

REVIEW ARTICLE

Oral Sustained Release Tablets: An Overview with a Special Emphasis on Matrix Tablet

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ABSTRACT

Among the various routes of drug delivery, oral route is the most preferred route. But conventional dosage form offers a few limitations which could be resolved by modifying the existing dosage form. Sustained and controlled drug delivery system helps in the maintenance of constant plasma drug concentration and retards the release rate of drug, thereby extending the duration of action. There are various formulation strategies for sustained-release tablets, among which matrix tablet serves as an important tool. Hence the problem like poor patient compliance, multiple dosing, see-saw fluctuations can be easily minimized. Matrix tablets can be formulated by either direct compression or wet granulation method by using a variety of hydrophilic or hydrophobic polymers. The rate of drug release from the matrix is primarily governed by rate and extent of water penetration, swelling of polymer, dissolution, and diffusion of the drug. Thus, a sustained release matrix tablet can offer better patient compliance and could be quite helpful in the treatment of chronic diseases. The present article concentrates on oral sustained-release tablets with a special emphasis on matrix tablets.

Keywords: Conventional tablet, Sustained-release, Controlled release, Polymer, Matrix tablet, Recent advancements.

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INTRODUCTION

The important role of a novel drug delivery system that improves the therapeutic effectiveness of incorporated drugs by providing sustained, controlled delivery and or targeting the drug to the desired site. Any drug delivery system aims to provide a therapeutic amount of drug to the specific site in the body to achieve promptly and then maintain the desired drug concentration.^[1] The design of oral sustained release delivery systems is subjected to several interrelated variables of considerable importance, such as the type of delivery system, the disease being treated, the patient, the length of therapy, and the properties of the drug. Sustain release system includes any drug delivery systems that achieve slow release of a drug over a prolonged period.^[2] Matrix tablets are considered to be the commercially feasible sustained action dosage forms that involve the least processing variables, utilize the conventional facilities and accommodate large doses of drug. There remains an interest in developing novel formulations that allow for sustained the drug release using readily available, inexpensive excipient by matrix-based formulation. During the last two decades, there has been a remarkable increase in interest in sustained release drug delivery system. This has been due to various factors like the prohibitive cost of developing new drug entities, expiration of existing international patents, the discovery of new polymeric materials suitable for prolonging the drug release, and the improvement in therapeutic efficiency and safety achieved by these delivery systems. Nowadays, the technology of sustained release is also being applied to veterinary products.^[3]

Gastrointestinal Tract (GIT)

The human gastrointestinal tract, or GI tract, or GIT is an organ system responsible for consuming and digesting foodstuffs, absorbing nutrients, and expelling waste. The tract consists of the stomach and intestines and is split into the upper and lower gastrointestinal tracts. The GI tract includes all structures across the mouth and the anus. On the other hand, the digestive system is a broader term that comprises other structures, including the digestive organs. The GI tract releases hormones to help regulate

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the digestive process. These hormones, including gastrin, secretin, cholecystokinin, and ghrelin. The track is divided into upper and lower tracts, and the intestines small and large parts:

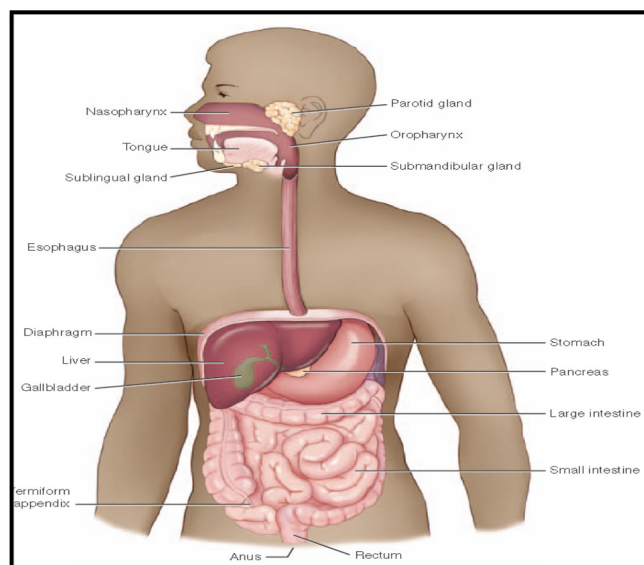


Figure 1.1 (a): Digestive systems

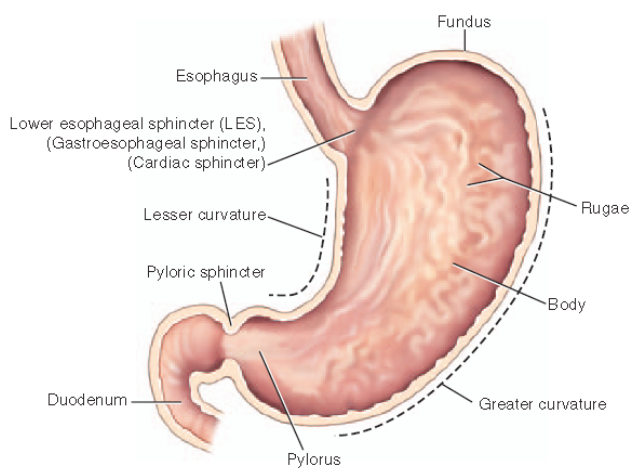


Figure 1.1 (b): Upper gastrointestinal tract (stomach)

