CONTROLLED DRUG DELIVERY SYSTEM

CONTENT: Introduction, Terminology/definitions, Rationale, Advantages, Disadvantages, Selection of Drug Candidates, Approaches to Design controlled Release Formulation, Physicochemical and Biologicalroperties.

INTRODUCTION

Controlled drug delivery system is one which delivers the drug at predetermined rate for locally or systematically for specified period of time**.**

TERMINOLOGY:

1.IMMEDIATE RELEASE DOSAGE FORM: It is also called as conventional dosage form. The dosage form release the drug present in the administration to achieve rapid systemic absorption.

2.MODIFIED RELEASE DOSAGE FORM:

The dosage form in which the rate of release of drug would takes place different from conventional type called as modified release dosage form.

3.SPECIFIC TARGETING:

This system refers to targeting the release of drug straight to a particular biological location in this case the target is adjacent or in the disease organ or tissue.

4.RECEPTOR TARGETING:

This system refers to targeting a specific biological receptor in this case the target is specific receptor for drug within an organ or tissue.

5.DELAYED RELEASE DOSAGE FORM: When the dosage form does not release the drug immediately after administration like immediate release dosage form but release drug in a predetermined time.

6.EXTENDED-RELEASE DOSAGE FORM:

If the dosage form reduces the frequency of dose at least by two-fold as compared to the frequency of administration of immediate release dosage form.

7.SUSTAINED RELEASE DOSAGE FORM:

If the drug exhibits a predetermined rate in order to maintain an approx. constant drug in concentration in body over a prolonged period.

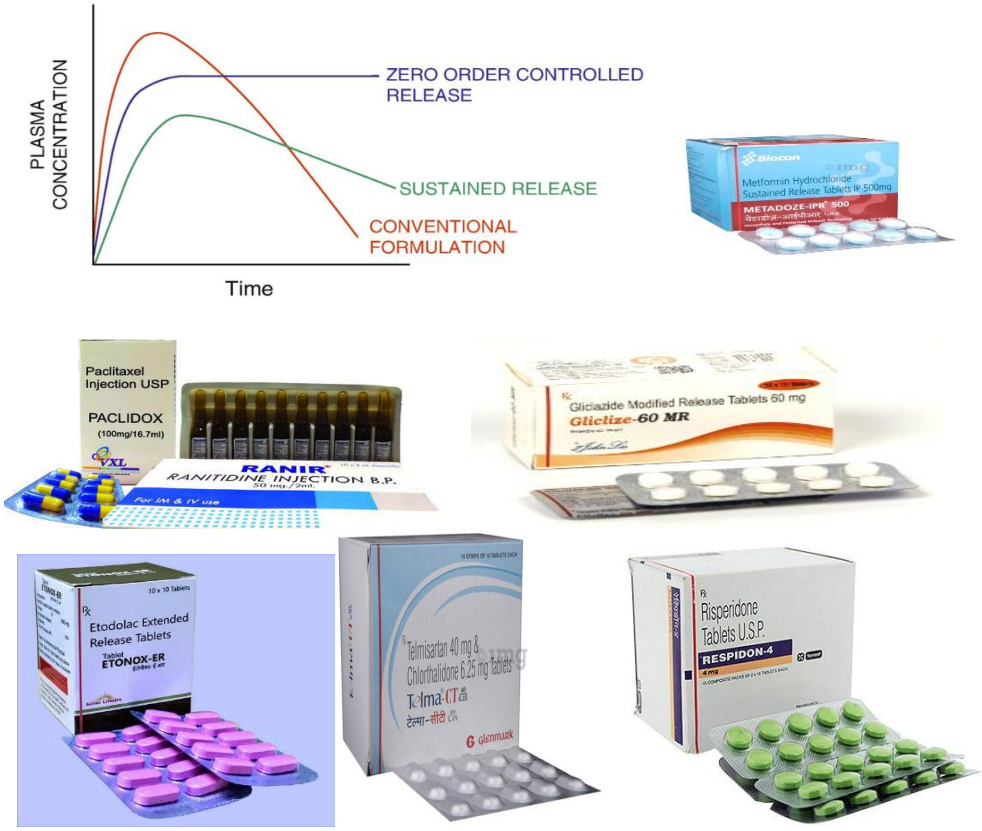


Fig.1-list of controlled drug delivery system.

RATIONALE:

The rationale of CDDS is to alter the pharmacokinetic and pharmacodynamics of pharmacologically active moieties by using NDDS or modifying the molecular structure or physiological parameters inherent in a selection of route of administration.

