



A Review: Formulation and Evaluation of Sustained Release Tablet

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Abstract

With constant release, side effects from medicinal medications can be minimized by minimizing fluctuations in the medicinal concentration in the body[3]. A dosage of medication form designed to delay the medicinal agent discharge so that it stays in the circulation throughout the body for an prolonged duration and maintains its plasma profile throughout time is referred to extended release. Tablets with constant release medication administration method have been created to gradually release the medication within. It manages the rate at which medications are released through a variety of ways[1]. The following formulation techniques have been used: matrix erosion, drug diffusion, and drug dissolution. The various aspects of sustained release tablets are the subject of the current review effort.[9]

Keywords: Sustained release, Controlled release, Classification, Drug design, Polymer

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I. Introduction

Treating diseases is the main objective of drug administration. Delivering a medicine in its pure form is never a good idea[5]. Rather, you should formulate it into a dosage form that enables you to maintain an eye on the drug's onset, intensity, and duration of effect. If a regulated medication administration method can deliver the medicine for a predetermined period with the least amount of toxicity, and more effectiveness, then it is ideal[7]. Novel and creative drug delivery systems are currently quickly replacing conventional drug dose forms. Drug administration by mouth is the most popular and useful mode of medication administration due to its high rate of patient adherence, cost effectiveness, absence of sterility limitations[6]. Oral medication administration has historically been the most common way to administer drugs due to its better potency, greater precision in dosing, convenience of production, and preference for tablets as an oral dosage form. Oral delivery accounts for almost half of the medication products available in the market[10]. The industry offers a wide variety of tablet varieties, varying from straightforward instant release formulations to intricate sustained release or modified release dosage forms. By gently releasing the medication, a sustained release drug delivery method aimed to maintain plasma drug levels[3]. Drug administration by mouth is the most popular and useful mode of medication administration due to its high rate of patient adherence, cost effectiveness, absence of sterility limitations, adaptability in dosage form design and simplicity in production. Oral medication administration has historically been the most widely used method of medication administration because its better potency, greater precision in dosing, convenience of production, and preference for tablets as an oral dosage form. Oral delivery accounts for almost half of the medication products available in the market[9]. The industry offers a wide variety of tablet varieties, varying from straightforward instant release formulations to intricate sustained release or modified release dosage forms. By gently releasing the medication, a sustained release drug delivery method aimed to maintain plasma drug levels[4]. By gently releasing the medication, a sustained release drug delivery method aimed to maintain plasma drug levels. For medications with a shorter half-life, the sustained release

drug delivery method is appropriate. One practical method for introducing prolonged release medication therapy is through matrix tablets since they are the most reasonably priced kind of sustained and controlled release solid dose forms[3].

Overview of drugs:-

DRUG USED	GROUP	TECHNIQUE APPLIED	POLYMER USE
Zidovudine	Anti-viral	Direct Compression	HPMC-K4M
Aspirin	Anti-inflammatory	Direct Compression	EudragitRS100
Naproxen	Morphine antagonist	Wet Compression	HPMC, CMC
Acarbose	Anti-diabetic	Direct Compression	HPMC, Eudragit
Ranitidine HCL	H2 antagonist	Wet Compression	Chitoson, Carbopol-940
Phenytoin Na	Anti-epileptic	Direct Compression	Tragacanth, Guar gum

Justification for SRDDS development

1. SRDDS formulations reduce the frequency of dose, and sustained release ensures that a medication is accessible during the course of the treatment at the site of action, enhancing the drug's clinical efficacy.
2. To lower treatment costs by lowering the number of doses needed.
3. To reduce toxicity from overdosing, which is frequently the case with typical dose forms.
4. Higher levels time period of action of a medication with a brief half-life.

Terms Associated with SRDDS

Delayed release

Drugs are dosed intermittently and repeatedly in delayed release systems. One or more dose forms of immediate-releasing units make up these system[6]. The basis for the release delay could be time or as a result of environmental factors, such as the pH of the gastrointestinal tract prolonged release

Prolonged release

a) Extended discharge

Extended discharge described as any alteration to a medicine or dose form that increases the duration of the drug's therapeutic effect.

a) Release under control

The mechanism for giving drugs is intended to administer the medication over a prolonged length of time at a predetermined pace[6]. While SRDDS operates on first order release⁵, this system operates on zero order release, which is independent of the drug's initial concentration.

