IMPLANTABLE THERAPEUTICS

By

Dr. S.Vidyadhara M.Pharm.Ph.D

Professor & Principal , CHIPS

WHAT ARE IMPLANTS.....???

- ✓ These are drug loaded devices administred into the subcutaneous region of the skin,by making a small incision on the skin surface, generally ment for delivering the drug at constant rate over a prolonged durationof time.

Ideal Requirements Of Implants

1. Environmentally stable.
2. Biocompatible.
3. Sterile.
4. Biostable.
5. Improve patient compliance.
6. Release the drug in a rate controlled manner which lead to enhanced effectiveness and reduced side effects.
7. Readily retrievable by medical personnel to terminate medication.
8. Easy to manufacture and relatively inexpensive.

Advantages

- Mainly meant for extended drug release over a prolonged duration at a steady state.
- Quiet suitable for chronic diseases & also for contraception purpose.

Disadvantages

- *Invasive*
- *Termination*
- *Danger of device failure*
- *Adverse reactions*
- *Biocompatible issues*

Approaches to design implantable therapeutics..

✓ 1) Controlled drug release by diffusion.....

MEMBRANE PERMEATION- CONTROLLED DRUG DELIVERY

A) NON POROUS MEMBRANES

B)MICROPOROUS MEMBRANES

C) SEMIPERMEABLE MEMBRANES

MATRIX DIFFUSION CONTROLLED DRUG DELIVERY USING;

A) LIPOPHILIC POLYMERS

B) HYDROPHILIC POLYMERS

C) POROUS POLYMERS

MICRO RESERVOIR DISSOLUTION CONTROL DRUG DELIVERY

A. HYDROPHILIC RESERVOIR/ LIPOPHILIC MATRIX

B. LIPOPHILIC RESERVOIR/ HYDROPHILIC MATRIX

Controlled drug delivery by activation process

- ✓ **Osmotic pressure – activated drug delivery**
- ➢ **Vapor pressure - activated drug delivery**
- ❖ **Magnetically - activated drug delivery**
- ○ **ultrasonic - activated drug delivery**
- ❑ **Hydrolysis - activated drug delivery**

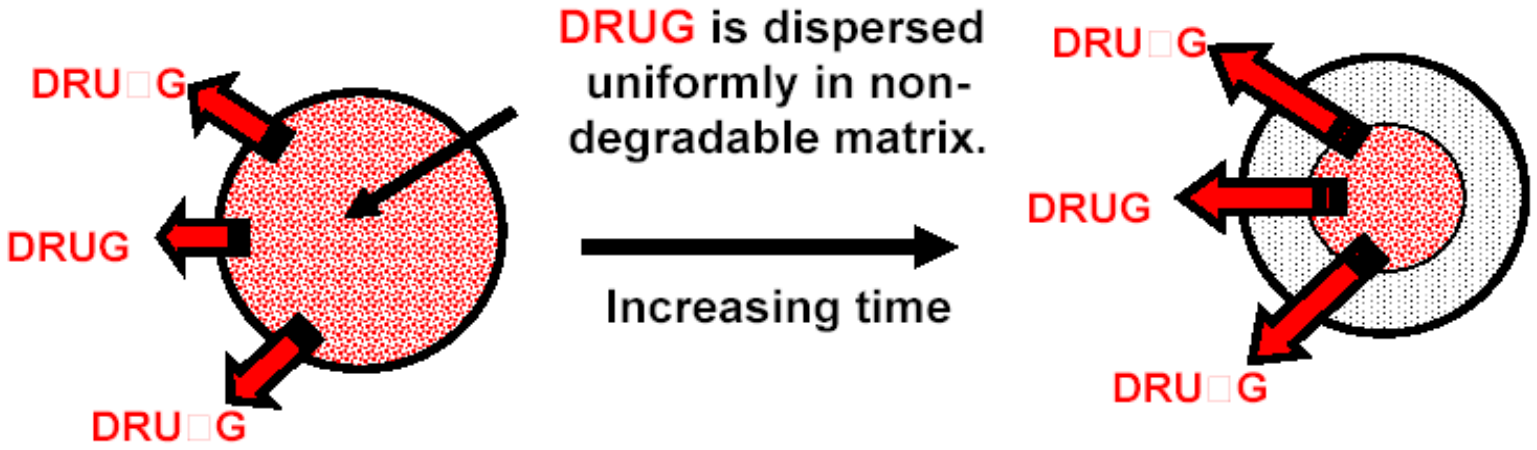
Controlled drug delivery by feed back regulated mechanism

- ❖ **Bioerosion regulated drug delivery**
- ❖ **Bioresponsive drug delivery**

Polymer membrane permeation- controlled drug delivery

In this type, the drug reservoir is encapsulated with in a compartment totally enclosed by a rate controlling polymeric membrane.

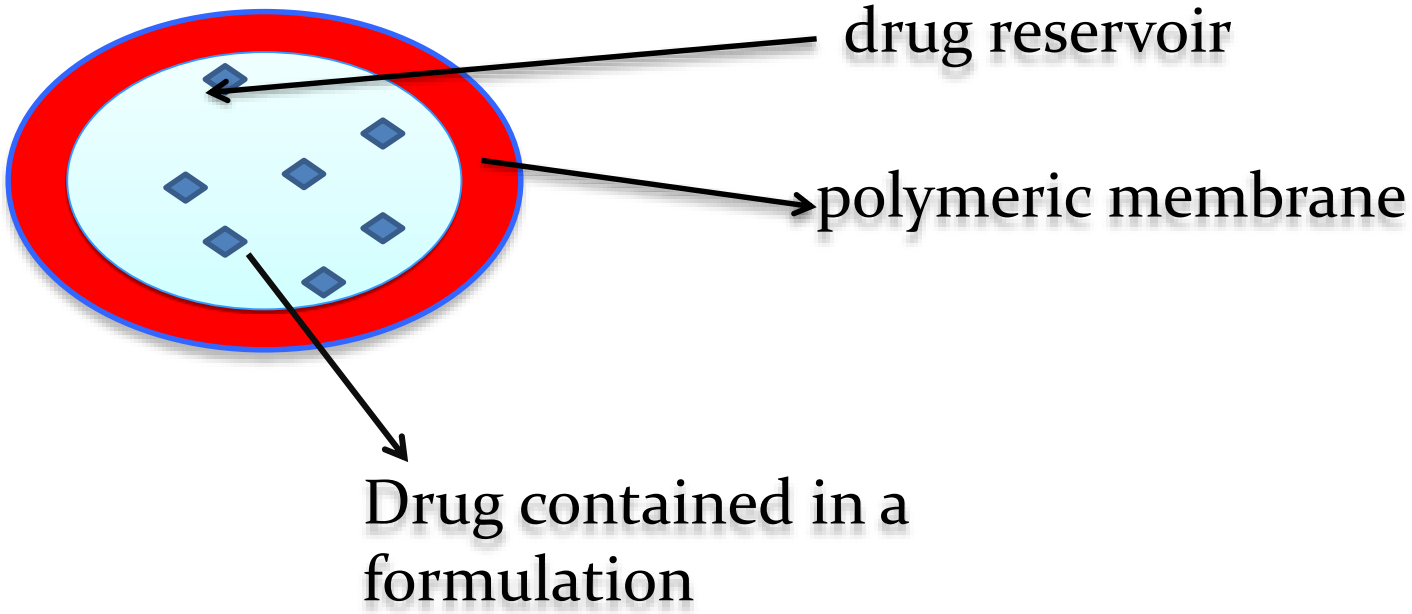
The drug reservoir can be either drug solid particles or a dispersion of drug solid particles in a liquid or a solid type dispersing medium

