beaker with constant stirring until the temperature rises to 5°C below the expected melting point. Then regulate the rate of increase to 1°C per minute. The temperature at which the sample is observed to rise in the capillary tube is taken as the melting point.

Method 3 This method is applied to petrolatums.

Procedure

Melt the sample slowly, with thorough stirring, until it reaches a temperature between 90°C and 92°C. Discontinue the heating, and allow the sample to cool to a temperature between 8°C and 10°C above the expected melting point. Chill the bulb of the thermometer to 5°C, wipe, dry, and, while still cold, thrust into the molten sample to such a depth that approximately the lower half of the bulb is submerged. Withdraw it immediately, hold vertically, cool until the attached sample becomes dull, then dip for 5 minutes in water having a temperature not higher than 16°C. Fix the thermometer securely in a test tube by means of a cork stopper so that the lower end is 15 mm above the bottom of the test tube. Suspend the tube in water contained in a beaker at a temperature of about 16°C, and raise the temperature of the bath to 30°C at a rate of 2°C per minute, then at a rate of 1°C per minute until it reaches the melting point. Read the temperature at which the first drop leaves the thermometer. If the variations between each of three determinations are not more than 1°C, take the average of the three. If any of the variations is greater than 1°C, make two additional determinations, and take the average of the five as the melting point.

32. Methanol Test

The Methanol Test is a method to determine methanol adhering in ethanol.

Reagents

(1) Standard Methanol Solution—To 1.0 g of methanol, accurately measured, add water to make exactly 1000 mL. To 5 mL of this solution, exactly measured, add 2.5 mL of methanol-free ethanol and water to make exactly 50 mL.

(2) Solution A—To 75 mL of phosphoric acid add water to make 500 mL, then dissove 15 g of potassium permanganate in this solution.

(3) Solution B—Add sulfuric acid carefully to an equal volume of water, cool, and dissolve 25 g of oxalic acid dihydrate in 500 mL of this dilute sulfuric acid.

Procedure

Pipet 1 mL of the sample, and add water to make exactly 20 mL. Use this solution as the sample solution. Transfer 5 mL each of the sample solution and the Standard Methanol Solution, accurately measured, to test tubes, add 2 mL of Solution A to each solution, and allow to stand for 15 minutes. Decolorize these solutions by adding 2 mL of Solution B, and mix with 5 mL of fuchsin-sulfurous acid TS. Allow to stand for 30 minutes at ordinary temperature. The sample solution has no more color than the Standard Methanol Solution.

33. Methoxyl Assay

The Methoxyl Assay is a method to determine methoxyl groups, in which the sample is heated with hydroiodic acid, the produced iodomethane is oxidized with bromine to give iodic acid, potassium iodide and dilute sulfuric acid are added, and the liberated iodine is titrated with sodium thiosulfate VS.

$$ROCH_3 + HI = CH_3I + ROH$$
$$CH_3I + 3Br_2 + 3H_2O = CH_3Br + 5HBr + HIO_3$$
$$HIO_3 + 5HI = 3I_2 + 3H_2O$$

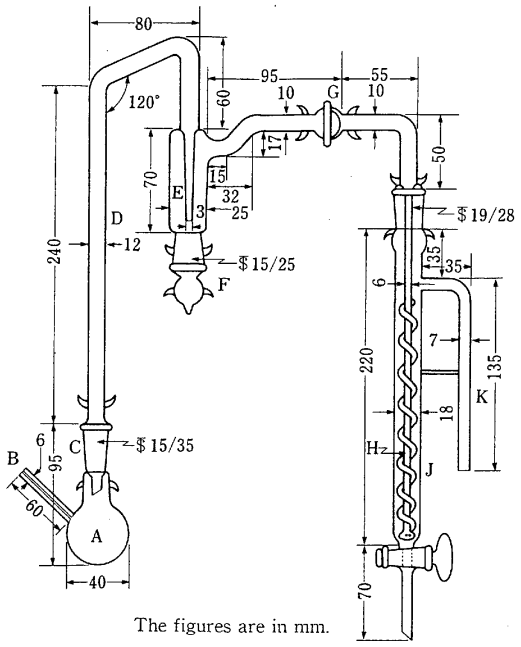
Apparatus

Use the apparatus illustrated in the figure.

Reagents

(1) Scrubbing solution—Prepare a suspension by mixing 1 g of red phosphorus with 100 mL of water.

(2) Absorbing solution—Dissolve 15 g of potassium acetate in 150 mL of a mixture of acetic acid (100) and acetic anhydride (9:1), and to 145 mL of the solution add 5 mL of bromine. Prepare the absorbing solution before use.



The figures are in mm.

A: Decomposition flask
B: Gas-introducing tube
C: Ground joint
D: Air condenser
E: Gas scrubber
F: Glass stopper
G: Ball joint
H: Gas duct
J: Absorption tube
K: Gas-expelling tube