the internal pressure and the drug solution will thus be pumped out.

If the flow rate of incoming liquid to the release unit is the rate-controlling process, the drug release rate can be described as:

$$M/t = CV/t \tag{30.3}$$

where V is the volume of incoming liquid. The flow rate of incoming liquid under steady-state conditions is a zero-order process and the release rate of the drug will therefore also be a zero-order process. The water flow is not affected by the flow and pH of the dissolution medium. However, the water flow rate and hence drug release rate can be affected by a number of formulation factors, such as the osmotic pressure of the drug solution within the release unit, the drug solubility, and the permeability and mechanical properties of the membrane.

Osmosis-controlled release systems can be designed as single-unit or multiple-unit tablets. In the first case, the drug solution can be forced out from the tablet through a single orifice (Fig. 30.17) formed in the membrane by boring with a laser beam. Alternatively, the drug solution can flow through a number of pores formed during the uptake of water. Such pores can be formed by the dissolution of water-soluble substances present in the membrane, or by straining of the membrane owing to the increased internal pressure in the release unit. In the case of multiple-unit release tablets, the transport occurs in formed pores.

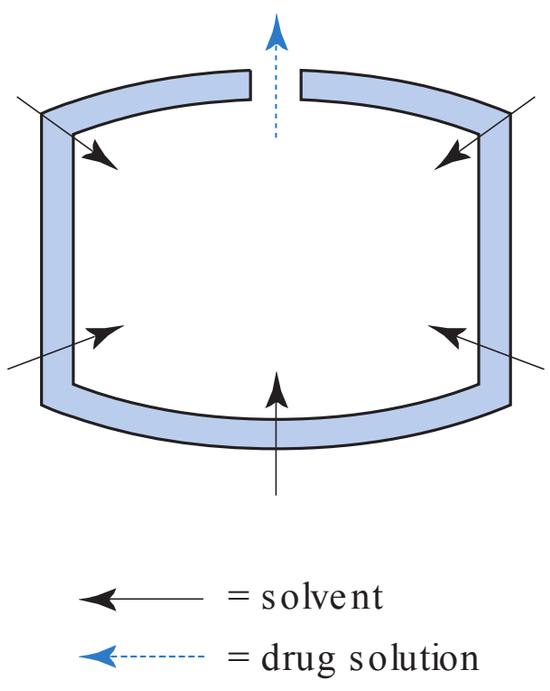

Fig. 30.17 • Schematic illustration of the mechanism of drug release from an osmosis-controlled release system designed as a single-unit tablet with a single release orifice.

Tablet testing

Test methods

In tablet formulation development and during manufacturing of tablets, a number of procedures are used to assess the quality of the tablets. Some test methods are described in pharmacopoeias and these tests are traditionally concerned with the content and the in vitro release of the active ingredient. Test methods not described in pharmacopoeias are sometimes referred to as non-compendial and concern a variety of quality attributes that need to be evaluated, such as the porosity of tablets. Below, some of the tests used in the quality evaluation of tablets are briefly described.

Uniformity of content of active ingredient

A fundamental quality attribute for all pharmaceutical preparations is the requirement for a constant dose of drug between individual tablets. In practice, small variations between individual preparations are accepted and the limits for this variation appear as standards in pharmacopoeias. Traditionally, uniformity of dose or dose variation between tablets is tested in two separate tests: uniformity of weight (mass) and uniformity of active ingredient.

The test for uniformity of weight is carried out by collecting a sample of tablets from a batch and determining their individual weights. The average weight of the tablets is then calculated. The sample complies with the standard if the individual weights do not deviate from the mean more than is permitted in terms of percentage.

If the drug substance forms the greater part of the tablet mass, any weight variation obviously indicates a variation in the content of active ingredient. Compliance with the standard thus helps to ensure that uniformity of dosage is achieved. However, in the case of potent drugs which are administered in low doses, the excipients form the greater part of the tablet weight and the correlation between tablet weight and amount of active ingredient can be poor (Fig. 30.18). Thus, the test for weight variation must be combined with a test for variation in content of the drug substance. Nevertheless, the test for uniformity of weight is a simple way to assess variation in drug dose, which makes the test useful as a quality control procedure during tablet production.