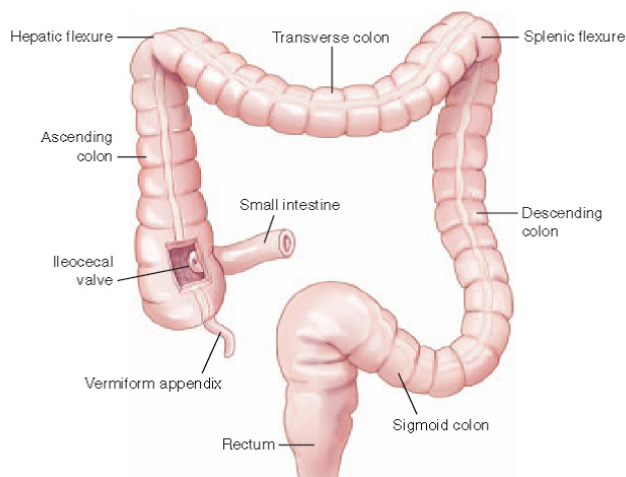


Figure 1.1 (c): Lower gastrointestinal tract (Intestine)^[4]

Upper Gastrointestinal Tract

The upper gastrointestinal tract composed of the esophagus, stomach, and duodenum. The exact demarcation across the upper and lower tracts is the suspensory ligament of the duodenum (also known as the Ligament of Treitz). This delineates the embryonic borders across the foregut and midgut and is also the division commonly used by clinicians to describe gastrointestinal bleeding as being of “upper” or “lower” origin.

Lower Gastrointestinal Tract

The lower gastrointestinal tract comprises most of the small intestine and all of the large intestine. In human anatomy, the intestine (or bowel, hose, or gut) is the segment of the gastrointestinal tract extending from the pyloric sphincter of the stomach to the anus and, in humans and other mammals, consists of two segments, the small intestine, and then large intestine. In humans, the small intestine is more likely subdivided into the duodenum, jejunum, and ileum while the large intestine is subdivided into the cecum, colon, rectum, and anal canal.

Principle of Sustained Release Drug Delivery

The conventional dosage forms release their active ingredients into an absorption pool immediately. This is illustrated in the following simple kinetic scheme in Figure 2.

The absorption pool represents a solution of the drug at the site of absorption, K_r , K_a , and K_e - first-order rate- constant for drug release, absorption, and overall elimination, respectively. Immediate drug release from a conventional dosage form implies that $K_r \gg K_a$. For non-immediate release dosage forms, $K_r \ll K_a$, i.e., the release of drug from the dosage form is the rate-limiting step. The drug release from the dosage form should follow zero-order kinetics, as shown by the following equation:

$$K_r = \text{Rate In} = \text{Rate Out} = K_e C_d V_d$$

Where, K_r : Zero-order rate constant for drug release- Amount/ time, K_e : First-order rate constant for overall drug elimination-time, C_d : Desired drug level in the body – amount/volume, and V_d : volume space in which the drug is distributed in liter.^[5]

The Following are the Rationale of Developing Sustained Release Matrix Drug Delivery System

- To extend the duration of action of the drug.
- To reduce the frequency of dosing.
- To minimize the fluctuations in the plasma level.
- Improved drug utilization.
- Less adverse effects.^[6]

Advantages of Sustained Release Matrix Drug Delivery System

- The frequency of drug administration is reduced.
- Patient compliance can be improved.
- Drug administration can be made more convenient as well.
- The blood level oscillation characteristic of multiple dosing of conventional dosage forms is reduced.
- Better control of drug absorption can be attained since the high blood level peaks that may be observed after the administration of a dose of a high availability drug can be reduced.
- The characteristic blood level variations due to multiple dosing of conventional dosage forms can be reduced.
- The total amount of drug administered can be reduced, thus: Maximizing availability with a minimum dose. Minimize or eliminate local side effects. Minimize or eliminate systemic side effects. Minimize drug accumulation with chronic dosing.
- Safety margins of high potency drugs can be increased, and the incidence of both local and systemic adverse side effects can be reduced in sensitive patients.
- Economy.

Disadvantages of Sustained Release Matrix Drug Delivery System

- Probability of dose dumping.
- Reduced potential for dose adjustment.
- Cost of single unit higher than conventional dosage forms.
- Increase the potential for the first-pass metabolism.
- A requirement for additional patient education for proper medication.

