The test for buoyancy and *in vitro* drug release studies are usually carried out in simulated gastric and intestinal fluids maintained at 37°C. In practice, floating time is determined by using the USP disintegration apparatus containing 900 ml of 0.1 N HCl as a testing medium maintained at 37°C. The time required to float the HBS dosage form is noted as floating (or floatation) time. Dissolution tests are performed using the USP dissolution apparatus. Samples are withdrawn periodically from the dissolution medium, replenished with the same volume of fresh medium each time, and then analysed for their drug contents after an appropriate dilution. Recent methodology as described in USP XXIII states "The dosage unit is allowed to sink to the bottom of the vessel before rotation of the blade is started. A small, loose piece of nonreactive material such as not more than a few turns of a wire helix may be attached to the dosage units that would otherwise float". However, standard dissolution methods based on the USP or British Pharmacopoeia (BP) have been shown to be poor predictors of *in vitro* performance for floating dosage forms. The specific gravity of FDDS can be determined by the displacement method using analytical grade benzene as a displacing medium.

Determining the buoyant capabilities of the floating dosage forms and the sinking characteristics of the NF forms a specially designed apparatus for measuring the total force acting vertically on an object immersed in a liquid. The *in vivo* gastric retentivity of a floating dosage form is usually determined by g-scintigraphy.

PROTOCOL: 1.1

Floating Microspheres

Materials

Drugs (Aspirin, salicylic acid, ethoxybenzamide, indomethacin, riboflavin)	0.1–1 g
Polymers	1.0 g
Eudragit S100, eudragit L100, eudragit L100-55	
Ethylcellulose (N-10-F)	
Hydroxypropylmethylcellulose (TC-5R)	
Hydroxypropylmethylcellulosephthalate (HP-55)	
Monostearin (wall membrane reinforcing agent)	0.5 g
Polyvinyl alcohol (PVA-120, dispersing agent)	
Dichloromethane	8 ml
Ethanol	8 ml

Principle

Emulsion solvent diffusion method

Procedure

1. Weigh drug (0.1–1.0 g), polymers (1.0 g), monostearin (0.5 g) and dissolve or disperse in a mixture of dichloromethane (8 ml) and ethanol (8 ml) at room temperature.

Higuchi Leeper pump is widely employed for veterinary use. This type of pump is either swallowed or implanted in body of an animal for delivery of antibiotics or growth hormones to animals. This presents advantage over other medications, which ought to be taken repeatedly, which is inconvenient in case of animals. This problem is overcome by using this device, which can be loaded with full dose and swallowed once, eventually leading to delivery of full course of medication in rumen.

HIGUCHI THEEUWES OSMOTIC PUMP

Higuchi and Theeuwes in early 1970s developed another variant of the Rose Nelson pump, even simpler than the Higuchi Leeper pump. This device is illustrated in Fig. 2.4. In this device, the rigid housing is provided by the semipermeable membrane. This membrane is strong enough to withstand the pumping pressure developed inside the device due to imbibition of water. The desired drug is loaded in the device only prior to its application, which extends advantage for storage of the device for longer duration. The release of the drug from the device is dictated by the salt used in the salt chamber and the permeability characteristics of the outer membrane. Small osmotic pumps of this form are available under trade name Alzet®. They are used frequently as implantable controlled release delivery systems in experimental studies requiring continuous administration of drugs. Diffusional loss of the drug from the device is minimised by making the delivery port in the shape of a long thin tube as shown in Fig. 2.5.

