# UNIT 1
# CONTROLLED DRUG DELIVERY SYSTEMS-2

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# Contents

- **Polymers for Control Drug Delivery System**
- **Classification Of Controlled Release System**

# Polymers for Control Drug Delivery System

Applications of polymers range from their

- use as binders in tablets
- viscosity builders and flow controlling agents in liquids, suspensions and emulsions.
- as film coatings to mask the unpleasant taste of a drug,
- to enhance drug stability
- and to **modify drug release characteristics**.

# Polymers for Control Drug Delivery System

- Polymer( natural or synthetic) is combined with a drug so that the drug is released from CDDS in predesigned manner.
- The release of the active agent may be constant over a long period,
- it may be cyclic over a long period, or
- it may be triggered by the particular environment or
- other external events.

# Polymers for Control Drug Delivery System

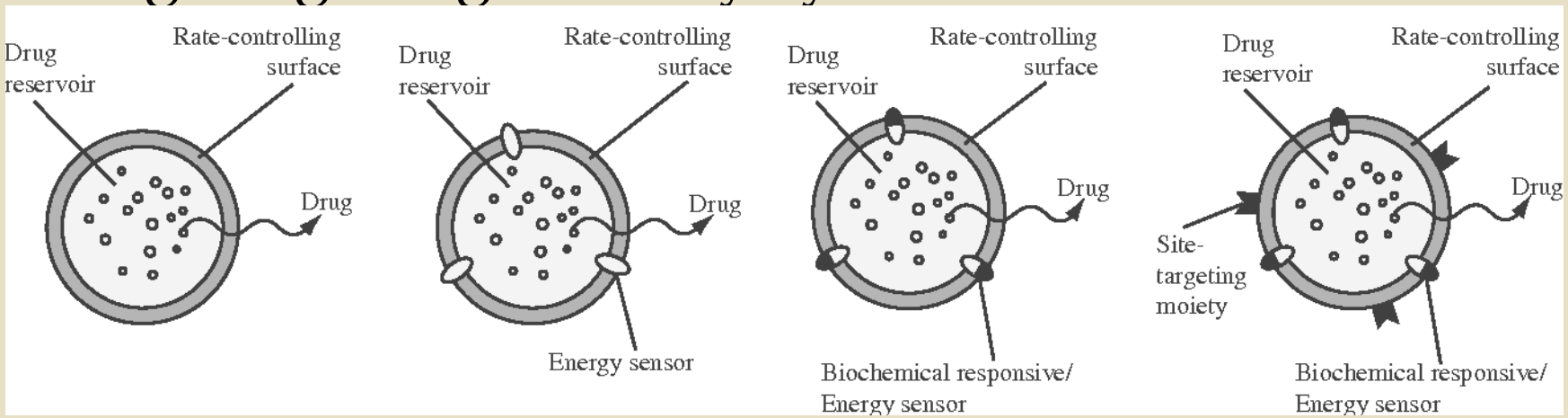
- Innovative pharmaceutical treatments require innovative methods of administration.
- Significant advances have been made in the development of various drug delivery devices with the help of polymers

DEFNITION:

- Polymers are defined as very large macromolecules consisting of repeating units of monomers

# Classification Of Controlled Release System

1. Rate pre-programmed drug delivery system
2. Activated modulated drug delivery system
3. Feedback regulated drug delivery system
4. Site targeting drug delivery system




https://www.semanticscholar.org/paper/Drug-Delivery%3A-Controlled-Release-Lin-Chien/69834df4208e8e14ee5da34d1dd49e88d6427499

# Classification Of Controlled Release System

### 1.Rate pre-programmed drug delivery system

- The release of drug molecule is preprogrammed at specific rate profile

### 2.Activated modulated drug delivery system

- The release of drug molecules from the delivery system is activated by some physical, chemical, or biochemical process and/or by energy supplied externally

### 3. Feedback regulated drug delivery system

- physiological response activates the release of drugs from the carrier
- rate of drug release is synchronized by the concentration of a triggering agent

