CONTROLLED DRUG DELIVERY SYSTEMS- GENERAL INTRODUCTION NDDS-VII SEMESTER

Dr. GarimaJoshi

Assistant Professor, Pharmacy, MLSU

Drug Delivery

- Drug delivery is the method of administering pharmaceutical compound to achieve a therapeutic effect in humans or animals.
- drug delivery can be done through various routes-

  the oral (through the mouth), topical (skin), trans-mucosal (nasal, buccal, sublingual, vaginal, ocular,rectal), parenteral(injection into systemic circulation) and inhalation routes.

- The drug delivery system can further be divided into two main types: 1. Conventional drug delivery system. 2. Novel drug delivery system
- The conventional dosage forms provide drug release immediately and it causes fluctuation of drug level in blood depending upon dosage form.
- Therefore to maintain the drug concentration within therapeutically effective range need novel drug delivery system(NDDS).
- NDDS is a combination of advanced techniques and newer dosage form with controlled/sustained drug release to target the at specific site.

Controlled drug delivery vs Conventional drug delivery

Conventional drug delivery

- Periodic administration
- High concentration can lead to undesirable effects
- Low concentrations can be ineffective
- Inconvenient
- No targeting

Controlled drug delivery

- Drug concentration rise quickly to effective level.
- Effective concentration is maintained for longer duration

Sustained release drug delivery system

☐ sustained release are drug delivery system that achieve slow release of drug over an extended period of time after administration of single dose.

☐ In other words, the drug release is simply extended in time i.e. the rate and duration are not designed to achieve a particular profile. Sustained release- steadily over a long period of time

Controlled Release Drug Delivery System

☐ Controlled release are drug delivery system which maintain constant level of drug in blood and tissue for extended period of time. It implies A predictability and reproducibility in drug release kinetics

☐ In other words, the rate and duration are designed to achieve A desired concentration.

Controlled release drug delivery system is a way of designing and formulating a medicine so that the release of drug from it occur in a controlled manner, desirable manner.

Advantages SR and CRDDS

- Improve absorption, utilization and there by enhancing bioavailability.
- Decreased local and systemic side effects reduced gastrointestinal irritation.
- Reduction in dosing frequency.
- Better patient acceptance and compliance.
- Reduced fluctuations in circulating drug levels.
- Reduction in the health care cost.
- Bioavailability of certain drugs can be increased.

Disadvantages of SR and CRDDS

- Dose dumping.
- Dose adjustment is difficult.
- Patient education is required for successful therapy.
- Patient need to substantial additional information as to the proper used sustained release product.
- Poor IVIVC.
- Higher cost of single unit as compared to cost of single conventional unit.
- Stability problems.

Pharmaceutical approaches for designing SR/CRDDS

a) Dissolution controlled release system

These system are most commonly employed in the production of enteric dosage forms. Drug present in the system having high aqueous solubility and dissolution rate.

It is further divided into matrix and reservoir type dissolution controlled release system

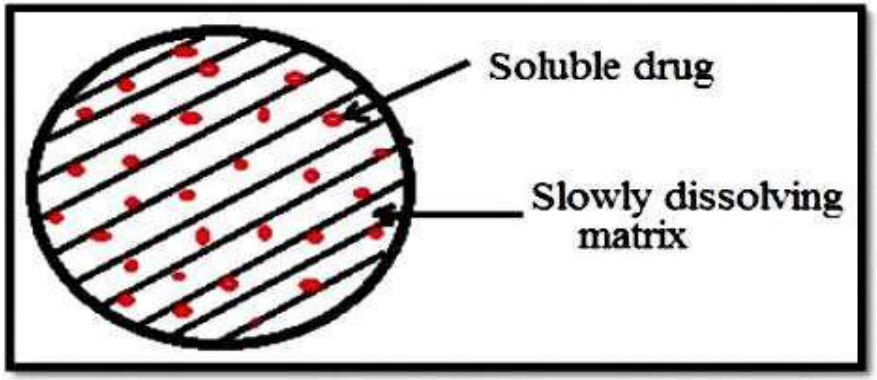
Dissolution controlled release system

• Control – Dissolution of the drug from the polymer matrix or encapsulated forms.
• The dissolution process at a steady state is described by Noyes Whitney equation:
dc / dt = k A/V (Cs – C)
dc / dt = (D/h) A (Cs – C)
where, dC/dt = dissolution rate
V = volume of the solution
k = dissolution rate constant
D = diffusion coefficient of drug through pores
h = thickness of the diffusion layer
A = surface area of the exposed solid
Cs = saturated solubility of the drug
C = conc. of drug in the bulk solution 42

