Shree H. N. Shukla Institute of Pharmaceutical Education and Research, Rajkot

B. Pharm
Semester-VII

Subject Name: Novel Drug Delivery System
Subject Code: BP704TT

CHAPTER-2- Unit:2- IMPLANTABLE DRUG DELIVERY SYSTEM

SYLLABUS:

Implantable drug delivery system:

Introduction, advantages and disadvantages, concept of implantsand osmotic pump

This subject is designed to impart basic knowledge on the area of novel drug delivery systems.

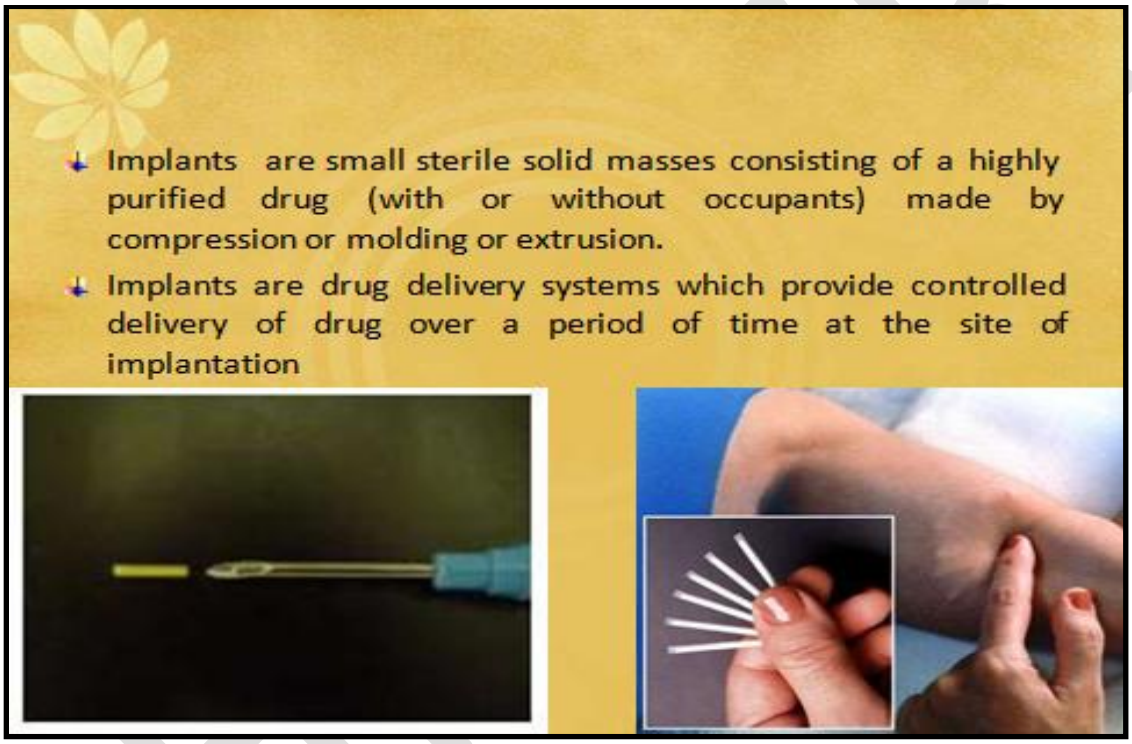
Learning objectives

Upon completion of the course the student shall be able to

1. To understand various approaches for development of novel drug delivery systems.
2. To understand the criteria for selection of drugs and polymers for the development of Novel drug delivery systems, their formulation and evaluation.

Implantable Drug Delivery System

What is Implantable Drug Delivery System (MDDS)



- Implants are intended for implantation in the body (usually subcutaneously) for the purpose of providing continuous release of the drug over long periods of time.
- Implants are administered by means of a suitable special injector or surgical incision.
- These are developed with a view to transmit drugs and fluids into the blood stream without the repeated insertion of needles
- These systems are particularly suited for delivery requirements of drugs such as insulin, steroids, antibiotics, analgesics.