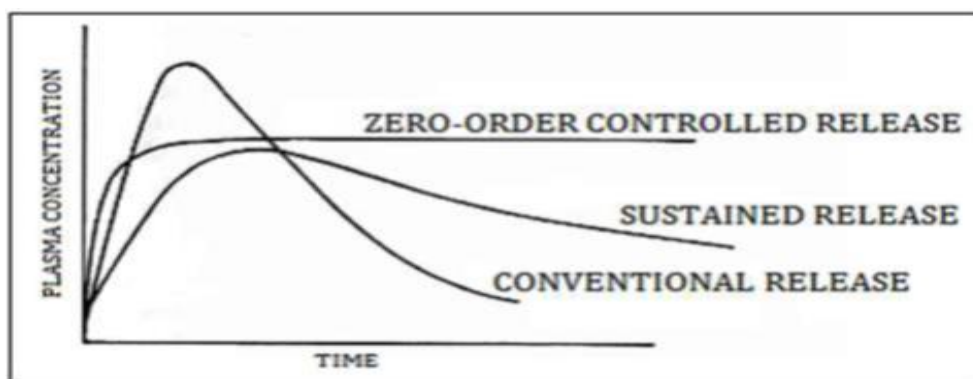


Figure 1. Rehabilitation range of various blood dosage types

Continued release matrix tablet benefits include:

- Patient compliance.
- A decrease in the "see-saw" variation.
- Treatment deficiencies improved.

The sustained release matrix tablet's drawbacks

- Diminished potentiality of modifying the dosage.
- The price is higher than for a customary dose form.
- Boost the possibility of initial pass metabolic process.
- Appropriate medicine requires patient instruction administration.
- It is possible for systemic availability to decrease.
- Dose dumping.

Parameters

Chart 1. Physicochemical factors in medication selection

Specification	Standards
Molecular weight	Not quite 600 Dalton
Soluble in water	Over 0.1mg/ml
Coefficient of partition	One to two
Constant dissociation	Medication that are acidic, $pka > 2.5$ alkaline medications, $pka < 11.0$
method of absorption	Inert
Consistency in GI environment	Stable at pH levels in the intestine
Ionization at the pH of physiology	At most 95%

Table 2. Pharmacokinetic factors in medication choice

Specification	Standards
50% life of elimination	2 to 6 hours
Total bioavailability	>75%
Rate of absorption constant	Elevated
Metabolic rate	Aproprately high
Overall clearance	Dosage shouldn't be factor
Medicinal concentration	Reduced Vd and lower C _{ss}

Table 3 Matrix tablet classification according to matrix porosity

Sort	Size of pores	Mechanism at play
large-scale porous structure	0.1-1 μm	Diffusion by a matrix
tiny permeable structure	50-200Å	Diffusion by matrix pore
non-permeable structure	-----	Diffusion by mesh networks

Formulation: - 1 .The Diffusion Sustained System: This system illustrates how medication molecules diffuse from a more focused area to a less focused one.

$$J = - D \frac{dc}{dx}$$

D is the A/t diffusion coefficient.

The formula $\frac{dm}{dt} = ADK.C$

A = Surface area

K = the medication's partition coefficient between its membrane and core.

L= Length of diffusion path, or, in the best scenario, the coat's thickness.

C = Difference in concentration in between the membrane

i) System of diffusion reservoirs:

This technology makes use of a polymeric material that is insoluble in water to cover the drug's core. The medication will split into the membrane and swap out the tablet or particle with the surrounding fluid[4] .Extra

medicine will interact with the surrounding materials and leak into the polymer, spreading to the edges. The diffusion process is responsible for the drug's release[7].

ii) Type of Diffusion Matrix:

A solid medication scattered throughout unsolvable matrix, & Usually, drug's removing rate depends on on affecting the rates of solid dissolution and drug diffusion. Higuchi created a suitable medication release equation[7].

$$Q = D/T [2A - C_s] C_s t^{1/2}$$

Where,

C_s = solubility medication into remove the media.

