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**Review Article**

# A Review on Sustained Release Matrix Tablet of Antihypertensive Drug

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## ABSTRACT

Now, the daily pharmaceutical industry is focused on developing common oral dosage forms as it becomes essential medical tool. This continuous-release formulation is designed to release the drug at a predetermined rate and keep the plasma drug overflow in a medical window with minimal side effects. The basic idea behind continuous drug delivery is to change the drug's biopharmaceutical, pharmacokinetic, and pharmacodynamics to reduce side effects, provide patient compliance, and treat the disease. Continued discontinuation of drug delivery improved patient compliance due to frequent drug administration, decreased flexibility in consistent drug levels, higher drug use, increased dosage of effective drug dosage, and reduced health care costs with improved treatment and shorter treatment duration. The main goal of the continuous-release forms is the development of drug treatment that has tested the relationship between the benefits and disadvantages of using a constant-release system. This review article contained basic information on the matrix type of the ongoing drug delivery system. Nowadays, there are very few drugs out of research and development, and existing drugs have a problem with resistance due to their unreasonable use, especially in the case of drugs such as antibiotics. Therefore, the mutation is an effective and efficient way to make a particular medication more effective with a slight change in drug delivery. Continuous extraction also provides a promising way to reduce the side effects of the drug by preventing fluctuations in the drug's therapeutic effect on the body. Drug administration through such a system involves controlled dispersal and distribution methods. If not correctly formulated, many medications can release the drug very quickly and may produce the drug's toxic effects orally. This article carries basic information about the structure of the release version and various similar types.

**KEYWORDS:** Sustained release, Matrix tablet, Oral drug delivery system, Antihypertensive drugs.

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## INTRODUCTION

The oral route is the most popular method used in drug administration due in part to the ease of administration and the fact that the physiology of the intestines provides greater flexibility in forming volume form than many other routes [1]. Terms of a stable release, long-term release, modified release, extended-release, or depot formation do use to identify drug delivery systems designed to achieve or extend the effect of continuous treatment by over-the-counter medications after single-dose administration [2].

The benefits of providing a single dose of a long-acting drug instead of multiple quantities have been evident in the pharmaceutical industry for a long time. The desire to maintain a blood level close to or similar to the drug often translates into better patient compliance, as well as the improved clinical efficacy of the drug in its intended use [3]. Because of the growing problems and costs involved in advertising for new drug companies, much attention does focus on developing continuous or controlled drug delivery systems [4]. The matrix system does widely used for constant release. It is a release system that expands and prevents the release of a dispersed or dispersed drug. A matrix does define as a well-mixed combination of one or more drugs containing a gelling agent, i.e., hydrophilic polymers [5]. The purpose of an extended-release dosage form is to maintain the level of the drug in the plasma for a long time.

### Advantages sustained Release Drug Delivery System [6]

### Clinical advantages

- Reduce the frequency of drug administration
- Improved patient compliance
- Decreased fluctuations in drug levels
- Reduction of total drug use compared to conventional treatment
- Reduce drug overdose through chronic treatment
- Reduction of drug toxicity (area/system)
- Stability of medical condition (due to similar drug levels)
- Improving the availability of bioavailability of certain drugs due to local control
- Economics for health care providers and patient

### Commercial / Industrial advantages

- Product life-cycle extension
- Product differentiation
- Market Expansion
- Patent extension

### Disadvantages of Sustained Release Drug Delivery System [6]

- Delay in the onset of drug action.
- Possibility of volume disposal in the case of incorrect design strategy.
- Increased chances of exceeding initial metabolism.
- Significant dependence on the G.I. duration of the dose form.
- Opportunities for slightly more accurate dose adjustment in some cases.
- The cost per unit volume is higher compared to the standard books.
- Not all medications are suitable for inclusion in the E.R. dosage form

### Specific Considerations for The Formation of Sustained Release Formulation [7]

- It is stored alone if an active compound has a long half-life (more than 6 hours).
- If the pharmacological activity of an active compound is not related to its blood levels, the release time is meaningless.
- If the absorption of an active compound involves active transport, the development of a timely product may be problematic.
- Finally, if an active compound has a shorter half-life, it will require a significant amount to maintain a more extended working capacity. In this case, a comprehensive treatment window does need to avoid poisoning; otherwise, the risk is unnecessary, which another management approach recommends.

**The Goal of Designing Delayed-Release Sustained or Controlled Delivery System [8]**

- Reduce dosing frequency or increase the drug's effectiveness by making a place in the action area, reducing the required dose, or providing a similar drug delivery.
- It can be a single dose during treatment regardless of the days or weeks, such as infection, or lifelong patients, such as hypertension or diabetes.
- It should bring the active business directly into the action area, reducing or eliminating adverse effects.
- It may need to be delivered to specific receptors or localized to cells or particular areas of the body. The safety limit for solid drugs increased, and the incidence of adverse local and systemic side effects was reduced in critical patients.