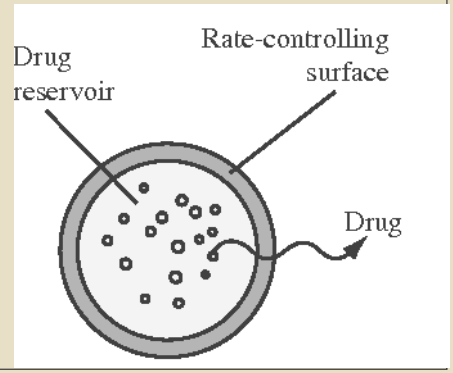
### 4. Site targeting drug delivery system

- (1)First order targeting: - drugs carrier release the drugs at the targeted site such as organ, tissue, cavity, etc.
- (2) Second order targeting: - drugs carrier release the drugs in the specific cell such as tumors cells not to the normal cells.
- (3) Third order targeting: - drugs carrier release the drugs to the intracellular site of targeted cells.

# Rate Preprogrammed Drug Delivery System

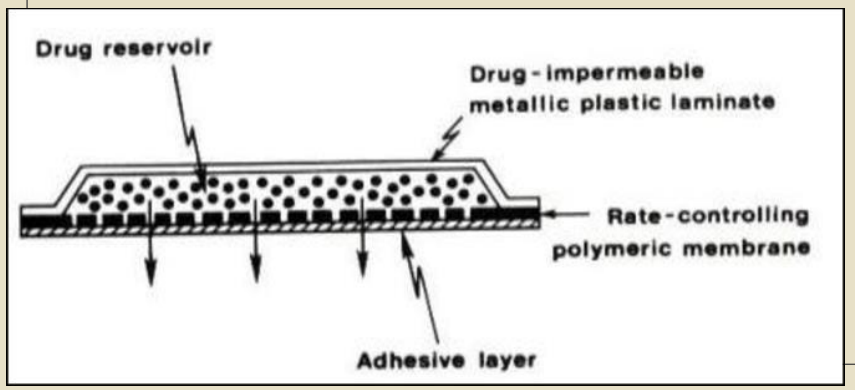
The release of drug molecule is preprogrammed at specific rate profile.

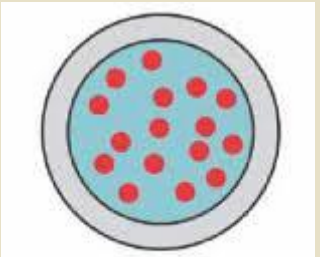
1. Polymer membrane permeation-controlled drug delivery system
2. Polymer matrix diffusion-controlled drug delivery system
3. Micro-reservior partition-controlled drug delivery  system



# 1. Polymer Membrane Permeation-Controlled Drug Delivery System

- Drug is totally or partially encapsulated within drug reservoir.
- Its drug releasing surface is covered by a **rate-controlling polymeric membrane** having a specific permeability.
- Drug reservoir may exist in solid, suspension or solution form.





Reservoir device

https://www.researchgate.net/figure/Cross-sectional-view-of-polymer-membrane-permeation-controlled-TDD-systems-The-drug-is_fig8_311444050

# Polymer Membrane Permeation-Controlled Drug Delivery System

- Polymeric membrane may be fabricated form of homogeneous or heterogeneous non-porous or partial microporous or semipermeable membrane.
- The encapsulation of drug formulation inside the reservoir compartment is done by **injection molding, spray coating, capsulation, microencapsulation, or other techniques**.
- Can be fabricated in different shapes and sizes.

The rate of drug release is defined by,

$$\frac{Q}{t} = \frac{K_{m/r}\, K_{a/m}\, D_d D_m}{K_{m/r}\, D_m h_d + K_{a/m}\, D_d h_m} \times C_R$$

Where,

$K_{m/r}$ & $K_{a/m}$ = partition coefficient of the drug molecule from reservoir to rate controlling membrane & from membrane to aq. Layer respectively.

$D_d$ & $D_m$ = diffusion coefficient of rate controlling membrane & aqueous diffusion layer respectively.