Primary objective is to ensure safety and to improve efficacy of drug as well as patient compliance.

For conventional dosage form only the dose and dosing interval can vary for each drug.

There exist therapeutic window of plasma cons below which therapeutic effect is insufficient and above which desirable or toxic effects are elicited**.**

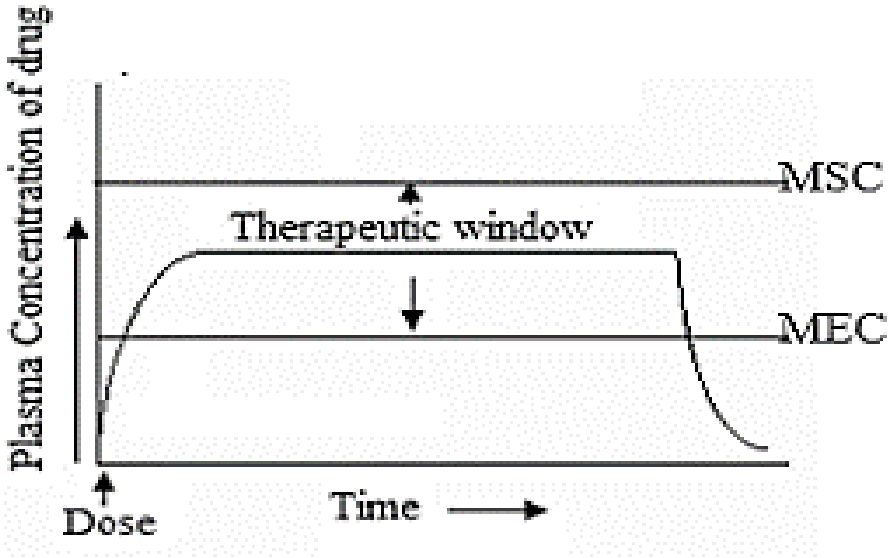


Fig.2- rationale plasma conc vs time.

ADVANTAGES:

1. Better patient compliance.
2. Reduce dose frequency.
3. Reduction of side effect.
4. Improve stability.
5. Improve bioavailability.
6. Minimum drug accumulation on chronic usage.

DISADVANTAGES:

1. Delayed onset of drug action.
2. Increase first pass metabolism.
3. Dose dumping.
4. High cost of drug.
5. Not used in unconscious patient.
6. Need of additional patient education.

SELECTION OF DRUG PRODUCTS:

Selection of drug candidates or characteristics that may make a drug unsuitable for controlled release dosage form-

- Short elimination half-life.
- Long elimination half life
- Narrow therapeutic index.
- Poor absorption.
- Extensive first pass metabolism.
- Active absorption**.**
- Slow metabolism**.**

APPROACHES TO DESIGN CONTROLLED RELEASE FORMULATION BASED ON THE FOLLOWINGS:

❖ DIFFUSION CONTROLLED SYSTEM:

No energy required. Drug diffuses from increase conc to decrease conc until equilibrium is attained and is directly proportional to conc gradient across membrane.

1) RESERVIOR TYPE DEVICE

a) Ficks law of diffusion:

Rate of drug released is explaind by

$$dMt/dt = DAK(c)/d$$

2) MATRIX DIFFUSION CONTROLLED SYSTEM:

i) SWELLEBLE POLYMER MATRIX:

It is also called as glassy hydrogels. Eg – lontab tablet.

ii) NON-SWELLEBLE POLYMER MATRIX :

It is also called as rigid matrix diffusion.

Higuchi equation: M= (DsCaP/T(2C0-PCa)t)1/2

M=KHt1/2.

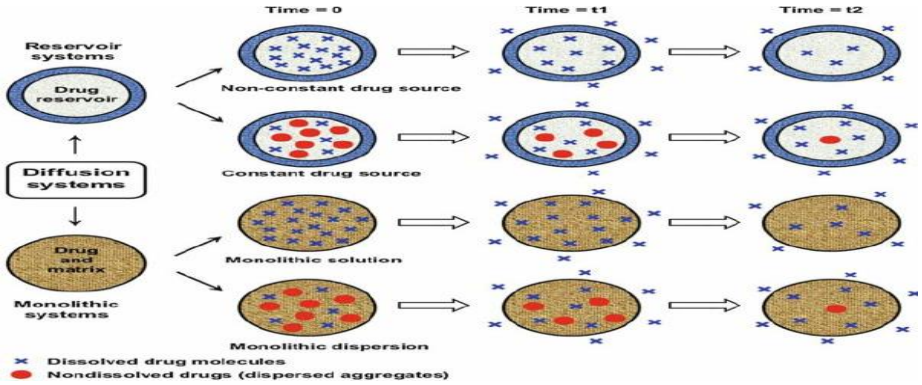


Fig.3- diffusion controlled released system.