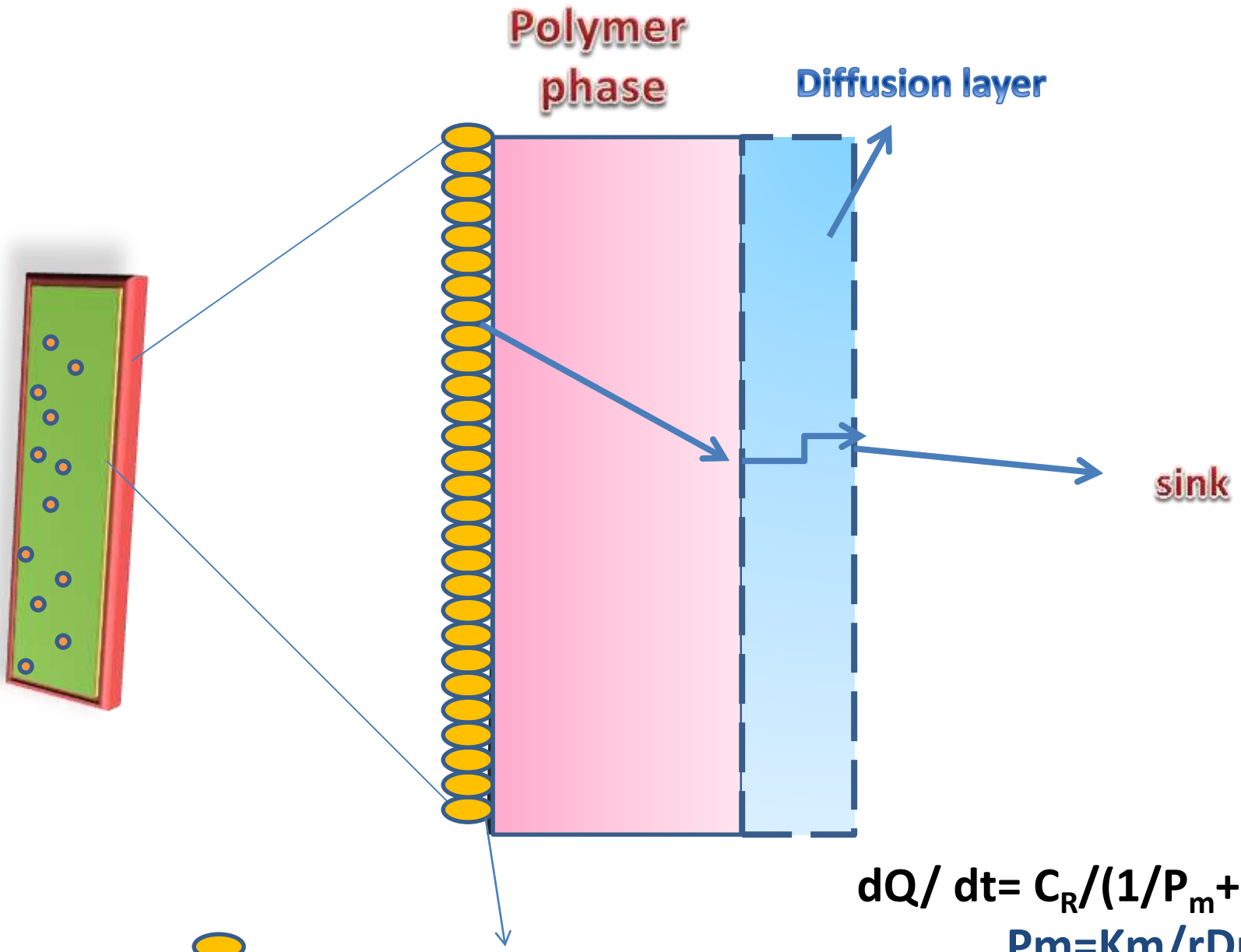


- Polymeric membrane can be fabricated from a homogeneous or a heterogeneous non porous polymeric material or a microporous membrane.

- Encapsulation of drug formulation in to the reservoir compartment can be done by

  Moulding
  Spray coating
  Microencapsulation





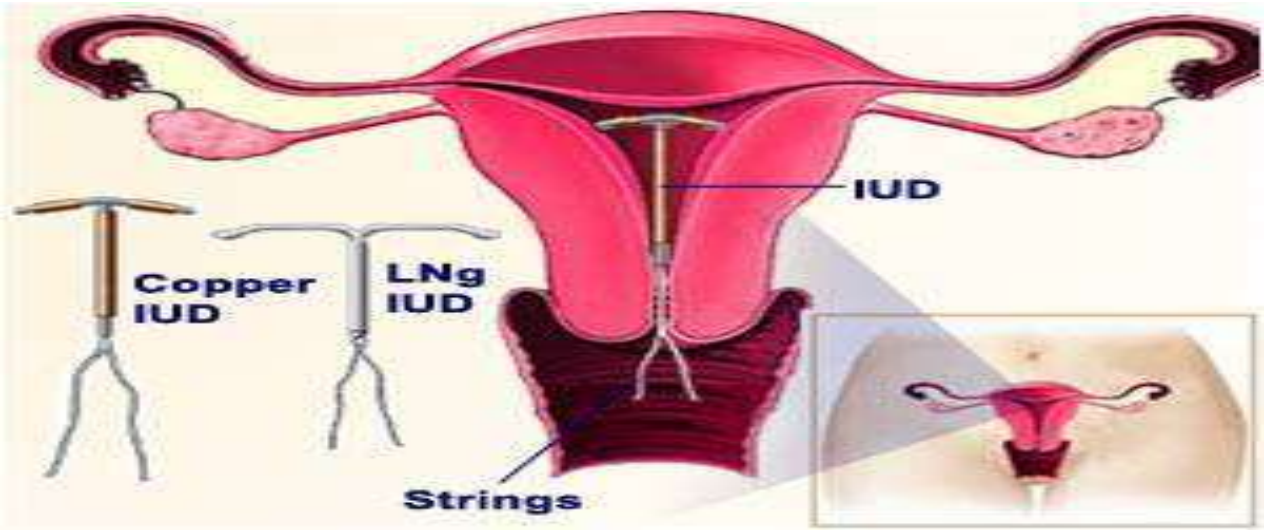
$$dQ/dt = C_R/(1/P_m + 1/P_d)$$

$$Pm = Km/rDm/\delta m$$

$$Pd = Ka/mDa / \delta d$$

Examples

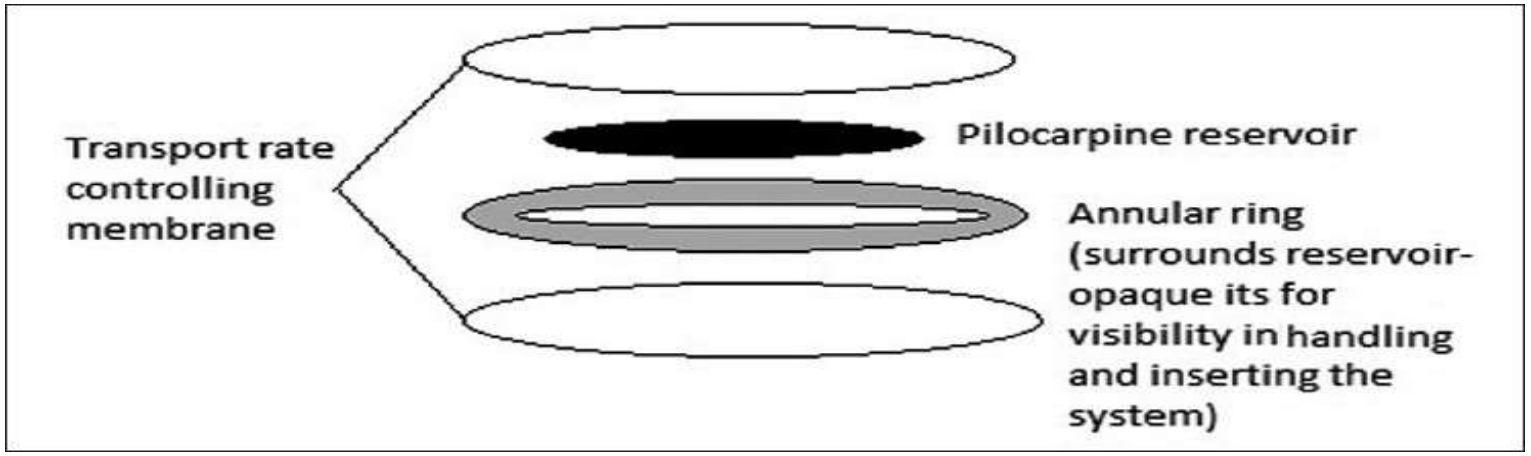
1) Progestasert IUD



The drug reservoir is a suspension of progesterone crystals in liquid silicon polymer is encapsulated in a T shaped Intra Uterine device(IUD) enclosed by a non porous membrane of Ethylene Vinyl acetate co-polymer.