**Antihypertensive drug**

Hypertension is an increase in BP > 140/90 mmHg. It could be mild, moderate, or severe. Prolonged hypertension damages the blood vessels of the heart, brain, and kidneys leading to complications.

**As per JNC recommendation, blood pressure may be classified as:**

Normal (SBP<120 and DBP <80mmHg)
Prehypertension (SBP 120-139 and 80-89 mmHg)
Stage 1 hypertension (SBP 140-159 and 90-99 mmHg)
Stage 2 hypertension (SBP >160 and >130 mmHg)

**Classification**

**(A) Diuretics**

- **Thiazides (**e.g., Indapamide, Hydrochlorothiazide)
- **Loop Diuretics (**e.g., Furosemide)
- **Potassium Sparing diuretics (**e.g., Spironolactone)

**(B) Drugs acting on renin-angiotensin system**

- **ACE Inhibitors** (e.g., Captopril, Lisinopril, Enalapril)
- **ARBs** (e.g., Losartan, Valsartan, Candesartan)
- **Renin inhibitors** (e.g., Aliskiren)

**(C) Sympatholytics**

- **Centrally acting drugs**
- **Ganglion blockers**
- **Adrenergic neuron blockers**
- **Adrenergic receptor blockers (Alpha Blockers, Beta Blockers)**

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- **Mixed alpha and beta blockers**

**(D) calcium channel blockers** (e.g., Nifedipine, Verapamil, Amlodipine)

**(E) Vasodilators**
- **Arteriolar dilators** (e.g., Diazoxide, Hydralazine)
- **Arteriolar and venular dilators** (e.g., Sodium nitroprusside)

**Modified Release Drug Delivery System [9]**

**Extended-release system**

Drug delivery system that allows at least double the dose compared to that drug introduced as an immediate-release program.

**The process of continuous release**

It includes any drug delivery system that gains a slow release of the drug in the long run and not, especially at a predetermined price.

**Controlled release system**

Includes any drug delivery system in which a drug delivers at a predetermined price over a long period.

**Long-term discharge plan**

It does design to release the drug slowly and provide continuous drug delivery over the long term.

**The release system is delayed**.

It is a program designed to release a different drug component at one time or another immediately after administration, alt. However, the piece may be removed immediately after administering the dosage form.

**Biological Factors Affecting Design of Oral Sustained Release Dosage Form [9]**

**Biological half-life**

A drug with a biological half-life of 2-8 hours does consider a suitable candidate for the dosage form, as this may reduce the dosage frequency. However, this is limited to drugs with a shorter half-life that may require an excessive amount of the drug per unit dose to maintain continuous results, forcing the dosage form to be relatively limited. The medication usually has a shorter half-life than 2 hours for poor people with ongoing relief programs.

**Absorption**

The level, dosage, and consistency of the absorption of a drug are important factors when considering its composition in an extended-release system. The most important in the case of oral control is s Kr <<< Ka. If the drug absorbed by active transport or transport is limited to a specific area of GIT, this drug is a poor candidate for continuous-release systems. Considering that the drug delivery duration in the abdomen's suction area is between 9-12 hours, the maximum absorption of half-life should be 3-4 hours. It is in line with the minimum constant absorption rate of the Ka value of 0.17- 0.23 / hrs. required by about 80-95% absorption during a 9–12-hour transport time. In drugs with a shallow absorption rate (of << 0.17 / hrs.), the initial order release rate of less than 0.17 / hrs. results in a bioavailability that is unacceptable in most patients. Therefore, the slow-release drug will be challenging to develop into extended-release systems where the Kr <<< Ka condition must meet.

**Metabolism**

Metabolism leads to an active drug's inactivity or an inactive molecule. Metabolic modification of the drug occurs mainly in the liver. Metabolism does characterize by consistent metabolism or the appearance of a metabolite. As long as the rate and rate of metabolism predict, this is appropriately incorporated into the product structure. However, complex metabolic patterns make formation more difficult, especially if the biological activity does require metabolite. Suppose a drug in chronic treatment ingests or shows an enzyme concentration. In that case, it will make the person very poor to produce a continuous product due to the difficulty of maintaining the same blood level.

**Therapeutic Index:** It does widely used to measure the safety limit of a drug. TI = TD50 / ED50. If the T.I. value is long, it is a safe drug. Drugs with shallow therapeutic value are poor preservatives developed into long-acting products. The drug does consider safe if its T.I. level is above 10.