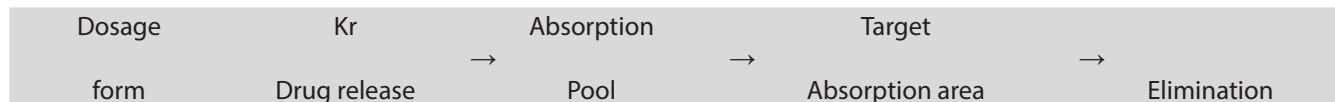


Figure 2: Schematic representation of the kinetics of sustained-release DDS

Table 1: Characteristics of drug unsuitable for peroral sustained-release forms:

Characteristic	Drugs
Not effectively absorbed in the lower intestine	Riboflavin, Ferrous salts
Absorbed and excreted rapidly short biological half-life < 1 hr	Penicillin G, Furosemide
Long biologic half-life (>12 hour.)	Diazepam, Phenytoin
Large dose required	> 1gm sulfonamide
Cumulative action and desirable side effect drug with low therapeutics indices	Phenobarbital, Digitoxin
Precise dosage titrated to individual is required	Anticoagulants, Cardiac glycosides ^[8]

- Decreased systemic availability in comparison to immediate release conventional dosage forms.
- Poor in vitro and in vivo correlation.^[7]

Criteria of Drug to be met to Formulate Sustained Release Dosage Forms

- Desirable half-life.
- High therapeutic index.
- Small dose.
- Desirable absorption and solubility characteristics.
- Desirable absorption window.
- First pass clearance.

Desirable Half-life

The half-life of a drug is an index of its residence time in the body. If the drug has a short half-life (less than 2 hours), the dosage form may contain a prohibitively large quantity of the drug. On the other hand, a drug with an elimination half-life of eight hours or more are sufficiently sustained in the body, when administered in conventional dosage form, and sustained release drug delivery system is generally not necessary in such cases. Ideally, the drug should have a half-life of 3-4 hours.

High Therapeutic Index

Drugs with low therapeutic index are unsuitable for incorporation in sustained-release formulations. If the system fails in the body, dose dumping may occur, leading to fatalities, eg. Digitoxin.

Small Dose

If the dose of a drug in the conventional dosage form is high, its suitability as a candidate for sustained release is seriously undermined. This is chiefly because the size of a unit dose sustained-release formulation would become too big, to administer without difficulty.

Desirable Absorption and Solubility Characteristics

Absorption of poorly water-soluble drug is often dissolution rate limited. Incorporating such Compounds into sustained-release formulations is therefore unrealistic and may reduce overall absorption efficiency.

Desirable Absorption Window

Certain drugs, when administered orally, are absorbed only from a specific part of the gastrointestinal tract. This part is referred to as the 'absorption window'. Drugs exhibiting an Absorption window like fluorouracil, thiazide diuretics, if formulated as sustained release dosage forms, are unsuitable.

First Pass Clearance

As discussed earlier in the disadvantages of a sustained delivery system, delivery of the drug to the body in desired concentrations is seriously hampered in case of drugs undergoing extensive

hepatic first-pass metabolism when administered in sustained release forms.^[9,10]

Classification of Matrix Tablets

Based on Retardant Material Used

Matrix tablets can be divided into 5 types.

• Hydrophobic Matrices (Plastic matrices)

In this method of obtaining sustained release from an oral dosage form, the drug is mixed with an inert or hydrophobic polymer and then compressed into a tablet. Sustained release is produced due to the fact that the dissolving drug has diffused through a network of channels that exist between compacted polymer particles. Examples of materials that have been used as inert or hydrophobic matrices include polyethylene, polyvinyl chloride, ethylcellulose, and acrylate polymers and their copolymers. The rate-controlling step in these formulations is liquid penetration into the matrix. The possible mechanism of release of drug in such type of tablets is diffusion. Such types of matrix tablets become inert in the presence of water and gastrointestinal fluid.^[11]

• Lipid Matrices

These matrices prepared by the lipid waxes and related materials. Drug release from such matrices occurs through both pore diffusion and erosion. Release characteristics are, therefore, more sensitive to digestive fluid composition than to totally insoluble polymer matrix. Carnuba wax, in combination with stearyl alcohol or stearic acid, has been utilized for a retardant base for many sustained-release formulations.^[12]

• Hydrophilic Matrices

Hydrophilic polymer matrix systems are widely used in oral controlled drug delivery because of their flexibility to obtain a desirable drug release profile, cost-effectiveness, and broad regulatory acceptance. A matrix is defined as a well-mixed composite of one or more drugs with a gelling agent (hydrophilic polymer). The polymers used in the preparation of hydrophilic matrices are divided into three broad groups.

Cellulose derivatives: Methylcellulose 400 and 4000 cps, hydroxyethylcellulose, hydroxypropylmethylcellulose (HPMC) 25, 100, 4000, and 15000 cps; and Sodium carboxymethyl-cellulose. Non-cellulose natural or semi-synthetic polymers: Agar-Agar; carob gum; alginates; molasses; polysaccharides of mannose and galactose, chitosan and modified starches. Polymers of acrylic acid: Carbopol-934, the most used variety.

• Biodegradable Matrices

These consist of the polymers which comprised of monomers linked to one another through functional groups and have unstable linkage in the backbone. They are biologically degraded or eroded by enzymes generated by surrounding living cells or by non-

enzymatic processes into oligomers and monomers that can be metabolized or excreted. Examples are natural polymers such as proteins and polysaccharides, modified natural polymers, synthetic polymers such as aliphatic poly (esters), and poly anhydrides.

• *Mineral Matrices*

These consist of polymers which are obtained from various species of seaweeds. An example is Alginic acid, which is a hydrophilic carbohydrate obtained from species of brown seaweeds (Phaeophyceae) by the use of dilute alkali.^[13]

On the Basis of Porosity of Matrix: Matrix tablets can be divided into 3 types

• *Macroporous Systems*

In such systems, the diffusion of the drug occurs through pores of a matrix, which are of size range 0.1 to 1 μm . This pore size is larger than the diffusion molecule size.