❖ DISSOLUTION CONTROLLED SYSTEM:

- Noyes Whitney equation: dc/dt =K(Cs-Cb)
- Modified noyes whitney equation:

  (Dc/dt)d = DAKw/o (Cs - Cb)/Vh.

a) ENCAPSULATED DELIVERY SYSTEM:

Dissolution rate of coat depend upon stability and thickness of coating.

b) MATRIX DISSOLUTION SYSTEM:

It is also called as monolith dissociation controlled System.

Controlled dissolution performed by-

a) Altering porosity of table
b) Decrease its wettability
c) Dissolving at slower rate

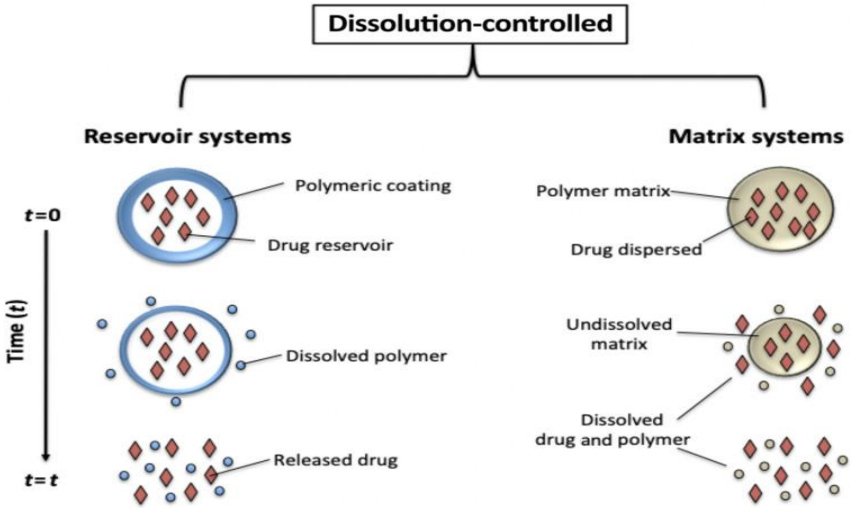
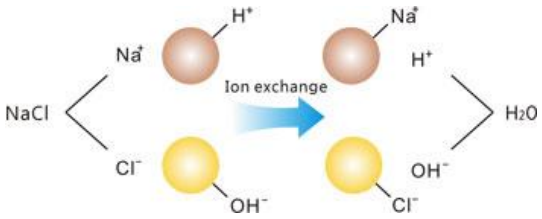


Fig.4-dissolution controlled release system.

❖ ION EXCHANGE RESINS:

1) Cation
2) Anion



A major drawback of controlled release system is dose dumping, resulting in increased risk of toxicity. Because there is better drug retaining property drug resinates prevent dose dumping.

PHYSICOCHEMICAL AND BIOLOGICAL PROPERTIES OF DRUG AS FOLLOWS-

Properties	Desired features
PHYSICOCHEMICAL	
1) Molecular size	<1000 Dalton
2) Aqueous solubility	microgram/ml for PH 1 to 7.2
3) Partition coefficient	High
4) Dissociation constant	Pka>2.5(Acidic) Pka<11.0(Basic)
5) Ionization at physiological PH	Not more than 95%
BIOLOGICAL	
6) Absorption rate	High
7) Elimination rate	2-6 hr
8) Metabolism rate	Not to high
9) Dosage form index	One
10) Therapeutic index	wide

MARKETED PREPARATIONS-

Product	Company	Drug	Therapeutic Category	Formulation type
Losec MUPS	Astra Zeneca	Omerprazole Magnesium	Antiulcer	Antiulcer
Esomeprazole	Astra Zeneca	Esomeprazole Magnesium	Antiulcer	Antiulcer
Troprol XL	Astra Zeneca	Metoprolol tartrate	Antihypertensive	Extended release
Prevacid SoluTab	Takeda	Lansoprazole	Antiulcer	Delayed release Orodispersible tablet
Theodur	Key	Theophylline	Antiasthmatic	Extended release

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