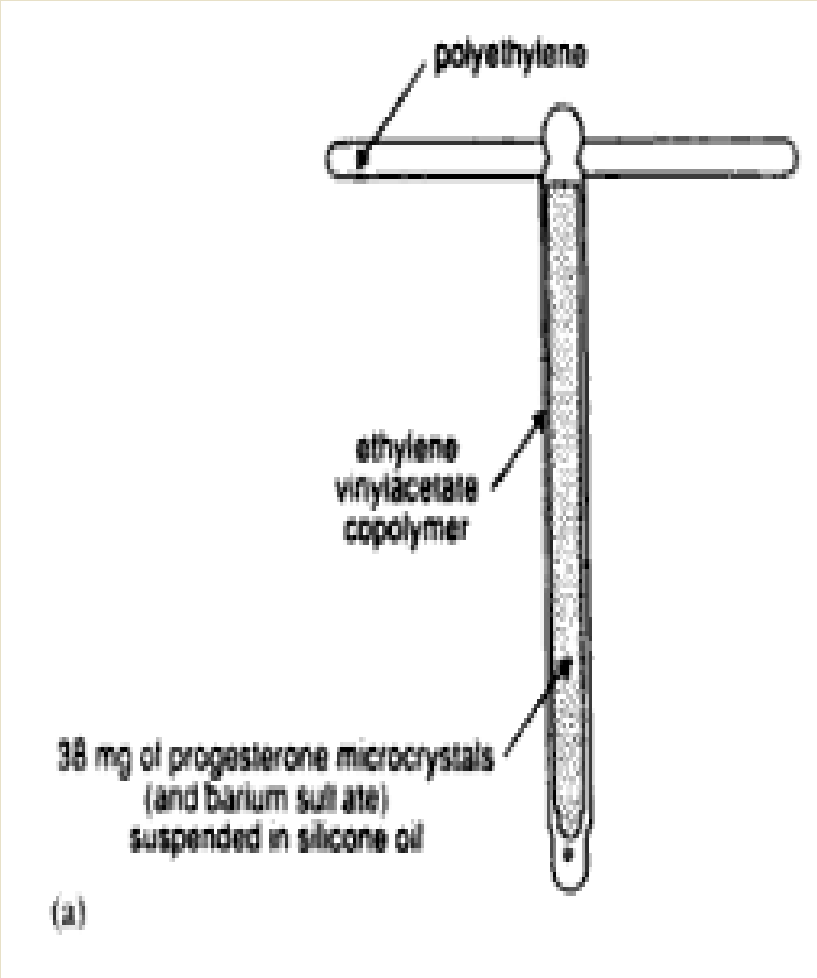
$h_m$ & $h_d$ = thickness of rate controlling membrane & aqueous diffusion layer respectively.

$C_R$ – drug conc. In reservoir compartment.

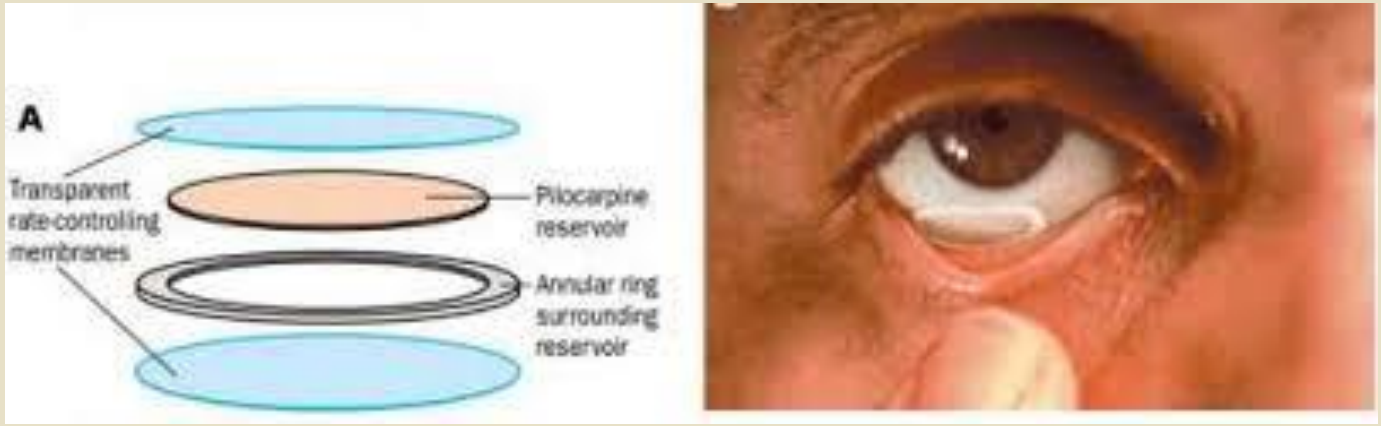
Release of drug molecules is controlled by :

- Partition coefficient of the drug molecule.
- Diffusivity of the drug molecule.
- The thickness of the rate controlling membrane.