➢Matrix system

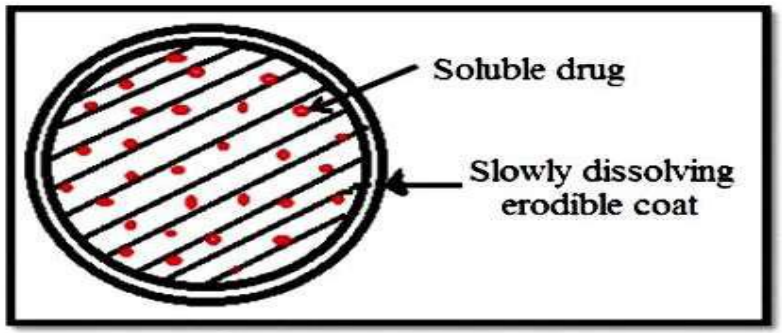
Matrix system are also called as monoliths since the drug is homogenously dispersed throughout a rate-controlling medium.

e.g. Bees wax, carnauba wax, hydrogenated castor oil.



➢Reservoir system

The drug particle are coated or encapsulated by one of the several microencapsulation Techniques with slowly dissolving materials like Cellulose, PEG, polymethacrylates, waxes, etc.



MATRIX type

- First order drug release.
- There are 2 methods:

1. Congealing &
2. Aqueous dispersion method

- The drug release is determined by dissolution rate of the polymer.
- Examples: 1. Dimetane extencaps 2. Dimetapp extentabs.

ENCAPSULATION type (Reservoir Type)

- The drug particle are coated or encapsulated by microencapsulation technique
- The pellets are filled in hard gelatin capsule, popularly called as 'spansules'.
- Once the coating material dissolves the entire drug inside the microcapsule is immediately available for dissolution and absorption.
- Here the drug release is determined by dissolution rate and thickness of polymer membrane which may range from 1 to 200µ

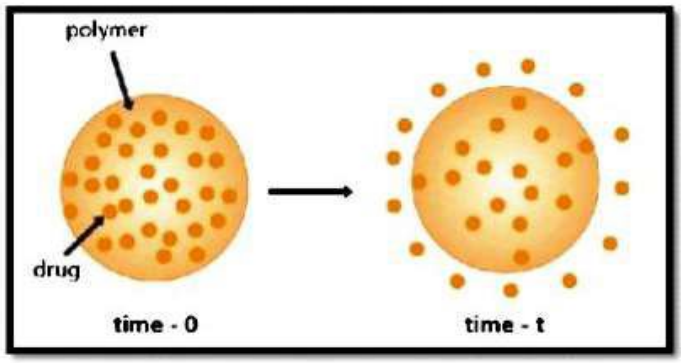
- it is also Called as Coating dissolution controlled system.
- Dissolution rate of coat depends upon stability & thickness of coating.
- One of the microencapsulation method is used.
- Examples: 1. Ornade spansules 2. Chlortrimeton Repetabs

B)Diffusion controlled release system

Movement of drug molecules from a region of a higher concentration to one of lower concentration.

➢Matrix system

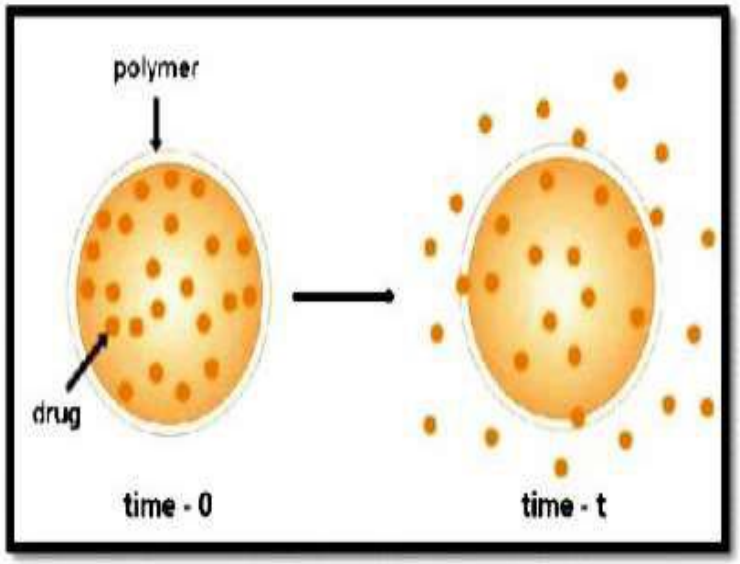
The drug is dispersed in an insoluble matrix of rigid nonswellable hydrophobic materials or swellable hydrophilic substances.



substances.