• *Microporous System*

Diffusion in this type of system occurs essentially through pores. For microporous systems, pore size ranges between 50–200 \AA , which is slightly larger than diffusant molecules size.

• *Non-porous System*

Non-porous systems have no pores, and the molecules diffuse through the network meshes. In this case, only the polymeric phase exists, and no pore phase is present.^[14,15]

Polymers used in the Matrix

The polymers most widely used in preparing matrix systems include both hydrophilic and hydrophobic polymers.

Hydrophilic Polymers

Hydroxyl propyl methylcellulose (HPMC), hydroxyl propyl cellulose(HPC), hydroxyl ethyl cellulose (HEC), Xanthan gum, Sodium alginate, poly(ethylene oxide), and cross-linked homopolymers and copolymers of acrylic acid.

Hydrophobic Polymers

This usually includes waxes and water-insoluble polymers in their formulation.

Waxes

Carnauba wax, beeswax, candelilla wax, microcrystalline wax, ozokerite wax, paraffin waxes, and low molecular weight polyethylene.

Insoluble Polymers

Ammoniomethacrylate co-polymers (Eudragit RL100, PO, RS100, PO), ethylcellulose, cellulose acetate butyrate, cellulose acetate propionate and latex dispersion of methacrylic ester copolymers.^[16]

Characteristics of an Ideal Polymer

- It should be versatile and possess a wide range of mechanical, physical, chemical properties.
- It should be non-toxic and have good mechanical strength and should be easily administered
- It should be inexpensive and easy to fabricate.
- It should be inert to host tissue and compatible with the environment.

Criteria Followed in Polymer Selection

- The polymer should be soluble and easy to synthesis.
- It should have finite molecular weight.
- It should be compatible with the biological environment.
- It should be biodegradable.
- It should provide good drug-polymer linkage.

General Mechanism of Drug Release From Polymer

There are three primary mechanisms by which active agents can be released from a delivery system namely,

Diffusion

Diffusion occurs when a drug or other active agent passes through the polymer that forms the controlled-release device. Diffusion occurs when the drug passes from the polymer matrix into the external environment. As the release continues, its rate normally decreases with this type of system since the active agent has a progressively longer distance to travel and therefore requires a longer diffusion time to release. In these systems, the combinations of polymer matrices and bioactive agents have chosen must allow for the drug to diffuse through the pores or macromolecular structure of the polymer upon the introduction of the delivery

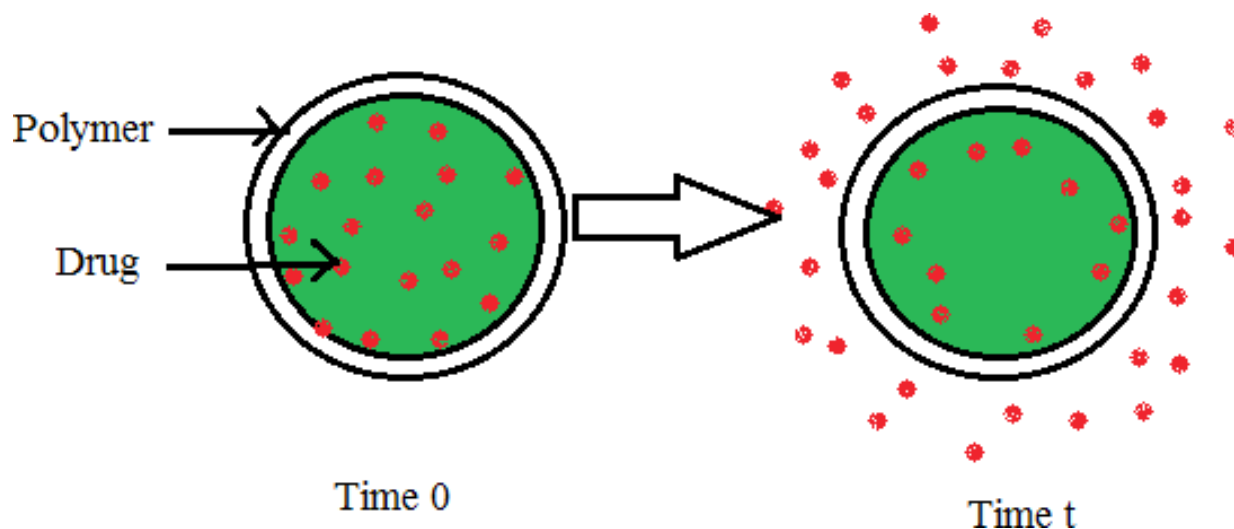


Figure 3: Diagrammatic representation of Diffusion type drug release

system into the biological environment without inducing any change in the polymer itself.^[17]

Degradation

Biodegradable polymer degrades within the body as a result of natural biological processes, eliminating the need to remove a drug delivery system after the release of the active agent has been completed. Most biodegradable polymers are designed to degrade as a result of hydrolysis of the polymer chains into biologically acceptable and progressively smaller compounds. For some degradable polymers, most notably the Polyanhydrides and Polyorthoesters, the degradation occurs only at the surface of the polymer, resulting in a release rate that is proportional to the surface area of the drug delivery system.