# Ex. Progestasert IUD




- The drug reservoir (suspension of **progesterone & barium sulphate** in silicone medical fluid) is encapsulated in the vertical limb of a T-shaped device walled by a **non-porous membrane of ethylene-vinyl acetate co-polymer**.
- It deliver progesterone continuously in uterine cavity at a daily dosage rate of at least 65 µg/day for contraception for 1 year.

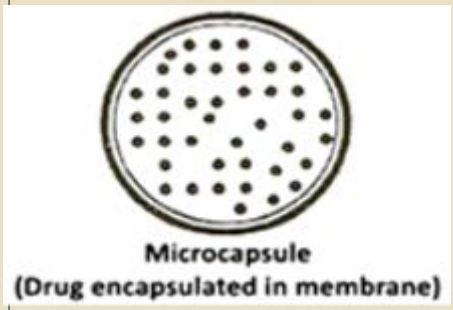



https://www.guwsmedical.info/intraocular-pressure/drug-delivery-systems.html

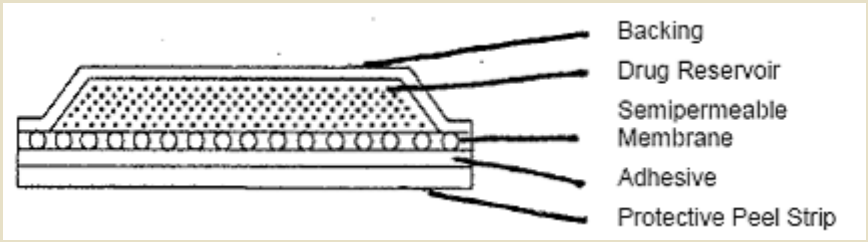
Ocuserts(Pilocarpin alginate)

- Norplant Subdermal Implant

(levonorgestrel crystals in silicon fluid)








https://www.rxlist.com/transderm-nitro-drug.htm

Transderm-Nitro

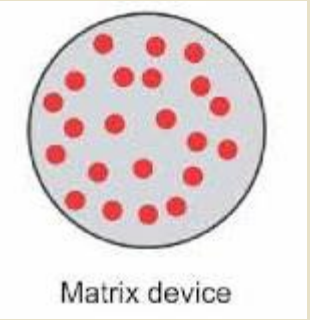
# 2. Polymer Matrix Diffusion-Controlled Drug Delivery System

- Drug reservoir is prepared by homogeneously dispersing drug particle in rate controlling polymer matrix from either a lipophilic or a hydrophilic polymer.

The drug dispersion in the polymer matrix is accomplished by either,

1) blending therapeutic dose of drug with polymer or highly viscous base polymer, followed by cross linking of polymer chains.

2) mixing drug solid with rubbery polymer at elevated temp.