Types of Implants

1. Biodegradable
2. Nonbiodegradable

Advantages

- Unattended continuous delivery within the therapeutic window
- Avoids the highly variable peak and trough concentrations Enhanced drug efficacy
- Minimized side effects
- Termination of therapy as and when required
- Patient compliance is also a benefit of continuous dosing with these implants as they operate for a long period of time once implanted

Disadvantages

- The reaction between host and implant.
- Implantation procedure is difficult in case of larger implants.
- Inadequate release.
- Requires small surgery for large implantation & painful.

Preparation of Implants

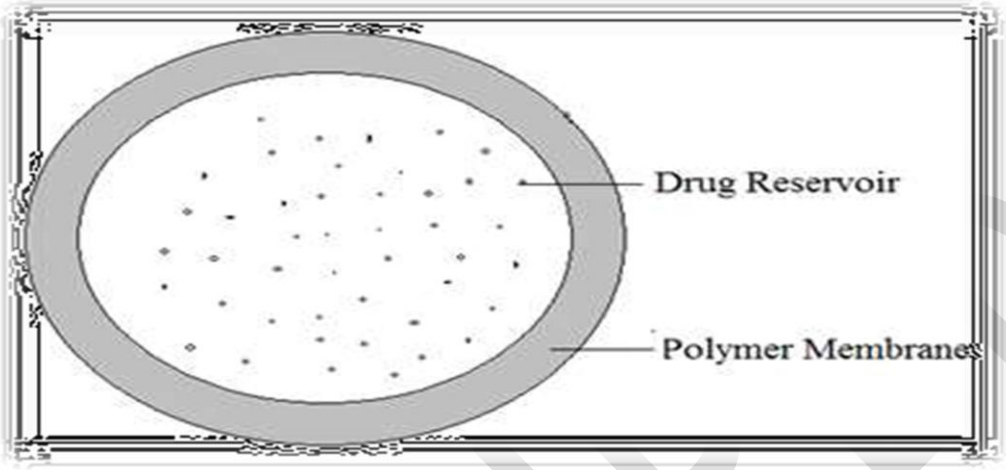
1. Compression
2. Molding
3. Extrusion

One Word Question Answer

SR NO.	QUESTION	ANSWER
1	The device which are drug delivery systems which provide controlled delivery of drug over a period of time at the site of implantation is called?	Implant
2	In which site Implants are intended for implantation in the body?	usually subcutaneously
3	Implants are administered by?	surgical incision
4	How many types of implants?	Two
5	Which type of drug release in implants?	Controlled release
6	How many ways implants are classified?	Three

Polymer Membrane Controlled Delivery System

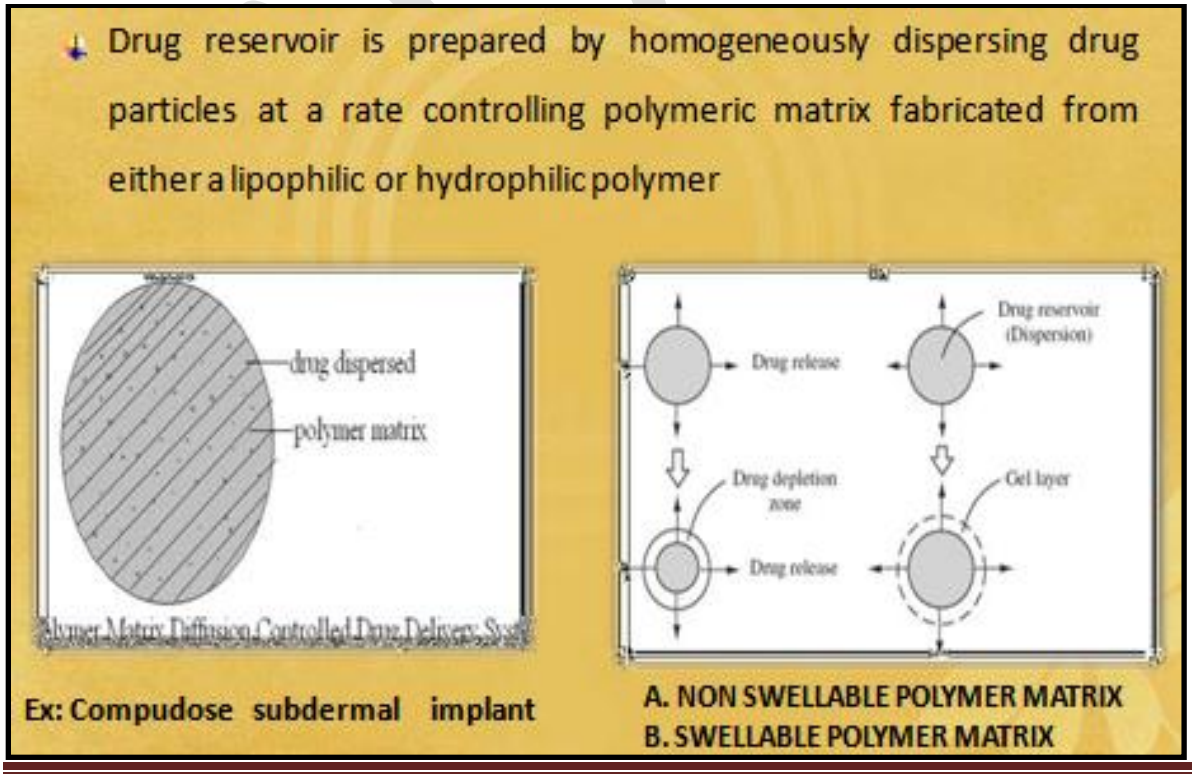
- Drug reservoir is encapsulated within a spherical compartment that is enclosed by a rate controlling polymeric membrane.
- **Drug reservoir:** solid particle/dispersion of solid particles in a liquid or solid dispersion medium
- **Polymer membrane:** nonporous/microporous/semipermeable