➢Reservoir system

These system are hollow containing an inner core of drug surrounded in a water insoluble polymer membrane.



INTRODUCTION

• This system is hollow containing an inner core of drug.

• The water insoluble polymeric material surrounds drug reservoir.

• The drug partitions into the membrane and exchanges with the surrounding
fluid by diffusion.

• The release drug from a reservoir device follows Fick's first law of diffusion.

$J = - D \, dc/dx$

Where, J = flux, amount/area-time

D = diffusion coefficient of drug in the polymer, area/time

dc/dx = change in conc. with respect to polymer distance

MATRIX Devices

• A matrix or monolithic device consists of an inert polymeric matrix in which a drug is uniformly distributed.

• Drugs can be dissolved in the matrix or the drugs can be present as a dispersion.

NOTE : Matrix may be HOMOGENEOUS or POROUS with water filled pores.

State of presentation of this form affects the various release patterns:

1. Dissolved drug (Fick’s Second law)
2. Dispersed drug (Fick’s First law)
3. Porous matrix (Higuchi’s theory for porous form)
4. Hydrophilic matrix (gelation & diffusion)

MATRIX Devices

• Rigid Matrix Diffusion

 Materials used are insoluble plastics such as PVP & fatty acids.

• Swellable Matrix Diffusion

1. Also called as Glassy hydrogels.Popular for sustaining the release of highly water soluble drugs.

2. Materials used are hydrophilic gums.

Examples : Natural- Guar gum, Tragacanth. Semisynthetic -HPMC, CMC, Xanthum gum. Synthetic -Polyacrilamides.

• Examples: Glucotrol XL, Procardia XL

RESERVOIR Devices

• The drug core is encased by a water-insoluble polymeric materials.

• The mesh (i.e., the space between macromolecular chains) of these polymers, through which drug penetrates or diffuses after partitioning, is of MOLECULAR LEVEL.

• The rate of drug release is dependent on the rate of drug diffusion but not on the rate of dissolution.

• In short, mass transport phenomena at molecular level occurs.

• Examples: Nico-400, Nitro-Bid

Methods of Prep. (RESERVOIR Devices)

- Mostly it involves :
  - o Coated Beads/Pellets
  - o Microencapsulation

Coated Beads/Pellets (RESERVOIR Devices)

- BEADS/PELLETS

Coating of drug solution onto preformed cores.

Covering of core by an insoluble (but permeable coat).

NOTE: Pan coating or air-suspension technique is generally used for coating.

NOTE: Pore forming additives may be added to the coating solution

Microencapsulation (RESERVOIR Devices)

- This technique used to encapsulate small particles of drug, solution of drug, or even gases in a coat (usually a polymer coat).
- Generally, any method that can induce a polymer barrier to deposit on the surface of a liquid droplet or a solid surface can be used to form microcapsules.

Design considerations of controlled release

- Route of drug delivery
- Target site
- Patient condition
- Polymer consideration- Glass transition temperature, Diffusion characteristics, compatibility, ease of formulation, fabrication
- Drug considerations-Physicochemical properties, stability, solubility, partitioning, charge protein binding

c) Ions Exchange Based SR/CR Formulations:

Ion-exchange systems generally use resins composed of water insoluble cross-linked polymers. These polymers contain salt-forming functional groups in repeating positions on the polymer chain. The drug is bound to the resin and released by exchanging with appropriately charged ions in contact with the ion-exchange groups

d) Dissolution & Diffusion Controlled Release System:

Drug is encapsulated in partially soluble membrane, pores are created due to soluble parts of coating film which permits entry of aqueous medium into core and drug dissolution starts by diffusion of dissolved drug out of system. Mixture of water soluble PVP and water insoluble ethyl cellulose is used for this purpose.

Osmotic Pressure Based SR/CR Formulations:

In this system, the flow of liquid into the release unit driven by a difference in osmotic pressure between the inside and the outside of the release unit is used as the release-controlling process.

Water penetration/Osmotic Pressure Controlled NDDS :

Drug may be osmotically active or drug may be combined with osmotically active salts like NaCl.