The rate of the drug release from this system,

$$\frac{Q}{t} = (2AC_R D_p)^{1/2}$$

Where,

$Q/t^{1/2}$ - rate of release of drug

A – initial drug loading dose in the polymer matrix

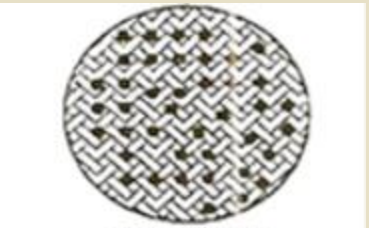
$C_R$ – drug solubility in polymer

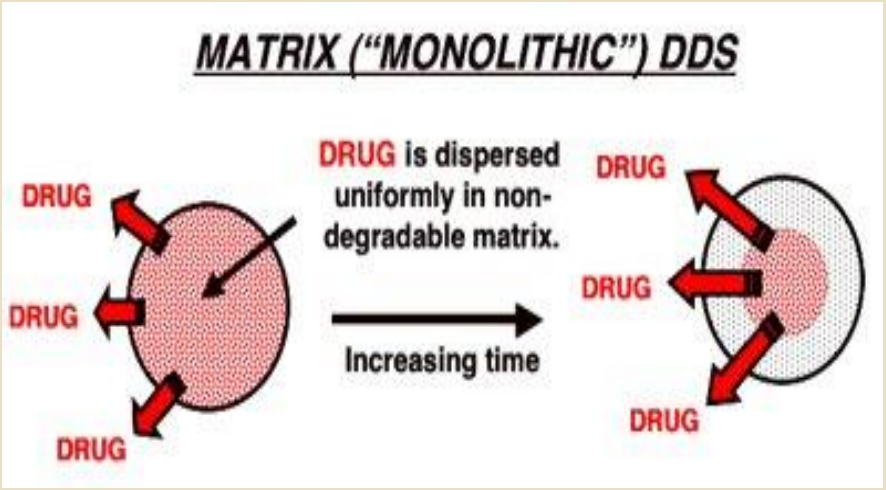
$D_p$ – diffusivity of drug in polymer matrix

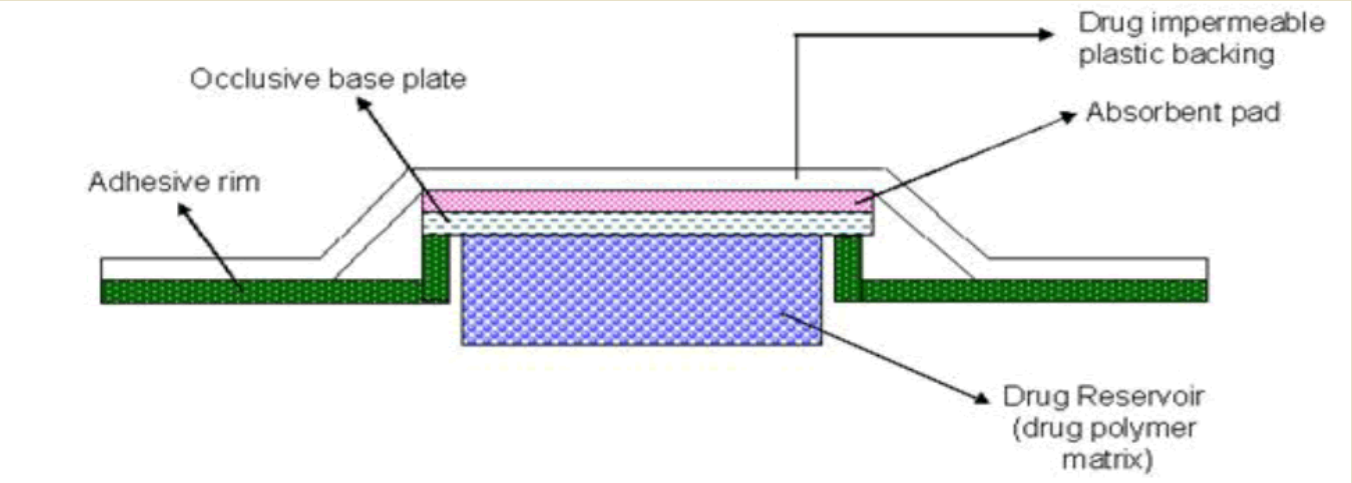
# Polymer Matrix Diffusion-Controlled Drug Delivery System

Release of drug molecule is controlled by

- Loading dose
- Polymer solubility of drug
- Drug diffusivity in polymer matrix.






http://www.rroij.com/open-access/transdermal-drug-delivery-systems-.php?aid=81831

Nitro-Dur :

•Nitro-Dur is a transdermal system contains nitroglycerin in acrylic-based polymer adhesives with a resinous cross-linking agent to provide a continuous source of active ingredient.

It is designed for application on to intact skin for 24 hrs to provide a continuous transdermal infusion of nitroglycerin at dosage rate of 0.5 mg/cm$^2$/day for the treatment of angina pectoris.