Ocusert system..

Encapsulated cell technology:
Schematic diagram of implant placed in vitreous cavity of human eye



➢In this a thin disc of Pilocarpine alginate is sandwiched between two transparent sheets of micro porous membrane fabricated from ethylene vinyl acetate co-polymer.

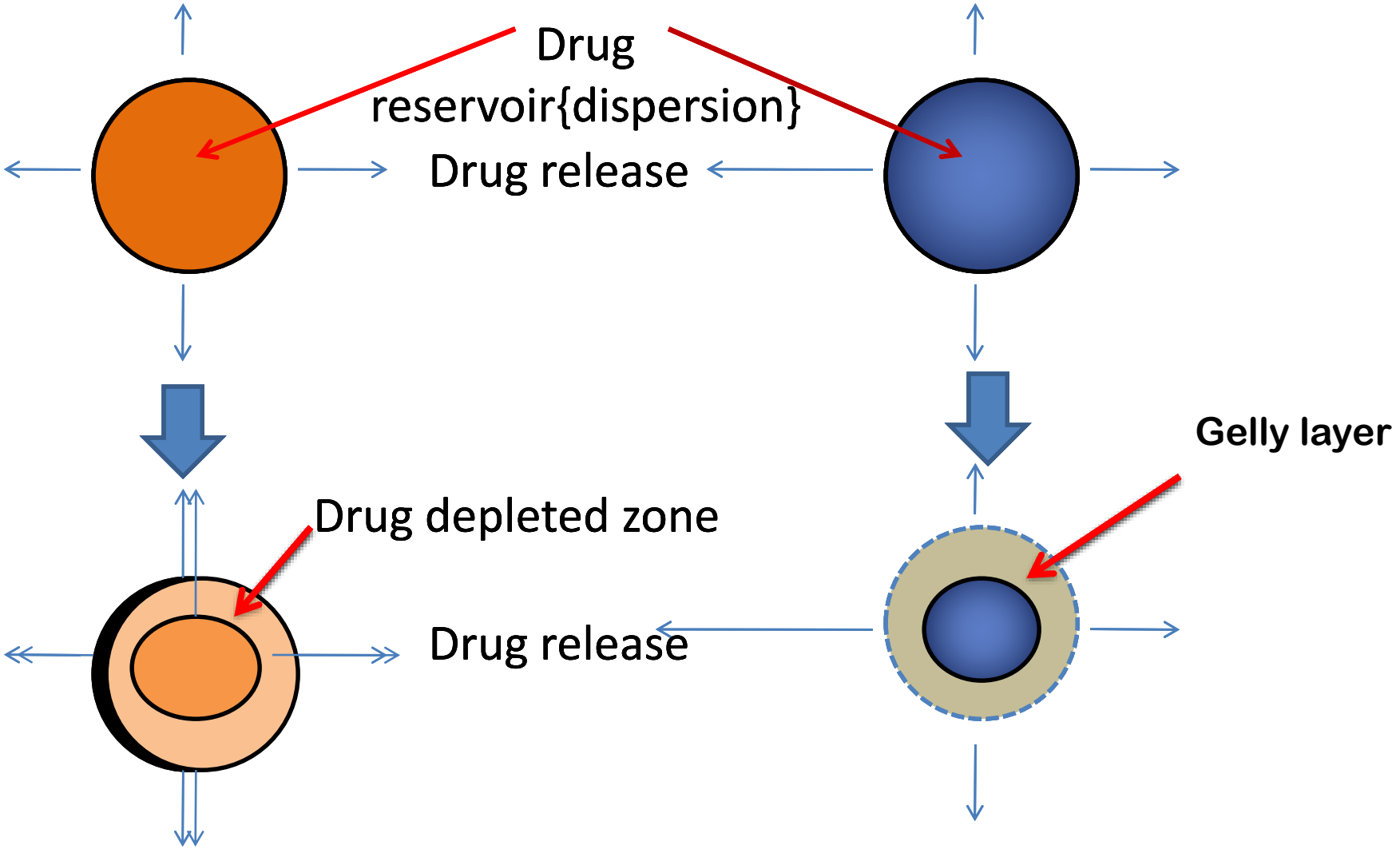
Matrix diffusion-controlled drug delivery

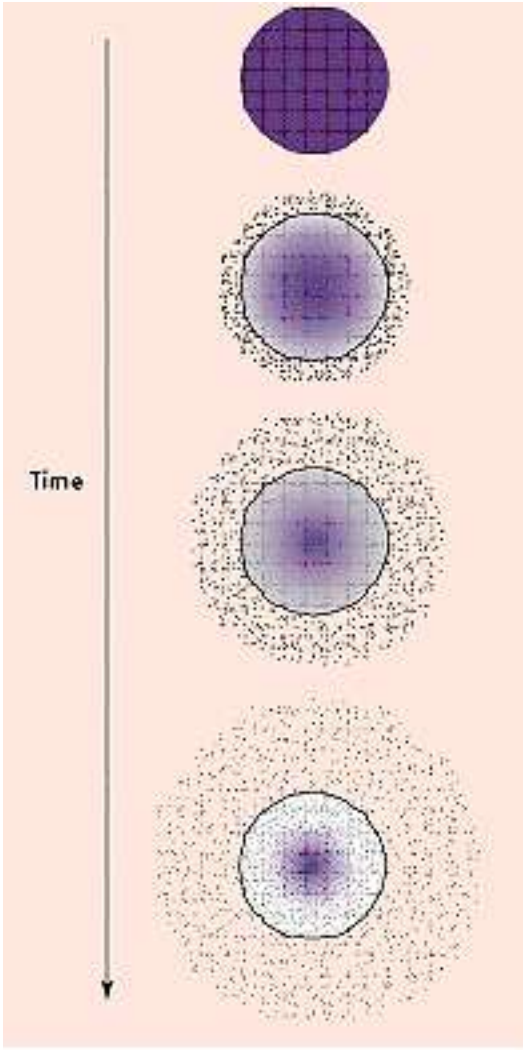
- In this type of controlled release drug delivery system the drug reservoir is formed by homogenous dispersion of drug particles in a rate controlling polymer matrix fabricated from either a lipophillic or a hydrophilic polymer

The drug dispersion in a polymer matrix is done by

1. Blending finely divided drug particles with a liquid polymer or a viscous base followed by cross linking of the polymer chain
2. Mixing the drug with a polymer at an elevated temperature
3. Dissolving drug and polymer in a common solvent followed by solvent evaporation at elevated temperature or under vacuum