Example

- ❖ NORPLANT subdermal implant
- ❖ Progestasert IUD
- ❖ Ocusert system

Polymer matrix diffusion controlled drug delivery systems



Membrane Matrix Hybrid Type Drug Delivery System

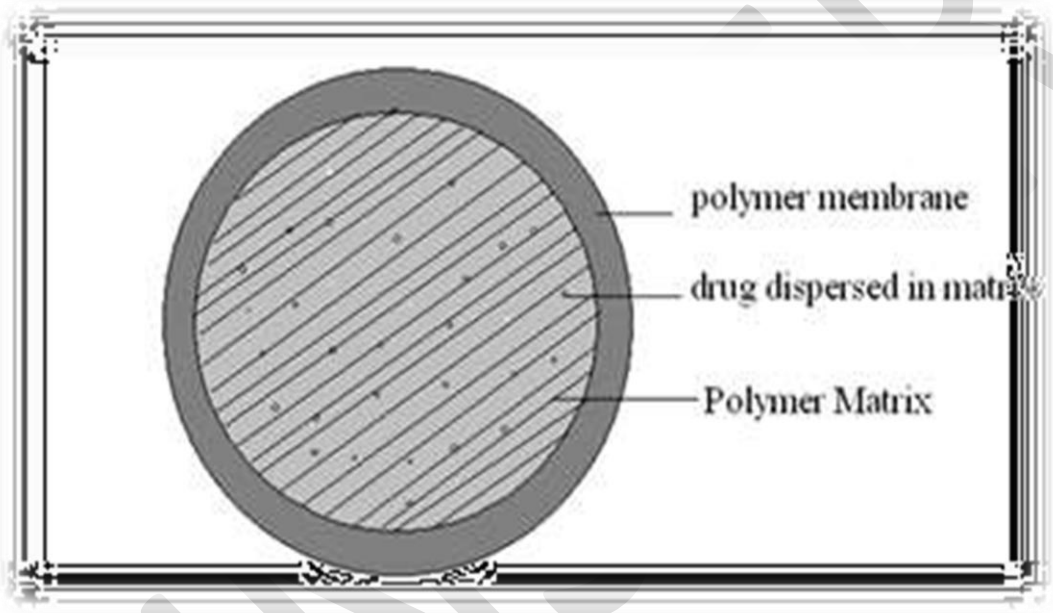
- It is a hybrid of Membrane permeation controlled DDS and Matrix diffusion controlled DDS.

Advantage:

- It achieves controlled release kinetics maintained by matrix controlled DDS.
- It minimizes the risk of dose dumping associated with membrane permeation controlled DDS.