T = Extensiveness the grid.

A = Quantity medication in the pill, grams per milliliter

The following equation can be used to get the release rate.:-

Release rate: $[C_1 - C_2] = AD/L$ Whereas

A = Area

D = Coefficient of diffusion

C₁ = Concentration of drugs in the core

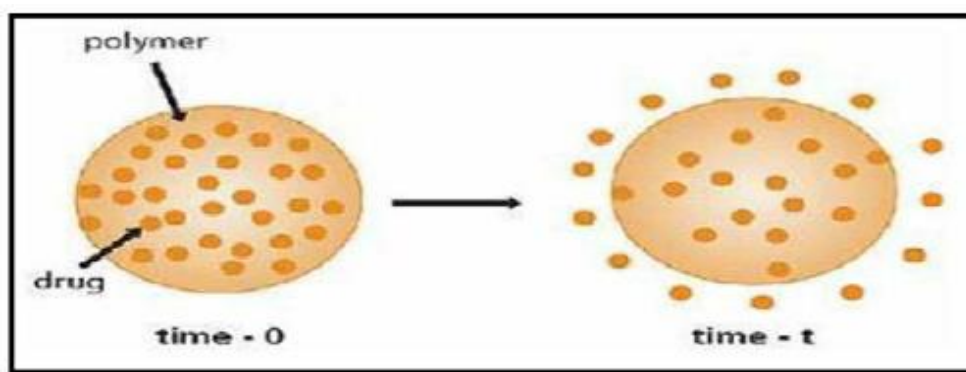


Fig. Diffusion sustain medication release represented diagrammatically using a matrix system

2.Systems for persistent dissolution:

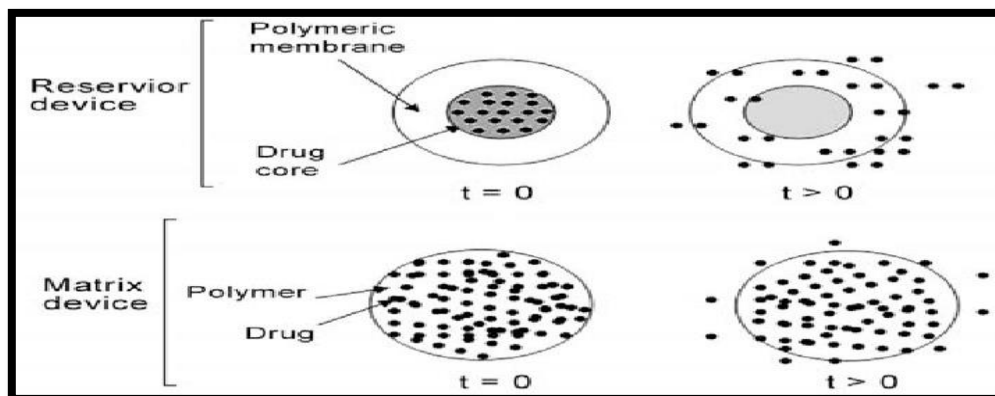
Drugs that dissolve gradually remain stable by nature, but drugs that dissolve quickly are reduced by employing the appropriate salt or derivative production to make them easier to dissolve in water[2]. Enteric coated dosage forms are typically manufactured using these techniques. For the purpose of shielding the stomach from medications like A coating of aspirin is placed; it dissolves in natural or alkaline media[2]. These prevents the medicine from releasing from the dose form until the intestine's higher pH is reached[5].

a) System of soluble reservoirs:

In such approach, a medicine has an erodible coating on it that dissolves gradually in the contents of the GI tract. Drug layers are alternated using rate-control coatings[10].

b) Soluble matrix system:

This system consists of a drug-impregnated tablet or sphere that will be slowly erosion.



3. Ion exchange methods:

Using ion exchange resin is a desirable way to distribute drugs continuously because it has a drug release feature[9]. Relies mostly regarding the ionic setting of the resins that contain drugs and are less susceptible to external factors like the pH concentrations of enzymes at the site of absorption. With this method, release of zero order kinetics is able to be fulfilled achieved. A more effective delivery method for a medication that is extremely vulnerable to enzymatic breakdown is an ion exchange-based device. resin for ion exchange which fall into one of the following categories[6]:

a) anion exchange resin;

b) cation exchange resin:

Polystyrene polymers with either acidic functional groups or phenolic carboxylic groups that are phenolic are frequently observed in cationic exchange resins.