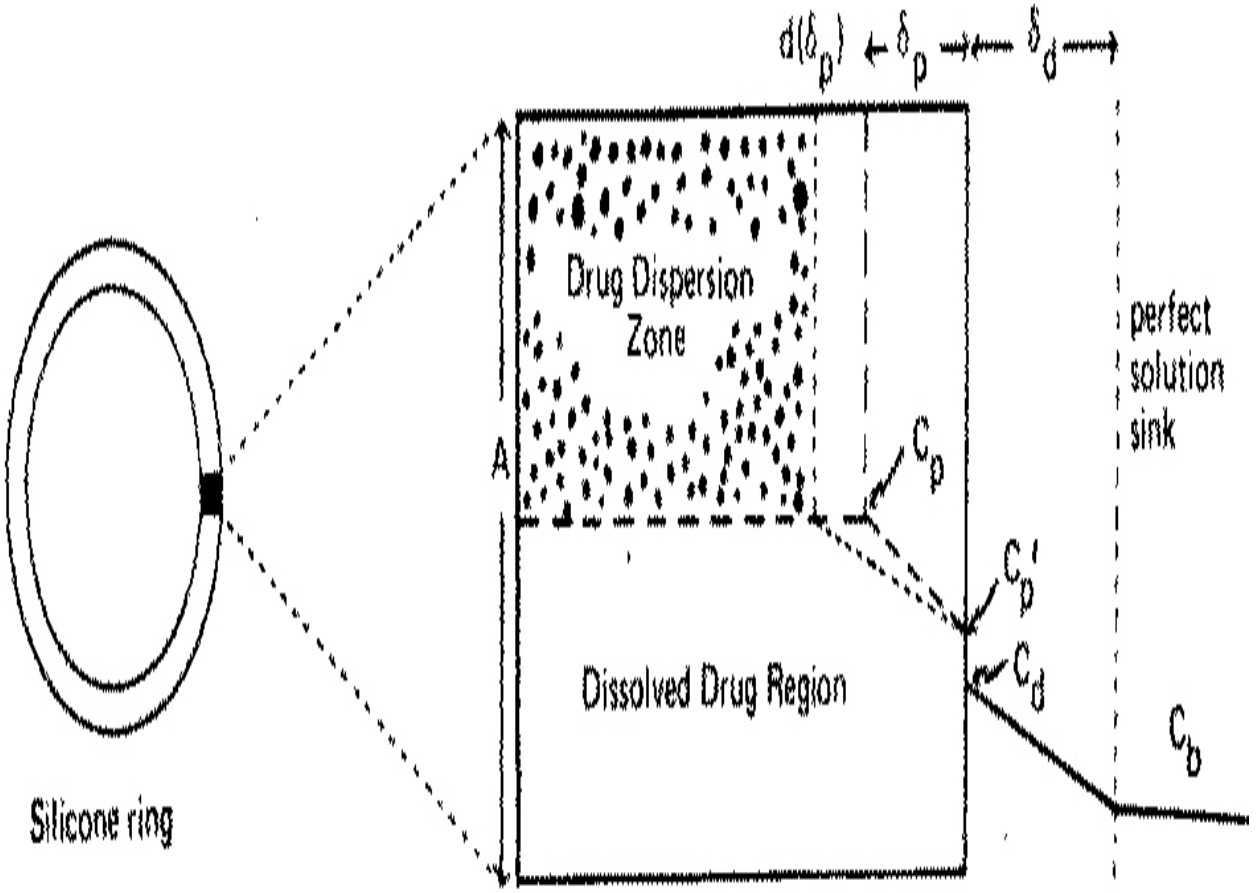
- The resultant drug polymer dispersion is then molded or extruded to form a drug delivery devices of various shapes
- Ex: Contraceptive vaginal ring, Syncro mate B implant, Compudose implant


Drug
reservoir{dispersion}
Drug release
Drug depleted zone
Drug release
Gelly layer
Lipophillic polymer
Non swellable matrix
Hydrophilic polymer
Swellable matrix

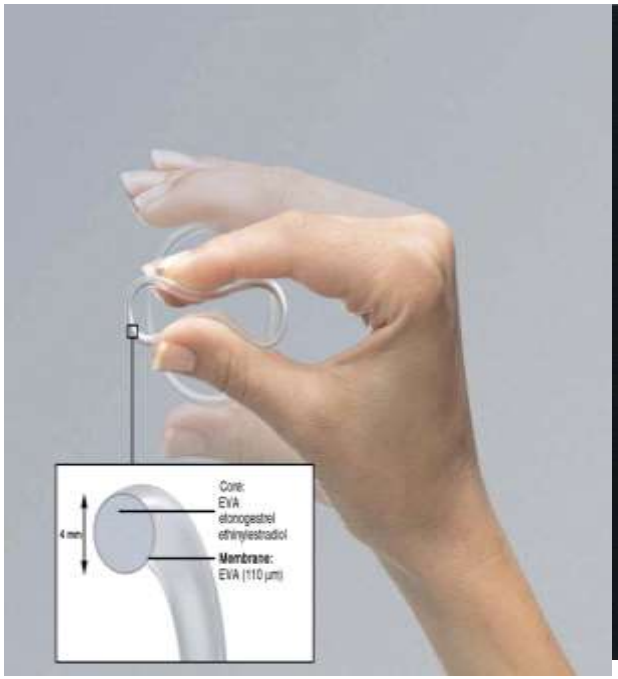


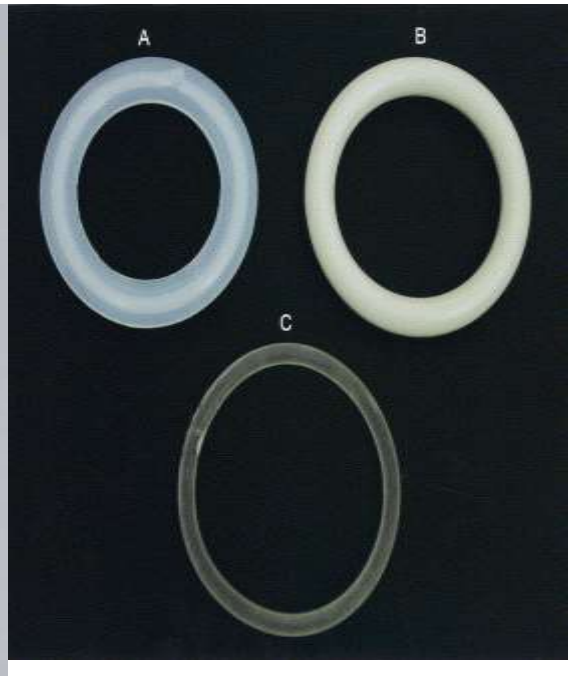
$$dQ/dt = (ACpDp/2t)^{1/2}$$

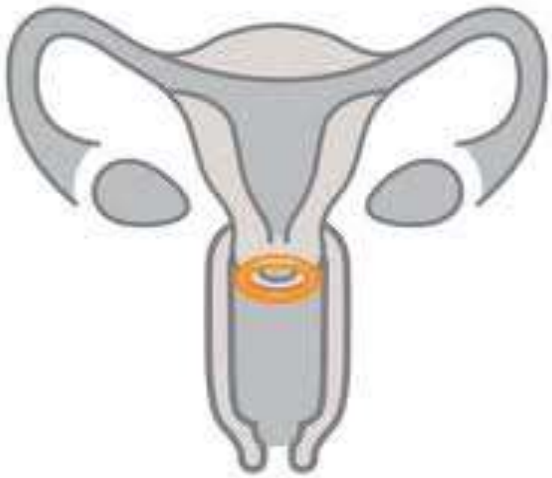
$$Q/t^{1/2} = (2ACpDp)^{1/2}$$



Contraceptive Vaginal Ring.....