Example:

NORPLANT 2 Subdermal Implant (Levonorgestrol releasing implant)



Activation modulated DDS

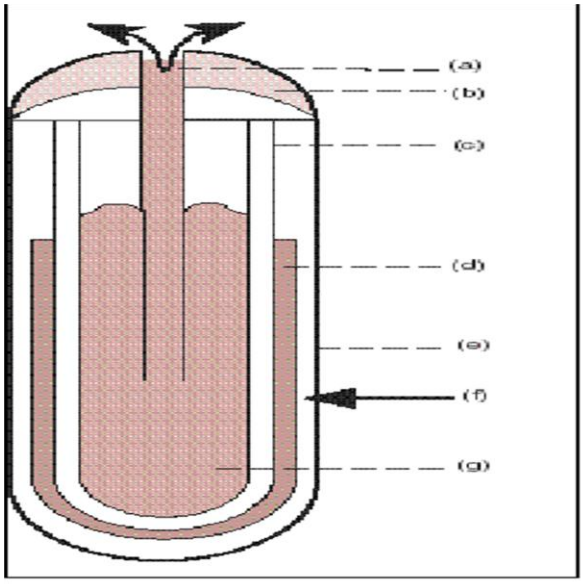
- The release of drug molecules from the delivery system is activated by some physical, chemical or biochemical process facilitated by an external energy supplier

Osmotic Pressure Activated Drug Delivery Device

- In this type of DDS, the drug in solution is released through a specialized laser drilled delivery orifice at a constant rate under a controlled gradient of osmotic pressure.
- **External component:**
  Rigid semipermeable housing made up of Substituted cellulosic polymers containing an osmotically active salt.
- **Internal compartment:**
  Drug reservoir enclosed by a flexible partition layer and osmotic agent impermeable polyester bag.

One Word Question Answer

SR NO.	QUESTION	ANSWER
1	solid particle/dispersion of solid particles in a liquid or solid dispersion medium is called	Drug reservoir
2	Nature of polymeric membrane is?	nonporous/microporous/semipermeable
3	Ocusert system is one type of example of?	Polymer matrix diffusion controlled delivery system
4	What is a hybrid of Membrane permeation controlled DDS and Matrix diffusion controlled DDS.	Membrane matrix hybrid type system
5	In which system, the drug in solution is released through a specialized laser drilled delivery orifice at a constant rate under a controlled gradient of osmotic pressure.	Osmotic pressure activated system
6	Drug reservoir enclosed by a flexible partition layer and osmotic agent impermeable polyester bag.	Internal compartment



The elements of an osmotic pump:
(a) drug solution leaving through delivery portal;
(b) removable cap;
(c) impermeable reservoir wall;
(d) osmotic agent;
(e) semipermeable membrane;
(f) water entering through semipermeable membrane; and
(g) reservoir.

Vapor Pressure Activated Drug

- In this system, the drug reservoir in a solution formulation is contained inside an infusate chamber.
- It is physically separated from the vapor pressure chamber by a freely movable bellows.
- The vapor chamber contains a vaporizable fluid, which vaporizes at body temp. & creates a vapor pressure.
- Under the vapor pressure created, the bellows move upward & forces the drug solution in the infusate chamber to release, through a series of flow regulators & the delivery cannula into the blood circulation at a constant flow rate.

