(especially with a high calorie meal). Pellets can get trapped too, but there is an improved chance of fortuitous emptying through the pyloric sphincter. Pellets will tend to distribute through the small intestine. They are also at less risk of dose dumping; if a tablet coating fails, then the whole dose can be dumped; with a pellet formulation, the disruption of one pellet coating may release only a small fraction of the total drug dose.

Osmotic systems

Osmotic pump systems are another form of membrane-controlled release drug delivery system, but work in a different way to that described previously. A drug is included in a tablet core which is water soluble, and which will dissolve (or suspend) the drug in the presence of water. The tablet core is coated with a semi-permeable membrane which will allow water to pass into the core. As the core components dissolve, a hydrostatic pressure builds up and forces (pumps) drug solution (or suspension) through a hole drilled in the coating (Fig. 31.11). The rate at which water is able to pass through the membrane and how quickly the drug solution (or suspension) can pass out of the hole govern the rate of drug release. The orifice needs to be small enough to prevent diffusion, but large enough to minimize hydrostatic pressure (600 μm to 1 mm diameter is normal). The orifice can be made by laser drilling, indentations in tablet (not fully covered by coating) or the use of leachable substances (pore formers).

The rate at which the drug solution/suspension is forced out can be modified by changes in the viscosity of the solution formed inside the system. The essential difference between an osmotic pump system and a 'classic' membrane-controlled system is that for the osmotic pump, only one diffusion process is required (in this case 'water in').

Osmotic pump systems require exposure to sufficient fluid in order to build up an internal osmotic pressure. This will depend on fluid levels in the gut. Like any other non-disintegrating dosage form, they are reliant on being at the site of drug absorption for sufficient time to release their drug load. For example, if the osmotic system was designed to have drug release over 12 hours, it needs to be in the stomach and intestine for this amount of time, otherwise drug release will be incomplete.

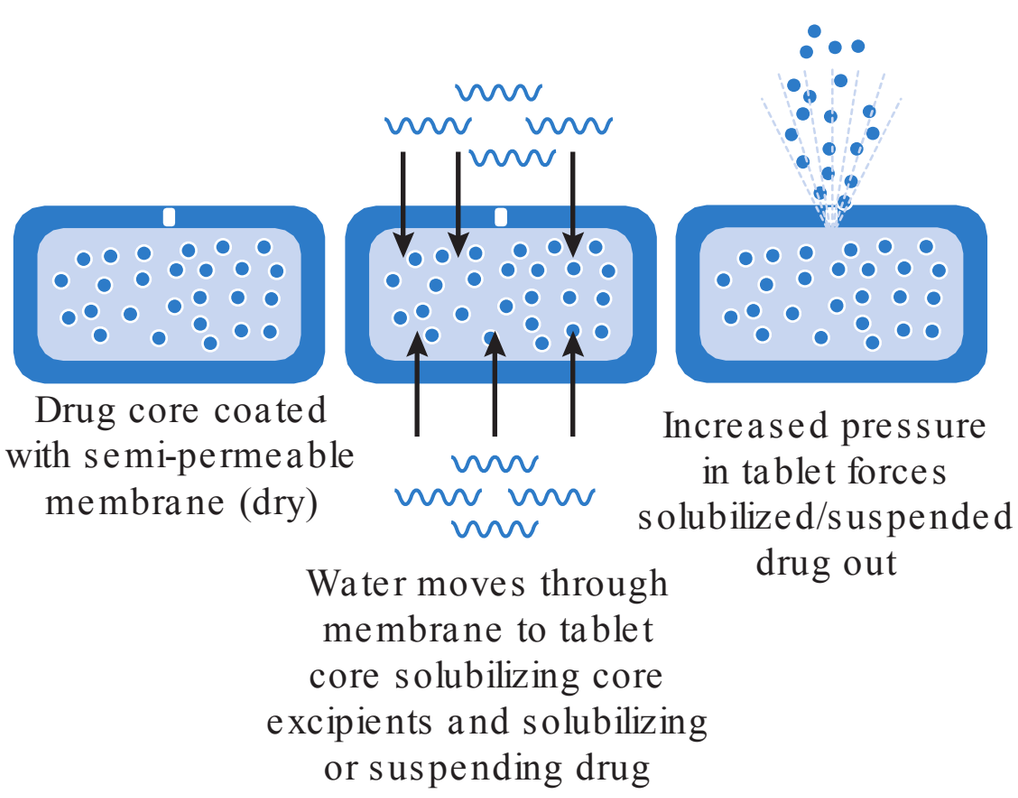

Fig. 31.11 • Release mechanisms from an osmotic pump delivery system.

Gastroretention

Gastroretention is the mechanism by which a dosage form is retained in the stomach, generally for the purposes of improving drug delivery. It has been proposed as a mechanism by which drug absorption in the upper gastrointestinal tract can be maximized. Gastroretentive approaches to drug delivery aim to overcome the physiological mechanisms in the stomach which would normally enable gastric emptying, so that a modified-release dosage form is retained for longer in the stomach. Drugs which may benefit from gastroretention include those for local action in the stomach (e.g. to treat *H. pylori*), drugs which have a narrow absorption window in the small intestine and drugs which are degraded in the colon.

Several approaches have been investigated, but none deliver true gastroretention. The approaches which have been used to try to achieve gastroretention are very varied and are summarized in Table 31.3. Success with gastroretention has been limited, mainly due to the challenge presented by the stomach and gastric emptying which is incredibly difficult to overcome by formulation methods alone.

Delayed release

Gastro-resistant coatings

The concept here is similar to that of membrane-controlled extended release, except that the membrane is designed to disintegrate or dissolve at a pre-determined point. The most common trigger for delayed release coatings is pH. Gastro-resistant coatings are polymer coatings which are insoluble at low pH, but are soluble at higher pH (e.g.