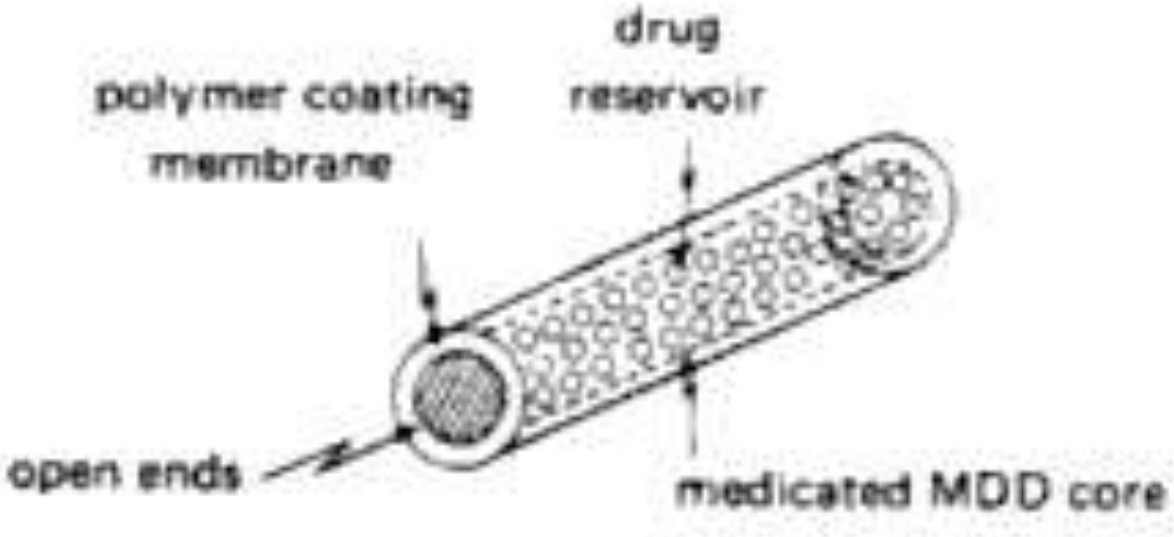


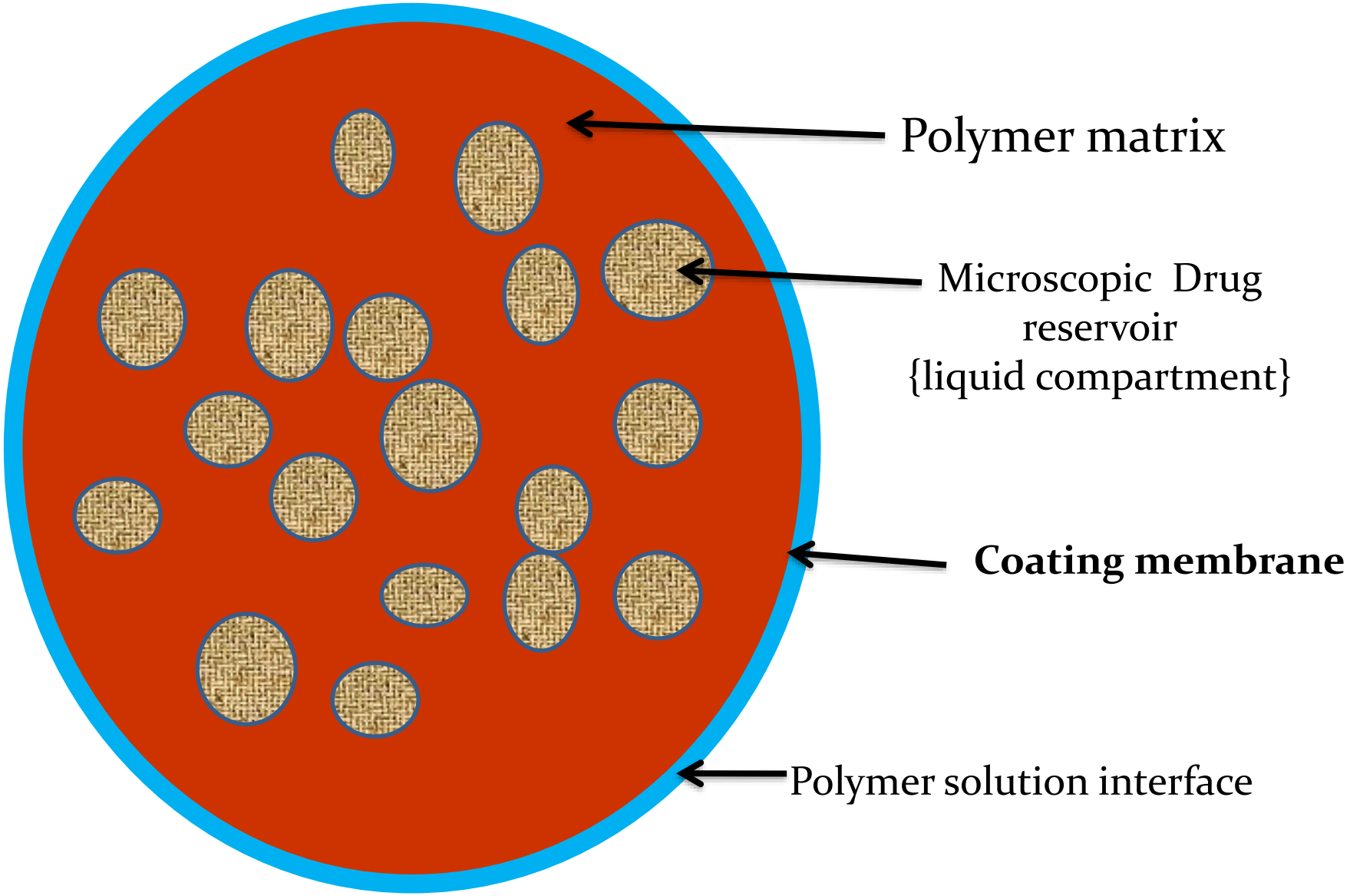
- It is fabricated by dispersing Contraceptive steroid ,e.g. Medroxy Progesterone acetate in viscous mixture of silicon elastomer then extruding the steroid- polymer dispersion into a mould to form a donut shape Vaginal ring.
- Others :Synchromate B implant,Compudo Implant

Microreservior partition-controlled drug delivery system

- In this type, drug reservoir is fabricated by micro dispersion of an aqueous suspension of drug in biocompatible polymer to form homogeneous dispersion.

  Ex. Syncromate-C.