**Physiological Factors Affecting Design of Oral Sustained Release Dosage Form [9]**

- Molecular Weight and Diffusivity For drug absorption, it is necessary to spread a wide range of biological membranes during its duration. In addition to the distribution of these physical layers, drugs in many controlled release systems must apply through the membrane that controls the polymeric level or matrix. Drugs weighing 150-400 cells are good candidates for continuous dosage forms. For drugs with a molecular weight greater than 500Da, their distribution coefficients in many polymers are usually so small that they are challenging to measure.
- Dosage size for standard dosage forms, the dosage size of 500-1000 mg is the highest appropriate dose for continuous dosage forms.
- Aqueous Soluble A portion of a drug absorbed into the bloodstream is a function of the value of a drug in the solution of the G.I. tract, i.e., penetration into the drug. For the drug to be absorbed, it must be dispersed in a liquid phase around the treatment area and separated from the permeable membrane. Therefore, a tree's aqueous solubility does use as an initial measure of its completion rate. Low-aqueous soluble drugs have low melting levels and often have oral bioavailability problems. The minimum melting point of the drug is 0.1 mg/ml for continuous extraction. Good aqueous-soluble drugs are ideal candidates for the development of constant oral release.
- Partition coefficient (K) Drugs with high K levels are highly soluble in oil, break down into membranes easily, and remain in the body for a long time. High K values positively affect poor water solubility but improve lipid solubility, and the drug will not separate the lipid membrane once it has entered. The K value at which the maximum activity does estimate at 1000/1 in n. -octanol/water. Drugs with a partition coefficient higher or lower than, in general, poor people to be produced into a dosage form for extended release.
- Drug Stability In those conservative medicines, the most effective control unit may be those that release only its intestinal contents. Release in the case of those dangerous drugs in the intestinal tract; the most appropriate control may be to remove its contents only in the stomach. Therefore, for drugs with serious stability problems in any area of G.I., the pamphlet is less suitable for designing controlled output systems that deliver the same content over the GIT length. **(Table 1)**

**Table 01:** Physicochemical Parameters for Drug Selection

| Parameters | Preferred value |
|---|---|
| **Molecular weight/ size** | < 1000 |
| **Solubility** | > 0.1 µg/ml for pH 1 to pH 7.8 |
| **Apparent partition coefficient** | High |
| **General absorbability** | From all G.I. segments |
| **Release** | Should not be influenced by pH and enzymes |
| **Elimination half-life** | Preferably between 0.5-8 hours |
| **Total clearance** | Should not be dose-dependent |
| **The apparent volume of distribution Vd** | The larger the Vd and MEC, the larger the required dose size. |
| **Absolute bioavailability** | It should be 75% or more. |
| **Intrinsic absorption rate** | It must be more significant than the release rate |
| **Dose size** | 0.5-1 gm |
| **Partition Coefficient** | High partition coefficient |
| **Stability** | Drugs should be stable in the intestine. |
| **Metabolism** | Drugs should not undergo first-pass metabolism. |
| **Therapeutic Index** | Should have a wide range of therapeutic index |
| **BCS Class** | BCS Class I and II are suitable for CR/ SR formulation development |

**Matrix Type of Sustained Release Drug Delivery System [9]**

The process by which drug molecules are dissolved or dispersed in a bio-compatible polymer produces the same device as drug molecules spread uniformly throughout. In this case, the drug molecules release by spraying the polymer on the surface of the device, where they are cast on the outer surface.

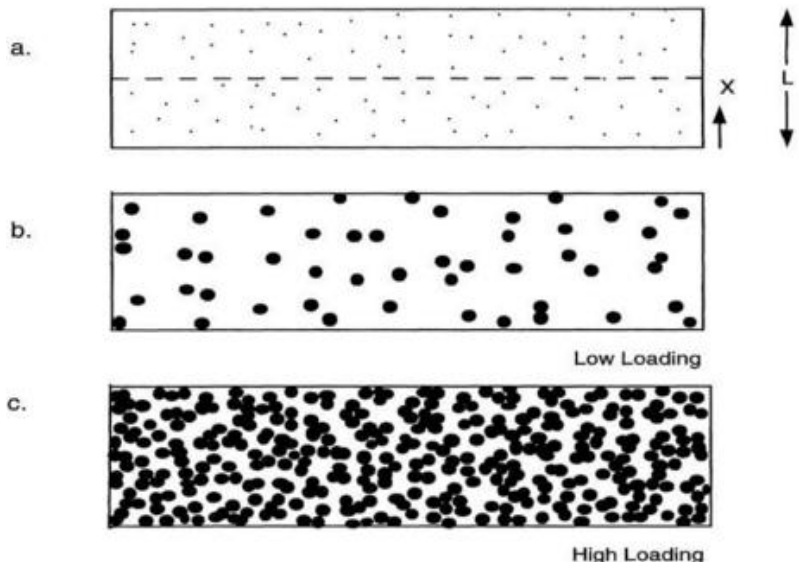

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**Fig. 1:** Schematic of matrix-type systems for controlled drug delivery. Matrix delivery systems can be constructed with drugs dissolved in the matrix material (a) or Particles of the drug dispersed to form a composite material (b and c).