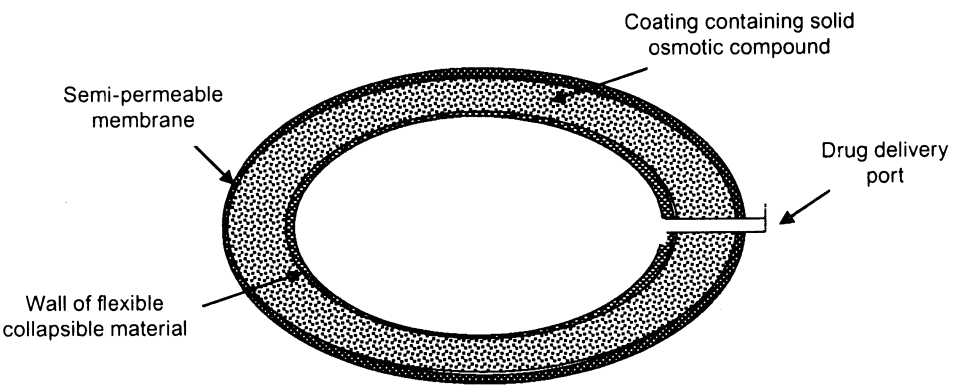

Fig. 2.4: *Higuchi Theeuwes pump design*

One modification of Higuchi Theeuwes pump utilises a mixture of citric acid and sodium bicarbonate in the salt chamber (patent 80-2) to generate the pressure required for delivery of drug. When contacted with water, the mixture produces carbon dioxide gas, which then exerts a pressure on the elastic diaphragm, eventually delivery of drug from device is obtained.

These multichamber tablets can be divided into two major classes based on whether one chamber expands into the other or they have got rigid walls and maintain their volume for the whole course of operation. The classes of tablets with expanding chamber are more important and are frequently employed by manufactures to produce osmotic devices and therefore will be discussed in priority.

TABLETS WITH A SECOND EXPANDABLE OSMOTIC CHAMBER

Tablets with two chambers separated by an elastic or movable barrier are particularly interesting and valuable because they allow delivery of drugs with limited solubility. This class of osmotic pump can further be classified into two groups one with internal film that moves from a rest to an expanded state or the volumes of the chambers communicating through opening provided in between.

In the tablets with a second expandable osmotic chamber, the water is simultaneously drawn into both the chambers in proportion to the osmotic gradient, eventually causing the increase in volume of the chamber and subsequently forcing the drug out from the drug chamber. Fig. 2.9 illustrates the mechanism of action of these devices. Conceptually, the device is related to Higuchi-Leeper pumps described earlier but in these devices, the semipermeable membrane forms the entire shell, and water is drawn simultaneously into both the chambers. The selection of matrix in which the drug is to be suspended presents a challenge in front of product formulation people. The matrix should have a sufficient osmotic pressure to draw water through the membrane into the drug chamber. Under hydrated conditions matrix have to be fluid enough to be pushed easily through a small hole by the little pressure generated by the elastic diaphragm.

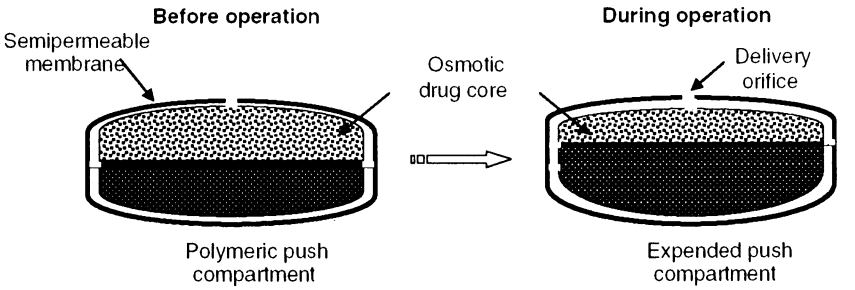

Fig. 2.9: *Drug delivery process of two-chamber osmotic tablet*

Among the successful approaches, incorporation of finely dispersed drug in hydrogel presents a most valuable alternative. Many of the useful hydrogel polymers were ionic materials such as sodium carboxy methylcellulose, which contains ionisable groups, which provide most of the osmotic pressure required to draw water through the semipermeable membrane. These polymers possesses dual property of being compressed in dry conditions and becomes fluid gels easily extrudable through the small delivery hole in hydrated conditions.

The controlled release nifedipine (Procardia XL) device is illustrated in Fig. 2.10. The device contains an external semipermeable membrane made up of cellulose acetate bearing

- Drill the dry coated tablet by a microdriller on both the sides of the tablets with 1.25-mm orifice. Composition of tablet materials; amount of plasticiser, membrane thickness, and coating solution can be changed as per requirement.

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