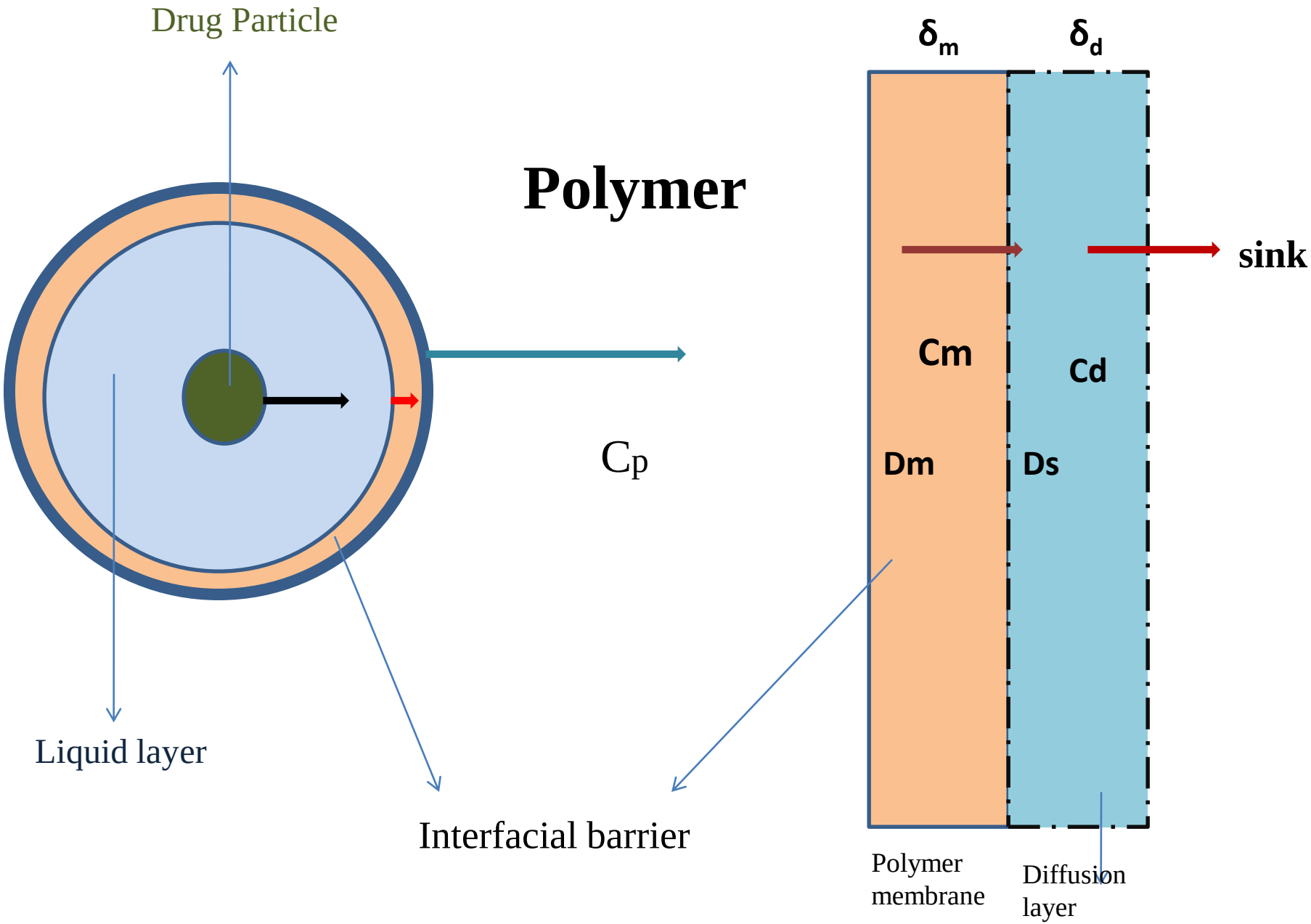

Polymer matrix
Microscopic Drug reservoir {liquid compartment}
Coating membrane
Polymer solution interface

Syncro-Mate-c Implant

- It is fabricated by dispersing the drug reservoir which is a suspension of Norgestromet in an aqueous solution of PEG 400 to form millions of microscopic drug reservoirs in a viscous mixture of Silicon elastomers.

Dual Release Vaginal Contraceptive Ring

- It is a suspension of progestin and an Estrogen in an aqueous solution of PEG 400 to form many microscopic drug reservoirs in a viscous mixture of silicon elastomers.


Drug Particle
Polymer
Cp
Liquid layer
Interfacial barrier
δm
δd
sink
Cm
Cd
Dm
Ds
Polymer membrane
Diffusion layer

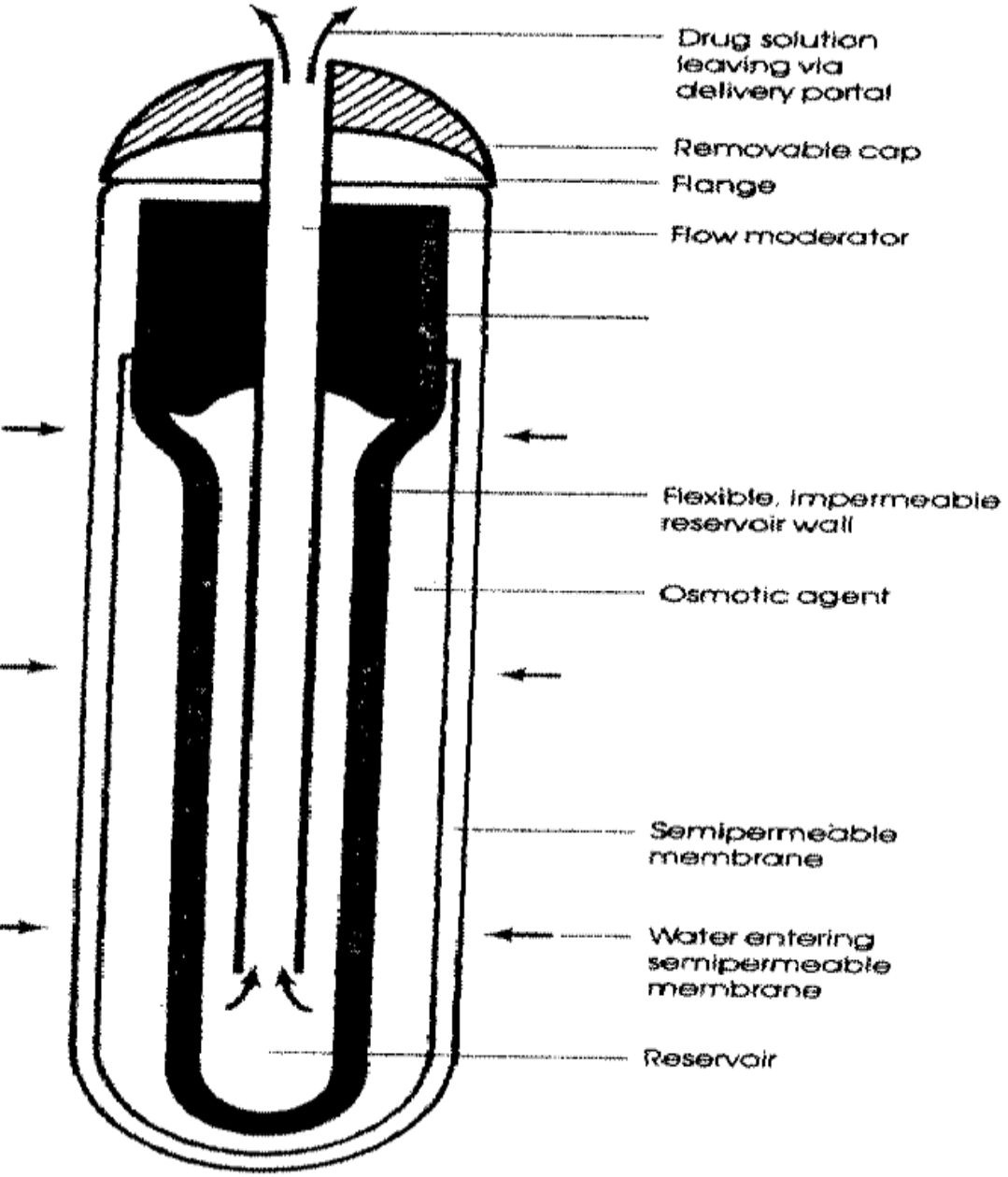
Controlled drug delivery by activation process

- ✓ In this type release of the drug is activated by some physical, chemical, or biological process and/or by the energy supplied externally and the rate of release is then regulated by the processes applied or input of energy

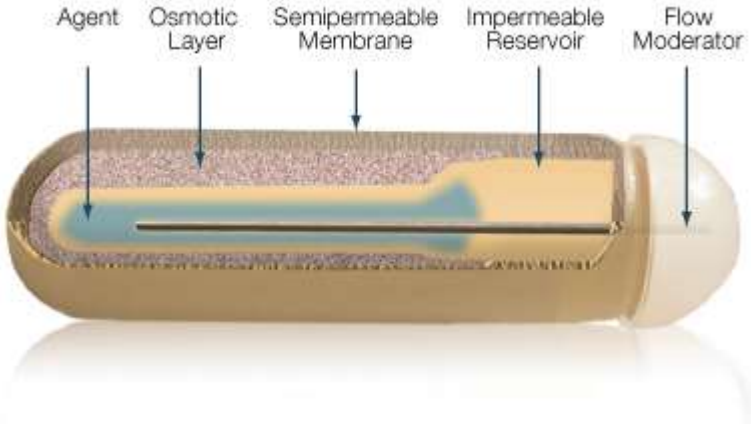
- ✓ Based on the processed applied these activation modulated drug delivery system can be classified in to