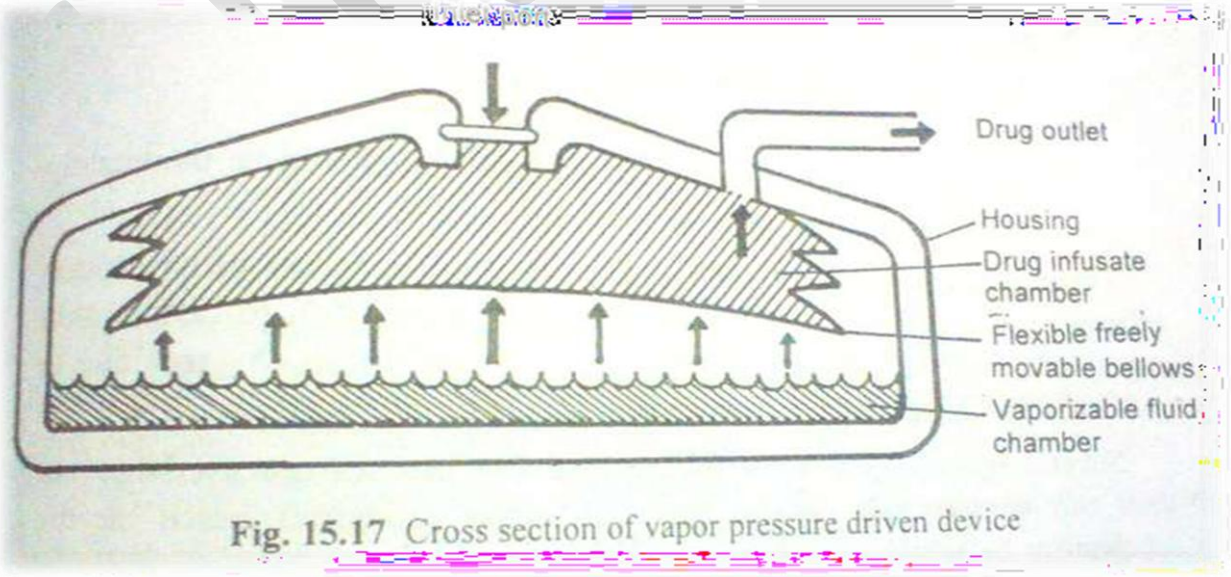


Fig. 15.17 Cross section of vapor pressure driven device

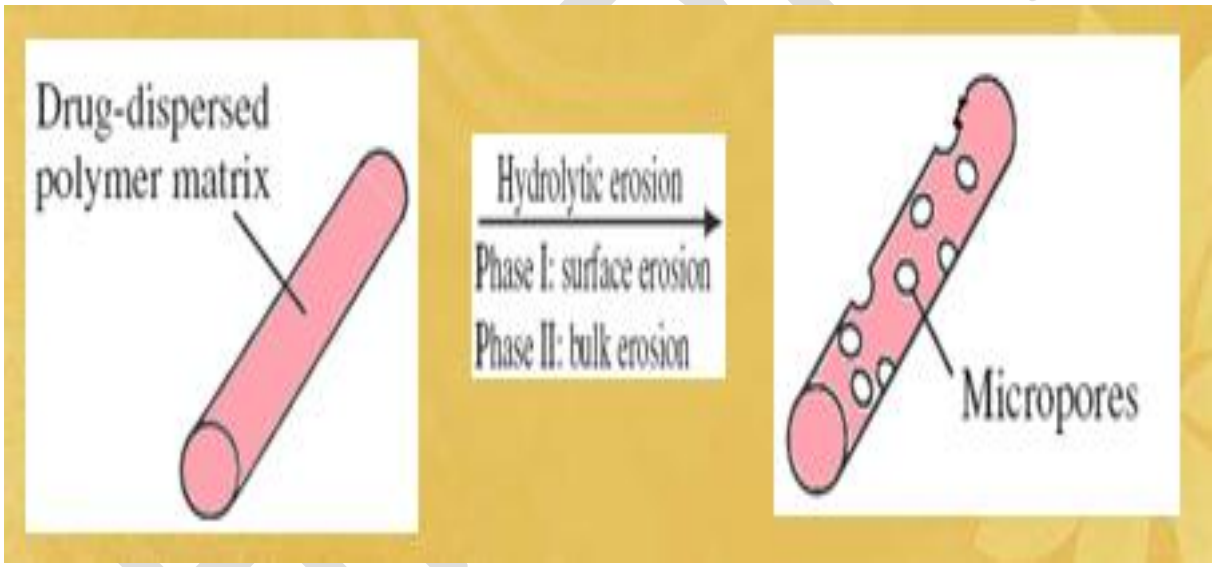
Ex: Infusaid , implantable infusion pump for Constant infusion of heparin in anticoagulation treatment Hydration

Activated Drug Delivery System

- Drug reservoir is homogeneously dispersed in a swellable hydrophilic polymeric matrix.
- After hydration, drug molecules are released by diffusing through the microscopic water saturated pore channels in the swollen polymeric matrix.
- Ex: Norgestomet releasing HYDRON implant