Swelling

They are initially dry and when placed in the body will absorb water or other body fluids and swell. The swelling increases the aqueous solvent content within the formulation as well as the polymer mesh size, enabling the drug to diffuse through the swollen network into the external environment.^[18]

Drug Release Mechanism of Sustained-release Drug Delivery Systems

Zero Order Kinetics

A zero-order release would be predicted by the following equation,

$$Q_t - Q_0 = K_0 t$$

Where,

- Q_t = Amount of drug release dissolved in time 't'.
- Q_0 = Initial amount of drug concentration in solution.
- $K_0 t$ = Zero-order rate constant.

When the data were plotted as cumulative % drug release verses time, if the plot is linear, then data obeys zero-order kinetics with slope equal to K_0 . This model represents an ideal release profile to achieve prolonged pharmacological action.

First Order Kinetics

A first-order release would be predicted by the following equation

$$\log Q_t = \log Q_0 - K_1 \frac{t}{2.303}$$

Where,

- Q_t = Amount of drug released in time 't'.
- Q_0 = Initial amount of drug concentration in solution.
- $K_1 t$ = First order rate constant.

When data were plotted as cumulative log % drug remaining versus time yields a straight line indicating that the release follows first-order kinetics, the constant K can be obtained multiplying slope values.

Higuchi's Model

Drug release from the matrix device by diffusion has been described by Higuchi's Diffusion equation

$$ft = Q = A \sqrt{(D(2C - C_s)C_s t)}$$

Where,

- Q = Amount of drug released in time 't'.
- D = Diffusion coefficient of the drug in the matrix.
- C_s = Solubility of the drug in the matrix.
- A = Porosity of matrix.
- t = Tortuosity.
- t = Time (h).

Peppas Korsmeyer Equation

In 1983 Korsmeyer et al. (Korsmeyer et al., 1983) developed a simple, semi-empiric model, when diffusion is the main drug release mechanism, relating exponentially the drug release to the elapsed time (t).

$$M_t/M_a = Kt^n$$

Where,

- K = Constant.
- n = Release.
- t = Time

M_t and M_a = Absolute cumulative amount of drug released at time 't'. This is used when the release mechanism is not well known or when more than one type of release phenomenon could be involved.

Hixon-crowell Equation

Drug released from the matrix device by diffusion has been described by Hixon-Crowell diffusion equation;

$$W_0^{1/3} - W_t^{1/3} = Kt$$

Where,

- W_0 = Initial amount of drug.
- W_t = Remaining amount of drug. t = Time.
- K = Constant (Kappa).

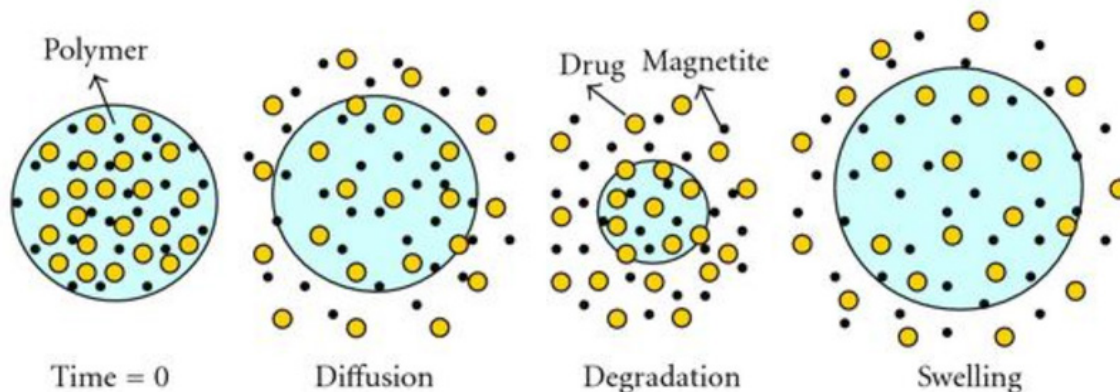


Figure 4: Schematic illustrations of diffusion, degradation, and swelling release mechanisms

This expression applies to pharmaceutical dosage form such as tablets where the dissolution occurs in planes that are parallel to drug surface if tablet dimensions diminish proportionally in such manner that the initial geometrical form keeps constant all the time.^[19]

Novel Trends in Sustained Release Drug Delivery Systems

For orally administered dosage forms, sustained drug action is achieved by affecting the rate at which the drug is released from the dosage form and or by slowing the transit time of dosage form through the gastrointestinal tract.

Single Unit Dosage Forms

This refers to diffusion controlled system where the therapeutic agent is evenly distributed (Dispersed/dissolved) throughout the solid matrix. This system can be classified as follows: Complex reservoir system or coated tablets or multi-layered system.

Hydrophobic/Swellable tablets

Optimum alkaloid such as morphine salts homogenized with its salt and fatty acid or any ethylene vinyl acetate copolymer (hydrophobic filler) and then compressed into tablets.

Semisolid Matrix Systems

In this system drug is incorporated in an oily "semisolid" hydrophobic carrier, and finally mass is typically filled into a gelatin capsule to prepare dosage form.