# 3. Microreservoir Partition-Controlled Drug Delivery System

Drug reservoir is fabricated by micro **dispersion of an aqueous Suspension of drug** in biocompatible polymer to form homogeneous dispersion.

Depending upon the physicochemical properties of drugs & desired rate of drug release, the device can be further coated with a layer of biocompatible polymer to modify the mechanism & the rate of drug release.

The rate of drug release is defined by,

$$\frac{dQ}{dt} = \frac{D_p D_d m K_p}{D_p h_d + D_d h_p m K_p} \left[ m S_p - D_l S_l (1-n) \frac{1}{h_l} \left( \frac{+1}{k_l} \frac{}{K_m} \right) \right]$$

Where,

n = the ratio of drug conc. At the inner edge of the interfacial barrier over the drug solubility in the polymer matrix.

m = a/b, a – ratio of drug conc. In the bulk of elution solution over drug solubility in the same medium.

b – ratio of drug conc. At the outer edge of the polymer coating membrane over drug solubility in the same polymer.

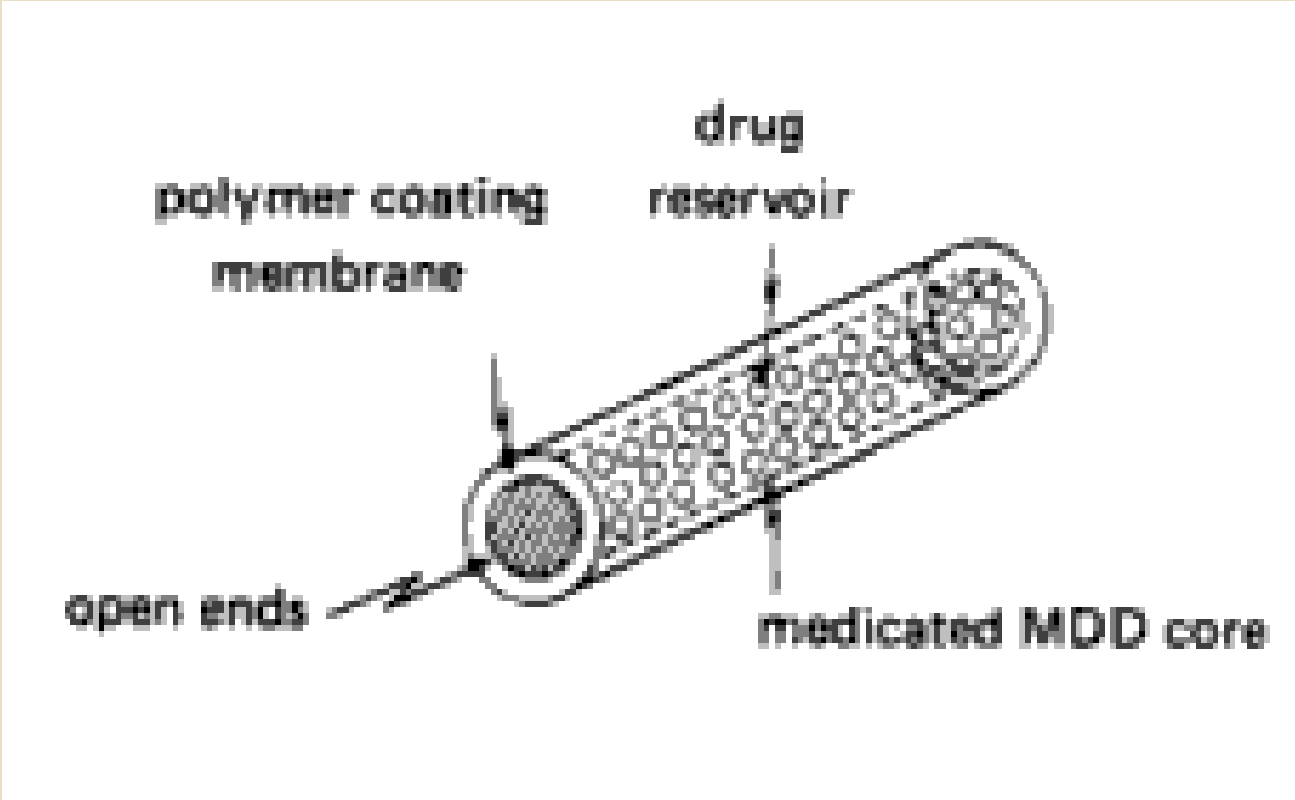
$K_l$, $K_m$ & Kp = partition coefficient for the interfacial partitioning of the drug from the liquid compartment to the polymer matrix, from the polymer matrix to the polymer-coating membrane & from the polymer coating membrane to the elution solution respectively.

