

CONCEPT OF IMPLANTS:

Implants for drug delivery are several types:

1. In-situ forming implants (*In-situ* depot forming systems):

a) *In-situ* precipitating implants:

- These implants are formed from drug containing in a biocompatible solvent.
- The polymer solution form implants after subcutaneous (S.C.) or intramuscular (I.M.) injection and contact with aqueous body fluids via the precipitation of polymers.

In-situ precipitating implants are formulated to overcome some problems associated to the uses of biodegradable microparticles:

- i) Requirement for the reconstitution before injection
- ii) Inability to remove the dose one injected.
- iii) Relatively complicated manufacturing procedures to produce a sterile, stable and reproducible product.

b) In-situ microparticle implants:

This type of implants is formed to overcome the disadvantages associated with **in-situ precipitating** implants.

These are:

i) High injection force.

ii) Local irritation at the injection site.

iii) Variability in the solidification rates.

iv) Irregular shape of the implants formed depending on the cavity into which the implants are introduced (implanted).

v) Undesirable high initial burst release of drugs.

vi) Potential solvent toxicity.

These in-situ implantable systems consist of internal phase (drug-containing polymer solution or suspension) and a continuous phase (aqueous solution with a surfactant, oil phase with viscosity enhancer and emulsifier).

The two phases are separately stored in dual-chambered syringes and mixed through a connector before administration.

2. Solid implants:

Solid implants are generally cylindrical monolithic devices implanted by a minor surgical incision or injected via a large bore needle into the S.C. or I.M. tissues.

Subcutaneous (S.C.) tissue is an ideal location because of its easy access to implantation, poor perfusion, slower drug absorption and low reactivity towards foreign materials.

- In these implants, drugs may be dissolved, dispersed or embedded in a matrix of polymers or waxes/lipids that control the releasing via dissolution and/or diffusion, bioerosion, biodegradation, or an activation process, such as hydrolysis or osmosis.
- These systems are generally prepared as implantable flexible/rigid molded or extruded rods, spherical pellets, or compressed tablets.
- Polymers used are silicone, polymethacrylates, elastomers, polycaprolactones, polylactide-co-glycolide, etc., whereas waxes include glyceryl monostearate.
- Drugs generally presented in such implantable systems are contraceptives, naltrexone, etc.

3. Infusion devices:

Infusion devices are intrinsically powered to release the drugs at a zero-order rate and the drug reservoir can be replenished from time to time.

Depending upon the mechanism by which these implantable pumps are power to release the drugs.

These are 3 types:

- i) Osmotic pressure activated drug delivery systems
- ii) Vapor pressure activated drug delivery systems
- iii) Battery powered drug delivery systems

Osmotic pumps:

- Osmotic pumps are designed mainly by a semi-permeable membrane that surrounds a drug reservoir (Fig. 8).
- The membrane should have an orifice that will allow drug release.
- Osmotic gradients will allow a steady inflow of fluid within the implant.
- This process will lead to an increase in the pressure within the implant that will force drug release through the orifice.
- This design allows constant drug release (zero order kinetics).
- This type of device allows a favorable release rate but the drug loading is limited.

- The historical development of osmotic systems includes seminal contributions such as the Rose-Nelson pump, the Higuchi-Leeper pumps, the Alzet and Osmet systems, the elementary osmotic pump, and the push-pull or GITSR system.
- Recent advances include the development of the controlled porosity osmotic pump, systems based on asymmetric membranes, and other approaches.

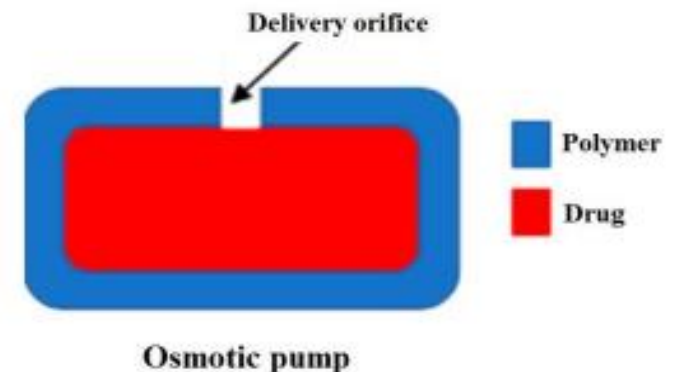


Fig. 8: Osmotic pump

Osmotic agents:

- Osmotic agents are used for the fabrication of the osmotic device maintain a concentration gradient across the membrane by generating a driving force for the uptake of water and assist in maintaining drug uniformity in the hydrated formulation.
- Osmotic agents usually are ionic compounds consisting of either inorganic salts such as sodium chloride, potassium chloride magnesium sulphate, sodium sulphate, potassium sulphate and sodium bicarbonate.
- Additionally, sugars such as glucose, sorbitol, sucrose and inorganic salts of carbohydrates can also act as effective osmotic agents.