Hydrolysis Activated Drug Delivery

- These systems are prepared from a bio-erodible or bio-degradable Polymer such as polylactide or poly(lactide-glycolide) copolymer.
- This device is activated to release the drug upon hydrolysis of polymer base by tissue fluid at the implantation site.
- Ex: ZOLADEX system



Controlled drug delivery by feed back regulated process

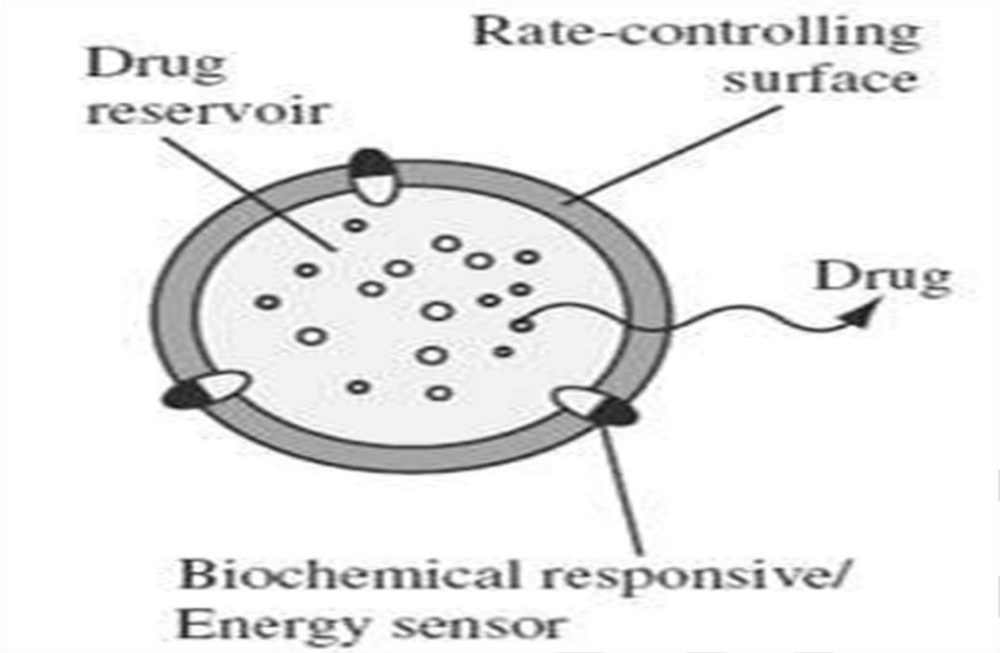
- The release of drug molecules is activated by a triggering system, such as a biochemical substance in the body, through some feedback mechanisms.
- The rate of drug release is regulated by the concentration of the triggering agent detected by a sensor built in the system.

