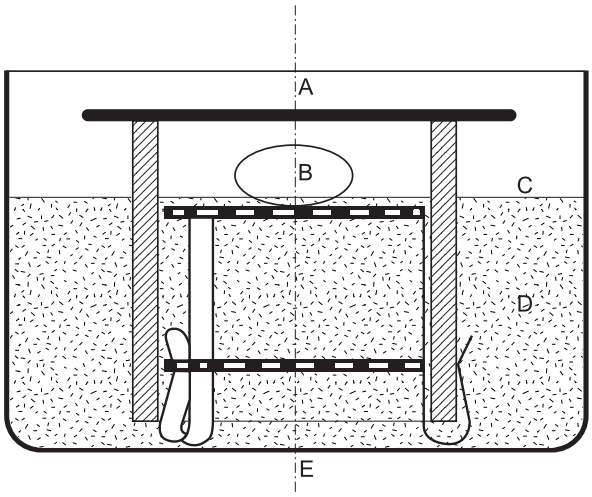

A. glass plate
B. vaginal tablet
C. water surface
D. water
E. dish, beaker

Figure 2.9.2.-2.

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2.9.3. DISSOLUTION TEST FOR SOLID DOSAGE FORMS

The test is used to determine the dissolution rate of the active ingredients of solid dosage forms (for example, tablets, capsules and suppositories).

Unless otherwise justified and authorised, either the paddle apparatus or the basket apparatus or in special cases, the flow-through cell apparatus may be used.

The following are to be prescribed for each preparation to which the dissolution test is applied:

- the apparatus to be used, including in those cases where the flow-through cell apparatus is prescribed, which flow-through cell (Figures 2.9.3.-4/5/6) is to be used,
- the composition, the volume and the temperature of the dissolution medium,
- the rotation speed or the flow rate of the dissolution medium,
- the time, the method and the amount for sampling of the test solution or the conditions for continuous monitoring,
- the method of analysis,
- the quantity or quantities of active ingredients required to dissolve within a prescribed time.

APPARATUS

The choice of the apparatus to be used depends on the physico-chemical characteristics of the dosage form. All parts of the apparatus that may come into contact with the preparation or the dissolution medium are chemically inert and do not adsorb or react or interfere with the test sample. All metal parts of the apparatus that may come into contact with the preparation or the dissolution medium must be made from a suitable stainless steel or coated with a suitable material to ensure that such parts do not react or interfere with the preparation or the dissolution medium. No part of the assembly or its environment contributes significant motion, agitation or vibration beyond that resulting from the smoothly rotating element or from the flow-through system.

An apparatus that permits observation of the preparation to be examined and the stirrer during the test is preferable.

Paddle apparatus. The apparatus (see Figure 2.9.3.-1) consists of:

- a cylindrical vessel of borosilicate glass or other suitable transparent material with a hemispherical bottom and a nominal capacity of 1000 ml; a cover is fitted to retard evaporation; the cover has a central hole to accommodate the shaft of the stirrer and other holes for the thermometer and the devices used to withdraw liquid;
- a stirrer consisting of a vertical shaft to the lower end of which is attached a blade having the form of that part of a circle subtended by 2 parallel chords; the blade passes through the diameter of the shaft so that the bottom of the blade is flush with the bottom of the shaft; the shaft is placed so that its axis is within 2 mm of the axis of the vessel and the bottom of the blade is 25 ± 2 mm from the inner bottom of the vessel; the upper part of the shaft is connected to a motor provided with a speed regulator; the stirrer rotates smoothly without significant wobble;
- a water-bath that will maintain the dissolution medium at 37 ± 0.5 °C.