1. Osmotic pressure activated
2. Vapor pressure activated
3. Magnetically activated
4. Hydrolytic-activated
5. Hydration activated

Osmotic pressure activated drug delivery system

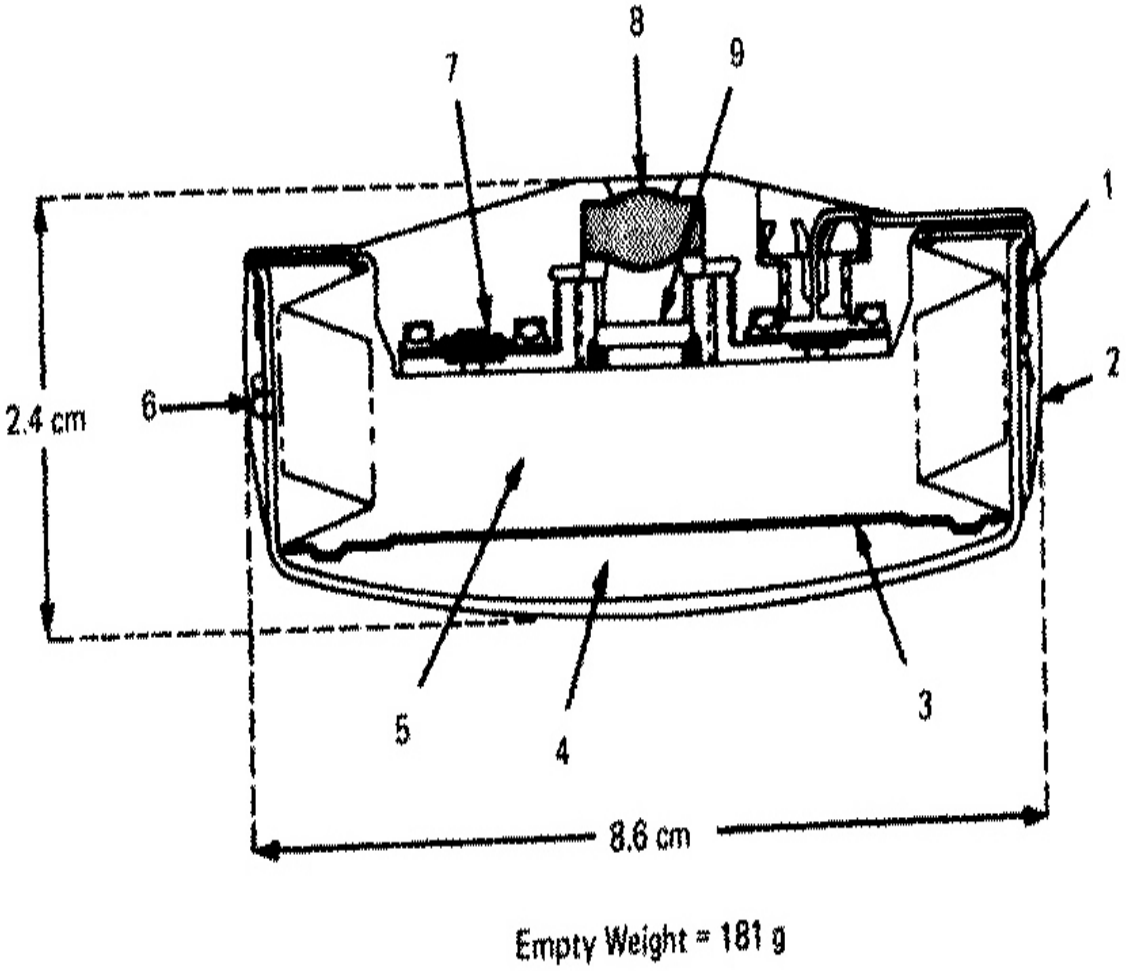


$$dQ/dt = P_w A_m / h_m(\pi_s - \pi_e)$$



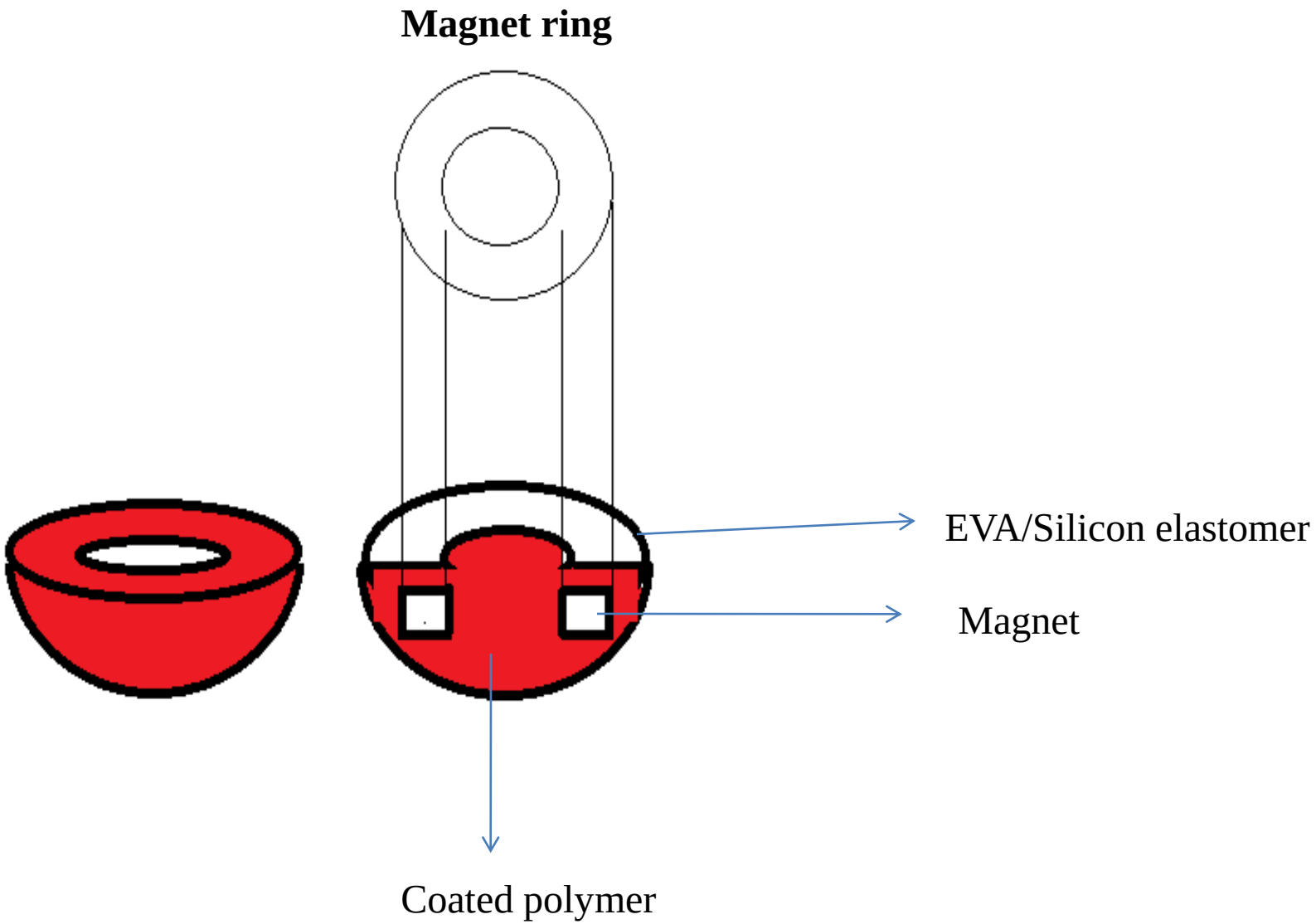
alzet®
OSMOTIC PUMPS

. Vapour pressure- Activated drug delivery



1. Flow regulator
2. Silicon polymer coating
3. Bellows
4. Flouro-carbon chamber
5. Infusate chamber
6. Flourocarbon fluid filling tube
7. Filter assembly

Magnetic- activated drug delivery……



. *Ultrasound- activated drug delivery*

- This implant utilizes ultrasonic energy to activate the delivery of drug from polymer, this system can be fabricated from either a nondegradable polymer such as ethylen vinyl acetate copolymer or bioerodible polymer such as poly[bis(p- carboxyphenoxy)alkane anhydride].
- Its modulation is still undergoing evaluation.