Dl, Dp & Dd = diffusivities of the drug in the lipid layer surrounding the drug particle, the polymer coating membrane enveloping the polymer matrix, & the hydrodynamic diffusion layer surrounding the polymer coating membrane with the thickness $h_l$, $h_p$ & $h_d$.

$S_l$ & $S_p$ = solubilities of the drug in the liquid compartments & in the polymer matrix, respectively.

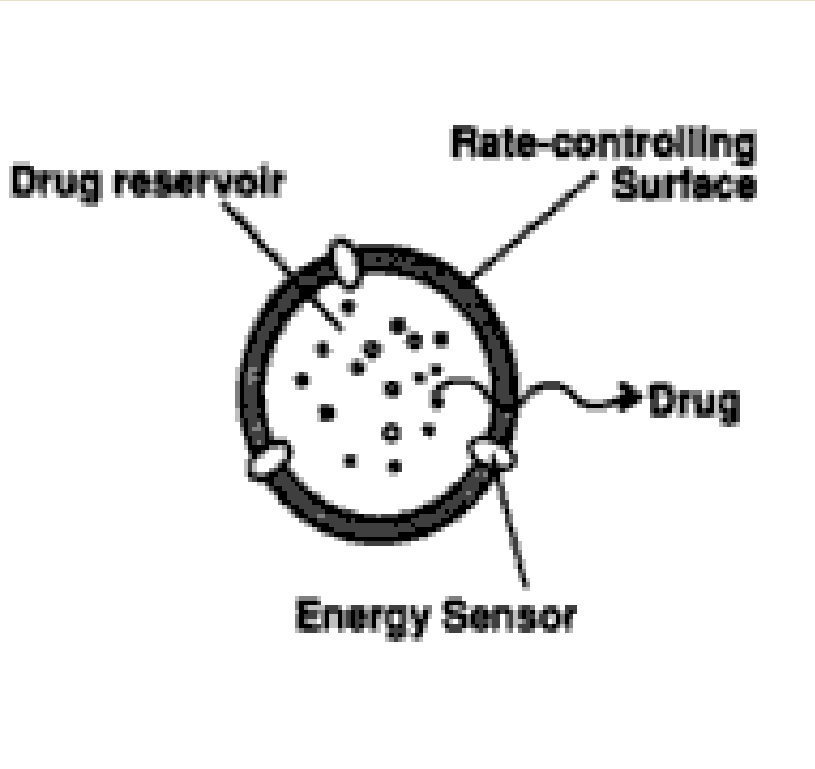
- Release of drug molecules from this type of system can follow either a dissolution or a matrix diffusion controlled process depending upon the relative magnitude of $S_l$ & $S_p$.
- Release of drug molecule is controlled by,
- Partition coefficient
- Diffusivity of drug
- Solubility of drug

# Ex. Syncro mate - c




- It is fabricated by dispersing the drug reservoir, which is a **suspension of norgestomet** in an aqueous solution of PEG 400, in a viscous mixture of silicone elastomer.

# 4. Activation Modulated Drug Delivery System




- The release of drug molecules from the delivery system is **activated** by some physical, chemical, or biochemical process and/or by energy supplied externally.

Based on nature of type of activation energy used they can be classified into

## 1. Physical means

a. Osmotic pressure-activated DDS

b. Hydrodynamic pressure-activated DDS

c. Vapor pressure-activated DDS

d. Mechanically activated DDS

e. Magnetically activated DDS

f. Sonophoresis activated DDS

g. Iontophoresis activated DDS

h. Hydration-activated DDS

## 2. Chemical means

a. pH- activated DDS

b. Ion- activated DDS

c. Hydrolysis- activated DDS

## 3. Biochemical means

a. Enzyme- activated DDS

b. Biochemical- activated DDS

# THANK YOU