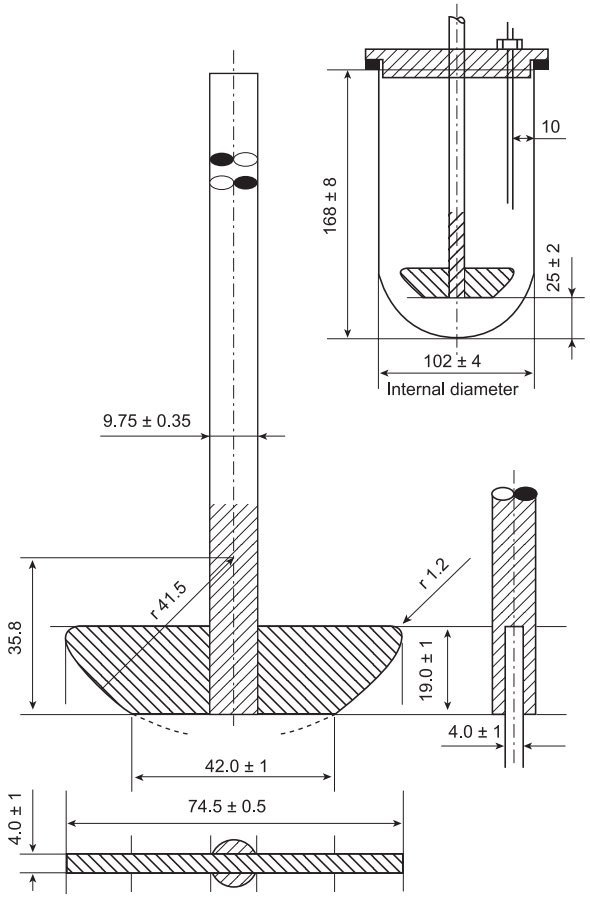

Figure 2.9.3.-1. – *Paddle apparatus*
Dimensions in millimetres

Basket apparatus. The apparatus (see Figure 2.9.3.-2) consists of:

- a vessel identical with that described for the paddle apparatus;
- a stirrer consisting of a vertical shaft to the lower part of which is attached a cylindrical basket; the basket has 2 parts: the upper part, with a 2 mm vent, is welded to the shaft and has 3 spring clips or other suitable device that allows removal of the lower part of the basket for introduction of the preparation to be examined and firmly

holds the lower part concentric with the axis of the vessel during rotation; the lower part of the basket is made of welded-seam cloth formed into a cylinder with a narrow rim of sheet metal around the top and bottom; unless otherwise prescribed, the cloth has a wire thickness of 0.254 mm in diameter and 0.381 mm square openings; a basket with a gold coating 2.5 µm thick may be used for tests carried out in dilute acid medium; the bottom of the basket is 25 ± 2 mm from the inner bottom of the vessel during the test; the upper part of the shaft is connected to a motor provided with a speed regulator; the stirrer rotates smoothly without significant wobble;

– a water-bath that will maintain the dissolution medium at 37 ± 0.5 °C.

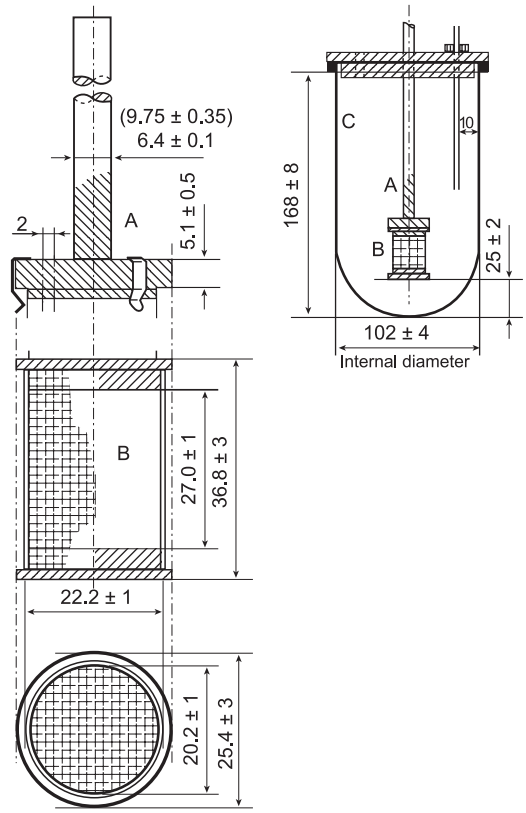

Figure 2.9.3.-2. – *Basket apparatus*
Dimensions in millimetres

Flow-through apparatus. The apparatus (see Figure 2.9.3.-3) consists of:

– a reservoir for the dissolution medium;

– a pump that forces the dissolution medium upwards through the flow-through cell;

– a flow-through cell (see Figures 2.9.3.-4/5/6) of transparent material mounted vertically with a filter system preventing escape of undissolved particles.

The flow-through cell shown in Figure 2.9.3.-6 is specifically intended for lipophilic solid dosage forms such as supposi-tories and soft capsules. It consists of 3 transparent parts which fit into each other. The lower part (1) is made up of 2 adjacent chambers connected to an overflow device.