Hydrolysis- activated drug delivery

Release of drug is activated by hydrolysis of a bioerodible polymer by the cell fluid at the implantation site.

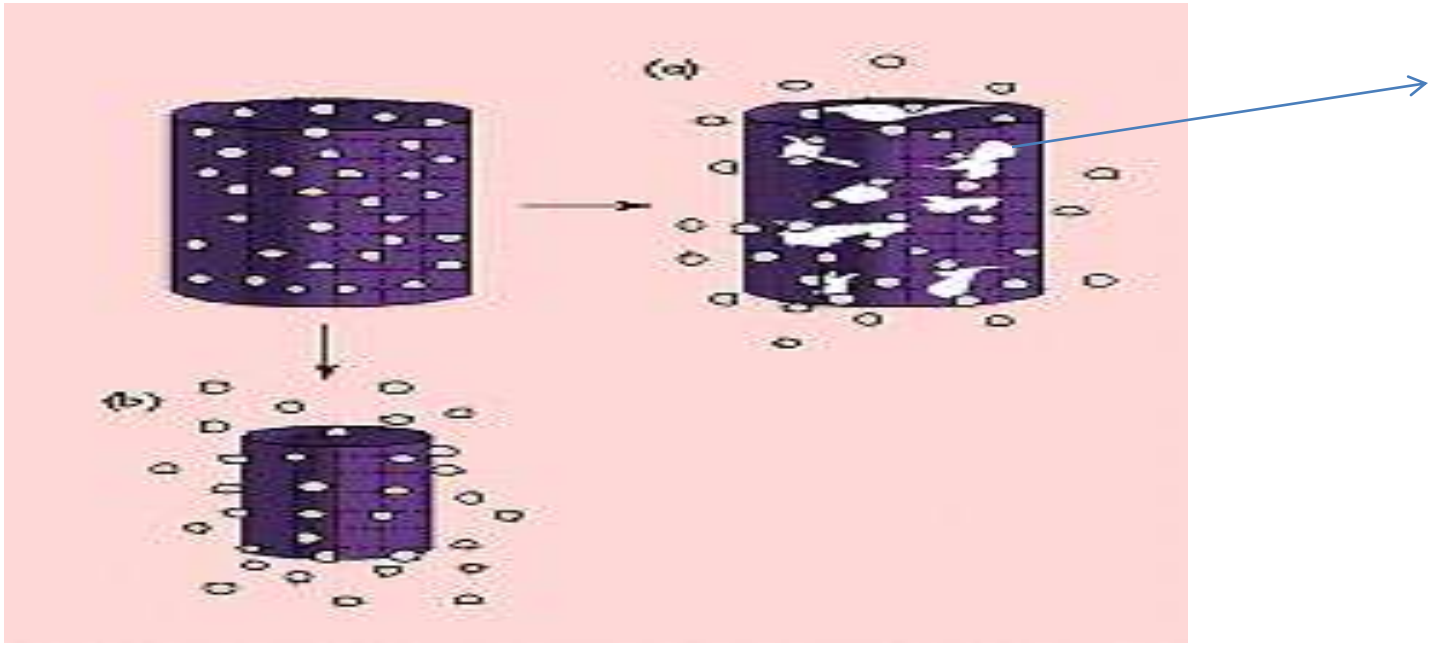
Biodegradable polymers like

1.Poly(lactide/glycolide) copolymer

2.Poly(orthoester)

3.Poly(anhydride) are used in fabrication of this type of implantable drug delivery system.

✓ This system is made by dispersing loading dose of a drug with in a bioerodible or biodegradable polymer , which is then molded in to pellet or a bead shaped implant.

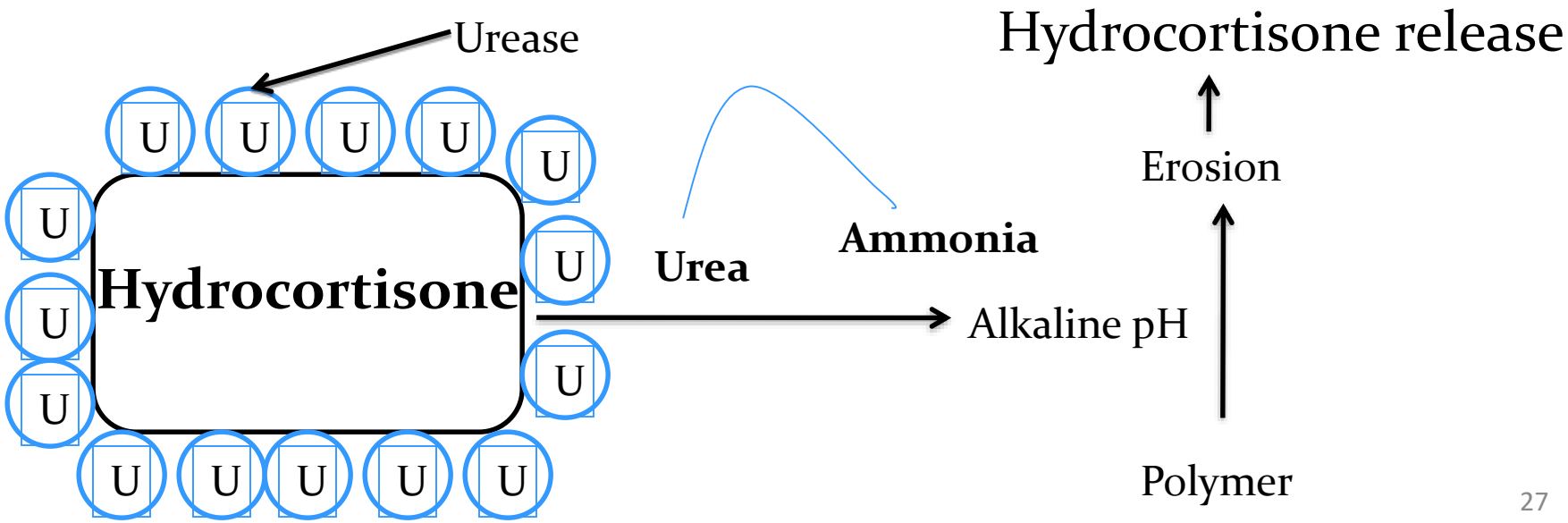


Controlled drug delivery by feed back regulated mechanism

- Using this group of controlled drug delivery system the release of a drug is activated by some biochemical molecule in the body and its concentration at the implantable site via feedback mechanism
- And the rate of controlled release of drug is regulated by the concentration of biochemical substance detected by a sensor in the feedback mechanism

Bioerosion regulated drug delivery system

- This system consist of a drug dispersed in to a biodegradable polymer matrix like poly vinyl methyl ether and is coated with immobilized urease in a neutral pH..
- Urease at the surface of drug delivery system metabolize urea to form ammonia causing increase in pH at which polymer degrades leading to drug release.



Medical aspects of implantation….

A) ***The Environment of Living Tissues***

B) ***Reaction of Host to Implant***

c) ***Reaction of implant to Host.***


Thank You