Ion Exchange Resins

The system is composed of a core tablet surrounded by a semipermeable membrane coating having a 0.4 mm diameter hole produced by laser beam. The tablet, particle or drug solution that allows transport of water into tablet with eventual pumping of drug solution out of the tablet through the small delivery aperture in tablet coating. E.g. Glucotrol XL (glipizide) tablets (Pfizer), Covera-HS® (verapamil HCl) tabs. (Searle).^[20,21]

Multiple Unit Dosage Forms

It represents a mixture of the dosage form, the source of which may either be homogenous or heterogeneous. The various forms which are available are multitablet system. Small spheroids

compressed tablets 3–4 mm in diameter may be prepared to have varying drug release characteristics. They them may be placed in gelatin capsule shells to provide the desired pattern of drug release coated beads, granules and microsphere In these systems, the drug is distributed on to beads, pellets, granules, or other particulate systems. Using conventional pan coating or air suspension coating, a solution of the drug substance is placed on small inert nonpareil seeds or beads made of sugar and starch or on microcrystalline cellulose spheres. Pellets prepared by coating inert drug pellet with film forming polymers. The drug release depends upon coating composition of polymers and amount of coatings. Microencapsulation is a process by which solids, liquids, or even gases may be enclosed in microscopic particles by formation of thin coatings of wall material around the substance. It utilizes principle of bioadhesion for optimum delivery of the drug from the device. Mucoadhesive system is suitable to increase the contact time of drug with absorbing membrane and localization of delivery of drug at targeted sites.^[22]

Protein Drug Eluting Cardiovascular Stents

Protein-eluting cardiovascular stents represent another potential application of protein sustained-release technology. The chemical drugs used on current drug eluting stents, although prevent after-stenting restenosis; inhibit healing of the blood vessel endothelium damaged by stent installation. The delayed endothelium recovery causes incident bleeding and thrombus forming. Several proteins have been found effective to suppress vascular smooth muscle proliferation and to stimulate vessel endothelium recovery when directly introduced to the stenting site. However, loading these proteins onto stents resulted in ineffectiveness. In these work, stents precoated with a layer of hydrophobic polymer was impregnated in a protein solution to adsorb proteins on the polymer surface. However, adsorbing proteins on hydrophobic polymer surfaces is a known cause for protein denaturing In addition, only limited amount of proteins can be adsorbed on a stent surface (< 20 µg/ stent).^[23]

Sustained release injectable formulations

Development of Sustained release injectable has occurred in the past few years. This was brought into existence to prolong the effect of drug at targeted site. This advancement also offers reducing dosing frequency, maximizing the efficacy– dose relationship, decreasing adverse side effects and enhancing

Table 2: Examples of Various SR DDS Approaches.^[25]

Sr. No.	Type of device	Product name	Active ingredient	Route	Manufacturer
1.	Diffusion (reservoir)	Estraderm	Estradiol	Transdermal	Alza/Novartis
		Norplant	Levonorgestrel	Sub-dermal implant	Wyeth-ayerst laboratory
		Ocusert	Pilocarpine	Ocular	Alza
		Progestasert	Progesterone	Intrauterine	Alza
2.	Diffusion (matrix)	Nitro-Dur	Nitroglycerine	Transdermal	Key Pharmaceutical
		Nitrodisc	Nitroglycerine	Transdermal	Searle
3.	Mixed (matrix reservoir)	Catapress-TTS	Clonidine	Transdermal	Alza/BoehingerIngelheim
4.	Hydro Dynamically	MedoparCR	Levodopa and Benserazide	Oral tablet	Roche
5.	Ion exchange	Colestid	Colestipol	Oral tablet or Granules	Upjohn
6.	Coating	Compazin	Prochlorperazine	Oral capsules	Smith Kline Beecham
7.	Nanocrystal technology	Rapamune	Sirolimus	Oral tablet	Elan/Wyefh-Ayerst Laboratory
8.	Osmotic pumps	Calan SR	Verapamil	Oral tablet	Alza/G. D. Searle

Table 3: List of various drugs which can be formulated as a matrix tablet with polymer and method used or its preparation

Sr. No.	Drugs	Category	Method used	Polymer used
1.	Ambroxol Hydrochloride	Secretolytic agent	Direct compression	Methocel K15MCR, PVP K30. ^[26]
2.	Diclofenac Sodium	Anti-inflammatory	Wet granulation	Pectin, Guar gum. ^[27]
3.	Metformin Hydrochloride	Antidiabetic	Direct compression	Chitosan, Ethylcellulose HPMC, Xanthan gum. ^[28]
4.	Cefpodoxime	Antibiotic	Direct compression	HPMC (K4M), HPMC (K100M) and Xanthan gum. ^[29]
5.	Risperidone	Antipsychotic	Direct compression	HPMC (K100), HPMC (K4M), Xanthan gum. ^[30]
6.	Lamivudine	Antiviral	Direct compression	HPMC (Methocel K15M CR) Avicel 102. ^[31]
7.	Isoniazid	Anti-tubercular	Direct compression	Guar gum, Tragacanth gum PEG-6000. ^[32]
8.	Terbutaline sulfate	Bronchodilator	Wet granulation	HPMC K200M, Ethylcellulose. ^[33]
9.	Indomethacin	Anti-inflammatory	Wet granulation	Hibiscusrosa-sinensis, Microcrystalline cellulose, Magnesium stearate. ^[34]
10.	Nateglinide	Antidiabetic	Wet granulation	Xanthan gum, Guar gum. ^[35]
11.	Zidovudine	Anti-viral	Wet granulation	HPMC, Xanthan gum, ethyl cellulose. ^[36,37]