The dissolution medium passes through chamber A and is subjected to an upwards flow. The flow in chamber B is downwards directed to a small-size bore exit which leads upwards to a filter assembly. The middle part (2) of the cell has a cavity designed to collect lipophilic excipients which float on the dissolution medium. A metal grill serves as a rough filter. The upper part (3) holds a filter unit for paper, glass fibre or cellulose filters.

– a water-bath that will maintain the dissolution medium at 37 ± 0.5 °C.

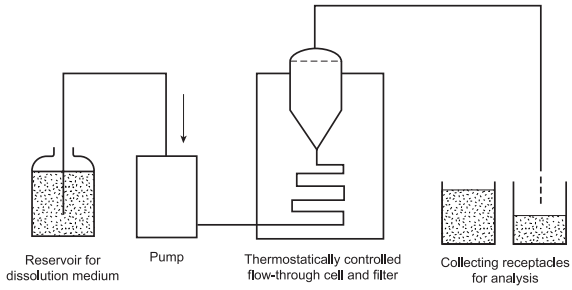

Figure 2.9.3.-3. – *Flow-through apparatus*

Dissolution medium. If the dissolution medium is buffered, adjust its pH to within ± 0.05 units of the prescribed value. Remove any dissolved gases from the dissolution medium before the test since they can cause the formation of bubbles that significantly affect the results.

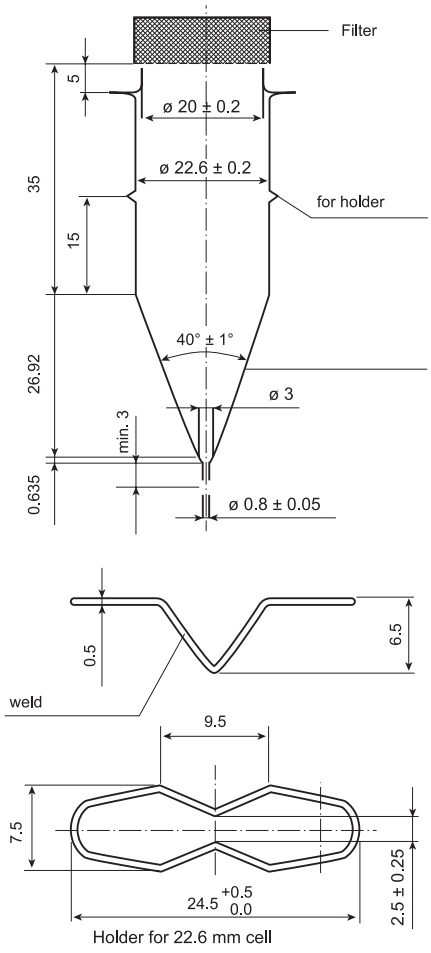

Figure 2.9.3.-4. – *Flow-through cell*
Dimensions in millimetres

METHOD

Paddle and basket apparatus

Place the prescribed volume of dissolution medium in the vessel, assemble the apparatus, warm the dissolution medium to 37 ± 0.5 °C and remove the thermometer.

Place one unit of the preparation to be examined in the apparatus. For the paddle apparatus, place the preparation at the bottom of the vessel before starting rotation of the blade; dosage forms that would otherwise float are kept horizontal at the bottom of the vessel using a suitable device, such as a wire or glass helix.

For the basket apparatus, place the preparation in a dry basket and lower into position before starting rotation.

Take care to avoid the presence of air bubbles on the surface of the preparation. Start the rotation of the apparatus immediately at the prescribed rate (± 4 per cent).

Flow-through apparatus

– Cells (see Figures 2.9.3.-4/5)