These are again of two types

1. Bioerosion regulated drug delivery
2. Bioresponsive drug delivery

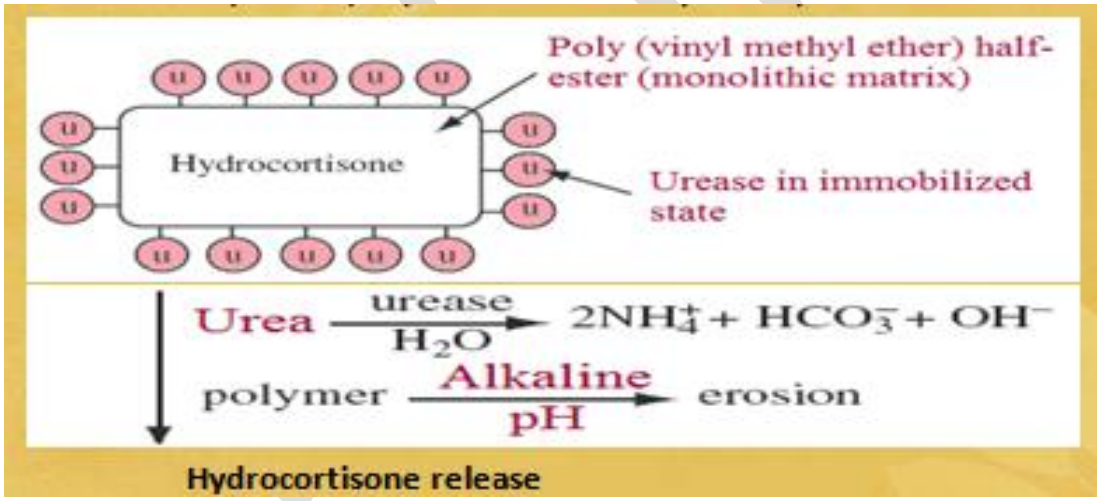
One Word Question Answer

SR NO.	QUESTION	ANSWER
1	The drug reservoir in a solution formulation is contained inside an infusate chamber is called?	Vapor pressure activated system
2	Which contains a vaporizable fluid, which vaporizes at body temp. & creates a vapor pressure.	Vapor pressure chamber
3	In which system, Drug reservoir is homogeneously dispersed in a swellable hydrophilic polymeric matrix.	Activated drug delivery system
4	In which system, the device is activated to release the drug upon hydrolysis of polymer base by tissue fluid at the implantation site.	Hydrolysis activated drug delivery
5	The release of drug molecules is activated by a triggering system, such as a biochemical substance in the body, through some feedback mechanisms is called?	Controlled drug delivery by feed back regulated process



BIO-EROSION REGULATED DDS

- This consists of bio-erodible drug dispersed polymer matrix fabricated from poly (vinyl methyl ether) half ester, which was coated with a layer of immobilized urease
- At neutral pH the polymer erodes very slowly.



Hydrocortisone release

- In the presence of urea, urease metabolizes urea to liberate ammonia
- This causes a rise in pH, rapid degradation of polymer and release of drug release

Bioresponsive Drug Delivery

- The drug reservoir is contained in a device enclosed by a bioresponsive polymer membrane whose permeability to drug molecules is controlled by concentration of biochemical agent in the tissue.

Ex: Glucose Triggered Insulin Delivery System

- Insulin reservoir is enclosed within a hydrogel membrane containing pendant NR_2 groups.
- In an alkaline solution the pendant NR_2 groups exist at neutral state and the membrane is unswollen and thus impermeable to insulin,
- As glucose penetrates the membrane it is oxidized by glucose oxidase enrapped in the membrane to gluconic acid.
- This causes protonation of NR_2 groups to $NR_2 H^+$
- This causes the membrane to swell and release of insulin.

Application

A. Cancer Treatment

- ***Gliadel Wafer:*** Delivers carmustine for the treatment of brain tumours directly at the site of tumour to prevent reoccurrence of tumours.
- ***Depocyte***: cytarabine releasing implantable DDS used to treat acute leukemia.
- ***Duros osmotic pump:*** Non-biodegradable implantable DDS used to deliver Leoprolide acetate in the treatment of prostate cancer.

B. Osteoporosis

- ***Micro chips:*** This device made by ELI Lilly & co-workers used to deliver Forteo drug used to increase bone density in patients suffering from severe osteoporosis.

C. Ocular Diseases

- **Lacrimedics:** These are collagen implants used to treat dry eye syndrome by partially blocking tear removing canals and they dissolve within 7-10 days.
- **Vitrasert:** delivers ganicyclovir used to treat AIDS related retinitis.

D. Contraceptives

- **Norplant:** delivers Norgestrol to achive contraception.
- Reactions of host to implant:
- Changes in permeability of polymer to body fluids.
- Environmental stress cracking.
- Chemical breakdown of polymeric material.
- Loss of tensile strength in case of hydrophobic polymers.

One Word Question Answer

SR NO.	QUESTION	ANSWER
1	Which system consists of bio-erodible drug dispersed polymer matrix fabricated from poly (vinyl methyl ether) half ester, which was coated with a layer of immobilized urease.	Bio-erosion regulated dds
2	In which system the drug reservoir is contained in a device enclosed by a bioresponsive polymer membrane whose permeability to drug molecules is controlled by concentration of biochemical agent in the tissue.	Bioresponsive drug delivery
3	Glucose Triggered Insulin Delivery System is one type of example of?	Bioresponsive drug delivery
4	Which pump used to deliver Leoprolide acetate in the treatment of prostate cancer?	Non-biodegradable implantable DDS
5	Which system delivers ganicyclovir used to treat AIDS related retinitis.	Vitrasert
6	Depocyte contain API of?	Cytrabine