patient compliance. This system also leads to alleviation of pain during administration and reducing costing of parenteral drug treatment. Safety issues relating to an injectable sustained-release system cannot be overlooked. Premature termination of treatment in case of drug toxicity can be extremely difficult for most of the parenteral sustained-release systems once administered. The adverse response of local tissues to the drug and/or the system on prolonged exposure can be clinically alarming. In recent years, the research in parenteral sustained-release technologies has been fuelled mainly by the advent of novel carriers. The growth of injectable sustained-release products in the pharmaceutical marketplace is also evidenced by the increasing number of products that have been granted regulatory approval during the last 5 years.^[24] Table 2 gives examples of various SR DDS.

DISCUSSION

The present article is focused on a sustained release matrix tablet. The goal of sustained-release could be easily and effectively ascertained via the approach of matrix tablets. As compared to conventional counterparts, matrix tablets offer better patient compliance, maintains constant plasma drug concentration level, reduces chances of toxicity, and once a day, drug therapy reduces the overall cost of treatment. Maintenance of drug concentration within a therapeutic range helps minimize the irrational use of drugs (esp. antibiotics) as well as helpful in the treatment of chronic diseases. Furthermore, it is a cost-effective approach.

CONCLUSION

It is concluded that oral sustained-release tablets provide the drug release in a modified form than their counterparts. It is effective to ascertain the therapeutic goals with maximum patient compliance. However, accurate adjustment of various physicochemical parameters is necessary. Matrix tablet is helpful in overcoming the problems associated with the conventional dosage form. Apart from various advantages associated with it cost-effective and once, daily dose is the key benefits associated with it. Due to its key benefits and better patient compliance, it can easily lead the market by replacing its counterparts.

REFERENCES

- Robinson DH, Mauger JW. Drug Delivery System. American Journal of Health-System Pharmacy. 1991; 48:14-23.
- Sato Y, Kawashima, Takeuchi H, Yamamoto H. Physicochemical properties to determine the buoyancy of microspheres (microballoons)

prepared by the emulsion solvent diffusion method. European Journal of Pharmaceutics and Biopharmaceutics. 2003; 55: 297-304.

- Hirtz J. The GIT absorption of drugs in man. A review of current concepts and method of investigation. British journal of clinical pharmacology. 1985; 19: 77-83 .
- Shilandb B.J Mastering Healthcare Terminology (Spiral Bound) - Text and Mosby's Dictionary of Medicine, Nursing and Health Professions 8e. Published on February 15, 2012 page – 174-184
- Diksha Thakur, Rambabu Sharma. Solid dispersion a novel approach for enhancement of solubility and dissolution rate: a review. Indian J. Pharm. Biol. Res.2019; 7 (3):5-11.
- Karna S, Chaturvedi S, Agrawal V, Alim M. Formulation approaches for sustained release dosage forms: a review. Asian J Pharm Clin Res. 2015; 8(5):46-53.
- Pundir S, Badola A, Sharma D. Sustained release matrix technology and recent advance in matrix drug delivery system: a review. International Journal of drug research and technology, 2017;28:3(1):8.
- Lieberman.H.A., Lachman.L., and kanig J L.,The theory and practice of industrial pharmacy, 3rd Edn, Published by: Varghese publishing house:430-456
- Shargel L, Wu-Pong S, Yu AB. Applied biopharmaceutics & pharmacokinetics. McGraw-Hill; 2007.
- Schall R, Müller Fr, Müller Fo, Luus HG. Bioequivalence of controlled-release calcium antagonists. Clinical pharmacokinetics. 1997; 32(1):75-89.
- Abdel-Rahman SI, Mahrous GM, El-Badry M. Preparation and comparative evaluation of sustained release metoclopramide hydrochloride matrix tablets. Saudi Pharmaceutical Journal. 2009; 17(4):283-8.
- Asghar LF, Mantha N. Design and evaluation of ethyl cellulose based matrix tablets of ibuprofen with pH modulated release kinetics. Indian journal of pharmaceutical sciences. 2008; 70(5):596.
- Gothi GD. Study on design and development of sustained release tablets of metoprolol succinate. Journal of Global Pharma Technology. 2010;3:2(2):69-74.
- Gurpreet Singh, Jayesh Dwivedi, Jeyabalan Govindasamy, Naresh Kalra, Rajesh Sharma. Formulation of Mouth Dissolving Tablets Using Solid Dispersion Technique: A Review. Indian J. Pharm. Biol. Res.2018; 6 (3):66-72.
- Dhat S, Aphale S, Bagul U, Tagalpallewar A, Vanshiv S, Shah N. Effect of Two Different Diluents On Release Profile of Aceclofenac From Sustained Release Matrix Tablets Using Gum Damar As Release Retardant. International Journal of Pharmacy and Pharmaceutical Sciences. 2011; 3(4):30713.
- Aulton ME. Pharmaceutics: The Science of Dosage Form Design. 2nd ed, London: Churchill livingstone; 2005.p. 296-298.
- Poddar RK, Rakha P, Singh SK, Mishra DN. Bio adhesive Polymers as a Platform for Drug Delivery: Possibilities and Future Trends. Research Journal of Pharmaceutical Dosage Forms and Technology. 2010; 2(1):1-6.
- Satturwar PM, Fulzele SV, Dorle AK. Biodegradation and *in vivo* biocompatibility of rosin: a natural film-forming polymer. AAPS Pharm SciTech. 2003; 4(4):434-9.