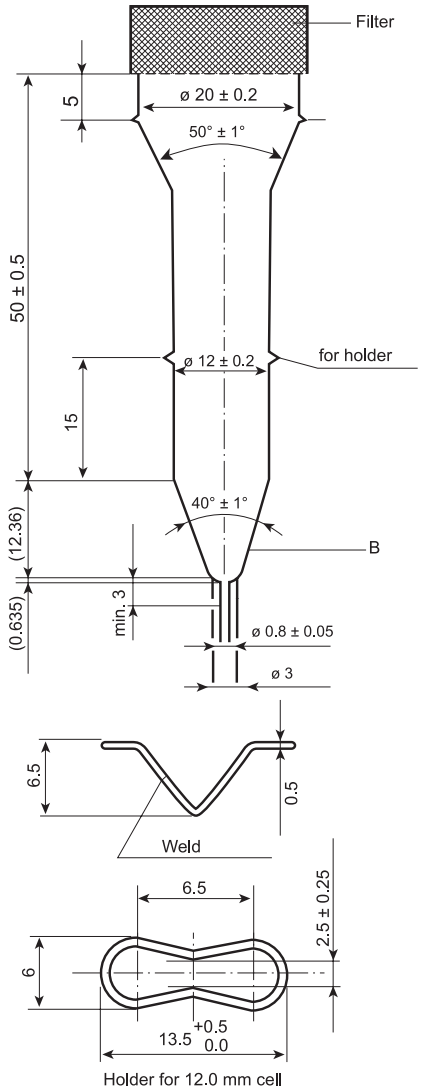

Figure 2.9.3.-5. – *Flow-through cell*
Dimensions in millimetres

Place 1 bead of 5 mm (± 0.5 mm) diameter at the bottom of the cone to protect the fluid entry of the tube and then glass beads of suitable size, preferably 1 mm (± 0.1 mm) diameter. Introduce 1 unit of the preparation in the cell on or within the layer of glass beads, by means of a holder. Assemble the filter head. Heat the dissolution medium to 37 ± 0.5 °C. Using a suitable pump, introduce the dissolution medium through the bottom of the cell to obtain a suitable continuous flow through an open or closed circuit at the prescribed rate (± 5 per cent).

– Cell (Figure 2.9.3.-6)

Place 1 unit of the preparation to be examined in chamber A. Close the cell with the prepared filter assembly. At the beginning of the test, chamber A requires air removal via a small orifice connected to the filter assembly. Heat the dissolution medium to an appropriate temperature taking the melting point of the preparation into consideration. Using a suitable pump, introduce the warmed dissolution medium through the bottom of the cell to obtain a suitable continuous flow through an open or closed circuit at the prescribed rate (± 5 per cent). When the dissolution medium reaches the overflow, air starts to escape through the capillary and chamber B fills with the dissolution medium. The preparation spreads through the dissolution medium according to its physico-chemical properties.

In justified and authorised cases, representative fractions of large volume suppositories may be tested.

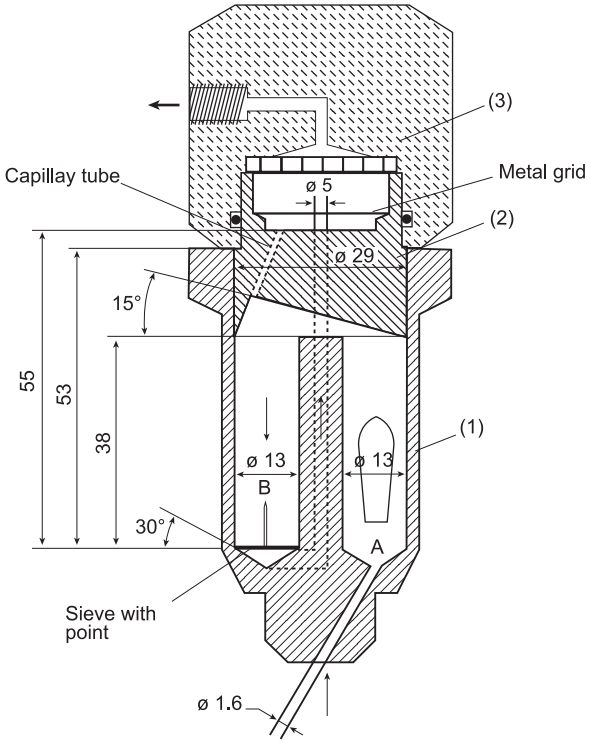

Figure 2.9.3.-6. – *Flow-through cell*
Dimensions in millimetres

SAMPLING AND EVALUATION

In the case of the paddle apparatus and the basket apparatus, withdraw at the prescribed time, or at the prescribed intervals or continuously, the prescribed volume or volumes 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.

In the case of the flow-through apparatus, samples are always collected at the outlet of the cell, irrespective of whether the circuit is opened or closed.

Except where continuous measurement is used with the paddle or basket method (the liquid removed being returned to the vessel) or where a single portion of liquid is removed, add a volume of dissolution medium equal to the volume of liquid removed or compensate by calculation.

Filter the liquid removed using an inert filter of appropriate pore size that does not cause significant adsorption of the active ingredient from the solution and does not contain substances extractable by the dissolution medium that would interfere with the prescribed analytical method. Proceed with analysis of the filtrate as prescribed.

The quantity of the active ingredient dissolved in a specified time is expressed as a percentage of the content stated on the label.