Anion exchange resin: Contains a fundamental functional group that can be used to remove anions from solutions that are acidic[6]. Ion exchange resins are used to maintain the effects of drugs by combining the right resin with drugs that have a negative or positive charge to produce insoluble poly salts[6].

4. pH-Independent Formulations:

Unwanted characteristics of the oral mode of administration result in an extended transit time[5]. To assist in keeping the pH steady and produce amino acid salts, citric acid, phthalic acid, phosphoric acid, or tartaric acid that have been mixed into combination are examples for pH independent medicine removing buffers. The process of creating a formulation for buffered continuous release typically involves combining an acidic or basic medication with adding one or more granulating agents to the mixture with the using the appropriate pharmaceutical excipients and adding a film-forming polymer to the mixture that permeates intestinal fluid^[4]. The buffering chemicals bring the fluid within to an appropriate constant pH when gastrointestinal fluid passes across the membrane, resulting in a steady pace of release of medication[2].

5. Adapted density formulas:

These have a restricted application if the dosage form's contents are not entirely discharged into the GI tract^[1]. In order to do this, different Tools to extend the medication delivery system's stay throughout the digestive system have been developed[3].

Elevated density method:

With these method, the pellet density should be at least 1-4 gm/cm³, which is bigger as compare to the density of typical stomach[8]. A heavy core can be coated with a medicine in this manner, or it can be combined with massive inert matter such as iron powder, titanium dioxide, as well as zinc oxide, and barium sulfate[5].

Low-density method:

Pop rice, popcorn, and globular shells whose densities are less than those of gastric fluid are all used as carriers of drugs for perpetual discharge[2]. Subsequently, a combination of medication and polymer, such as hydroxypropyl cellulose and ethyl cellulose, is applied to the undercoated shell. The finished product therefore slowly releases medication while floating in the stomach fluid with longer period[5].

Evaluation:

Prior to leaving a continuous release product onto the market, it is imperative to ensure the product's strength, safety, stability, and dependability through in-vitro and in analysis in vivo and the relationship between the two[9].

Plenty of people have created articles about analysis of protocols and parameters for formulations of sustained release.

1. **Weight Variation:** Each of the twenty tablets was weighed separately, and the average weight of the pills was next ascertained.

2. **Hardness:** With a Monsanto hardness tester in hand, a hardness test was performed values were averaged across tablets from every batch.

3. **Friability:** The tablets' friability was tested using the Roche friabilator, which spins for four minutes at a speed of 25 rpm.

4. **Thickness:** A micrometer screw gauge was used to measure the tablet thicknesses.

5. **Content Uniformity:** The calibration curve approach was used to determine the drug's quantity using a UV Visible spectrophotometer.

In vitro dissolution studies:

Drug release research in vitro dissolution studies is often decided in the Rotating Paddles device. Buffer is primarily employed as a dissolving medium[6]. The bath's temperature is kept at 37 degrees Celsius, and a sample of the drug-releasing dissolving media must be taken and replaced on a regular basis in the same amount. An ultraviolet photometer may be utilised to determine the drug's release levels[2].

A Stability Analysis:

Determine of Short-Term Stability: A short-term stability analysis of the ideal batch was conducted to find out how storage affected the in vitro release profile.

In vivo dissolution studies:

In Vivo Techniques Following attainment of a suitable the creation of an in-vitro in-vivo association. The many in-vivo assessment techniques include: Clinical reaction Data on blood levels, investigations on nutrition analysis and urine excretion research on radioactive tracer technology and toxicity[2].

II. Summary:

This review paper focused on the ingredients in matrix pills that last, their benefits, disadvantages. The above explanation concludes that matrix tablets can be used to address issues with patient adherence and dose form effectiveness that stem from the incapacity of conventional dosage forms to generate the necessary therapeutic response. The benefits include cost-effectiveness and the ability to take one dose at a time or every day. For prolonged release matrix tablets, leading to an refinement of the dosage form's layout.

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