19. Diwedi RO, Alexandar A, Chandrasekar MJ. Preparation and *in vitro* evaluation of sustained release tablet formulations of metformin HCL. Asian Journal of Pharmaceutical and Clinical Research. 2012; 5(1):45-8.
20. Hemnani M, Patel U, Patel G, Daslaniya D, Shah A, Bhimani B. Matrix tablet: A tool of Controlled drug delivery. American Journal of Pharm Tech Research. 2011; 1(4):127-43.
21. Robinson JR, Jantzen GM. Sustained-and controlled-release drug-delivery systems. In Modern Pharmaceutics, Fourth Edition 2002 May 24. CRC Press
22. Dokoumetzidis A, Macheras P. A century of dissolution research: from Noyes and Whitney to the biopharmaceutics classification system. International journal of pharmaceutics. 2006; 321(1):1-1.
23. Wu F, Jin T. Polymer-based sustained-release dosage forms for protein drugs, challenges, and recent advances. Aaps Pharm SciTech. 2008 ; 9(4):1218- 29.
24. Pundir S, Badola A, Sharma D. Sustained release matrix technology and recent advance in matrix drug delivery system: a review. International Journal of drug research and technology. 2017 Feb 28; 3(1):8.
25. Patnaik AN, Nagarjuna T, Thulasiramaraju TV. Sustained release drug delivery system: a modern formulation approach. International Journal of Research in Pharmaceutical and Nano Sciences. 2013; 2(5):586-601.
26. Moghal M, Islam M, Ahmed I, Islam M, Rahman H, Development and optimization of sustain release matrix tablet of Ambroxol Hcl using central composite design, IJPER 44(1):28-35, 2010.
27. Mediseti V.K., Avasarala H, KVRNS Ramesh, Padmasri S, Karthika D, Mouli C, Formulation and Evaluation of Sustained Release Hydrophilic Matrix Tablets of Diclofenac Sodium using Natural Almond Gum. Inventi Rapid NDDS. 2012;(4):1-6.
28. Corti G, Cirri M, Maestrelli F, Mennini N, Mura P Sustained-release matrix tablets of Metformin hydrochloride in combination with triacetyl-b-cyclodextrin, European Journal of Pharmaceutics and Biopharmaceutics.2008;(68):303–309.
29. Prasad A, Issac J, Verma A K Development of Sustained Release Cefpodoxime Matrix Tablets: An Investigation on Effects of Combination of Hydrophilic and Hydrophobic Matrix Formers. Inventi Impact: NDDS.2010;1 (2):1.
30. Haresh M, Thimmasetty J, Ratan G N, Formulation Development and In-vitro Evaluation of Sustained Release Matrix Tablets of Risperidone, Inventi Impact Pharma tech2003; (1):28-34.
31. Rahman Md.M., Ahsan Md.Q., Jha M K, Ahmed I, Rahman Md H, Effect of Mannitol on Release of Lamivudine Sustained Release Matrix Tablets“using Methocel K15M CR Polymer Inventi Impact: Pharm Tech. 2011;(1):58-62.
32. Jain D., Shukla S.B, Formulation and Evaluation of Sustained Release Matrix Tablets of Isoniazid. A Comparative Aspect Based on Polymer. Inventi Rapid: NDDS 2011; 2(1):1.
33. Hadi M, Rao S, Vineeth P, Azharuddin M. Formulation and Evaluation of once daily sustained release matrix tablet of terbutaline sulphate for treatment of Nocturnal asthma. Research Journal of Pharmaceutical dosage form and technology.5 (1):27-32, 2013.
34. Pagar H.B., Shinde U.P., Barhate S.D., Bari M.M., Janjale M.V., Agrawal Y.S., Formulation and Evaluation of Indomethacin Sustained Release Matrix Tablets. Inventi Rapid: NDDS:2011;4:1.
35. Madgulkar A.R., Bhalekar M.R., Warghade N.S., Chavan N.S., Preparation and Evaluation of Sustained Release Matrix Tablet of Nateglinide Effect of Variables. Inventi Rapid: NDDS.2011;2 (1):1.
36. Shanmugam S, Banthalarajan, ayyappan T, Sundermoorthy, Vetrichelvan T. Formulation and evaluation of Sustained release matrix tablet of zidovudine using different polymer, Research Journal of Pharmaceutical dosage form and technology.2011;3(1): 17-23.
37. Satinder Kakar, Ramandeep Singh, Ramandeep Kaur, Alok Semwal. Preparation and drug release assessment of mesalazine matrix tablets. Int. J. Pharm. Med. Res. 2014; 2(1):28-32.