**Advantages of Matrix System**

- Their production is expensive and does not require particular infrastructure.
- The drug can be protected from the acidic environment of the gastrointestinal tract, thereby increasing its stability.
- Improvement of patient compliance by reducing the frequency of dosing
- Reduce drug accumulation and related side effects

**Disadvantages of Matrix System**

- The zero-order release of a drug is often difficult to achieve.
- Drug withdrawal can be affected by physiological factors, the presence of food, the timing of abortion, and bowel movements.

**Classification of matrix tablets**

**Based on Retardant Material Used**

**Hydrophobic Matrices (Plastic matrices)**

Stable emissions do produce due to the dissolving solvent distributed through a network of existing channels between the composite polymer particles. In this method of obtaining continuous release in oral dosage form, the drug is mixed with an inert or hydrophobic polymer and pressed into the tablet. Examples of materials used as inert or hydrophobic matriculants include polyethylene, polyvinyl chloride, ethyl cellulose, and acrylate polymers and their copolymers. Such matrix pills become idle in the presence of water and intestinal fluid—a step to control the level of this formation of fluid infiltration into the matrix. A possible way of drug withdrawal from such types of pills is distribution **[10]**.

**Lipid Matrices**

These matrices do prepare by lipid wax and related substances. Drug release in such matrices occurs in both the distribution of pores and erosion. Extrusion elements are therefore more sensitive to forming digestive fluids than to an insoluble polymer matrix. Carnauba wax mixed with stearyl alcohol or stearic acid does use as a discarded base in many continuous products.

**Hydrophilic Matrices**

Hydrophilic polymer matrix systems do widely use in the delivery of oral contraceptives due to their flexibility in obtaining the desired drug release profile, cost-effectiveness, and wide acceptance of control. Drug formulation in gelatinous capsules or tablets using high-strength gelling hydrophilic polymers as base excipients with a particular interest in the field of controlled release. An ***infection matrix*** does define as a well-mixed compound of one or more chemicals containing a gelling agent (hydrophilic polymer). These systems are called **swellable controlled** release systems. The polymers used in the preparation of hydrophilic matrices do divide into three broad groups,

- **Cellulose derivatives:** Methylcellulose 400 and 4000cPs, Hydroxy ethyl cellulose; Hydroxypropyl methyl cellulose (HPMC) 25, 100, 4000, and 15000cPs; and Sodium carboxy methyl 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, is the most used variety **[11]**.

**Biodegradable Matrices**

These include polymers that combine monomers connected by functional groups and unstable connections to the spine. They are biologically damaged or degraded by enzymes produced by surrounding living cells or by a non-enzymatic process to oligomers and monomers that can be modified or extracted. Examples are natural polymers such as proteins and polysaccharides; natural polymers replaced; polymers produced as aliphatic poly (esters) and poly anhydrides **[12].**

**Mineral Matrices**

These include polymers found in various types of seaweed. E.g., Alginic acid is a hydrophilic carbohydrate found in brown seaweed species (Phaeophyceae) through refined alkali **[13]**.

**Based on the Porosity of Matrix [13]**

The matrix system divides according to its porosity, and as a result, Macro porous, Microporous and Non-porous systems identify.

**Macro-porous Systems**: In such systems, the diffusion of the drug occurs through pores of the matrix, which are in the size range of 0.1 to 1µm. This pore size is larger than the diffusion molecule size.

**Micro-porous System**: Diffusion in this type of system occurs essentially through pores. For microporous systems, pore size ranges between 50–200 A°, slightly larger than diffusion molecule size.

**Non-porous System**: Non-porous systems have no pores, and the molecules diffuse through the network meshes. Only the polymeric phase exists in this case, and no pore phase is present.

**Polymers Used in Matrix Tablet [14]**

**Table 2:** Polymers Use for Sustained Release Tablet

| Hydrophilic Polymers | | | Water Insoluble and Hydrophobic | Fatty Acids/Alcohols/Waxes |
|---|---|---|---|---|
| **Cellulosic** | **Non-Cellulosic** | **Non-Cellulosic (others)** | | |
| **Methylcellulose** | Sodium Alginate | Polyethene oxide | Ethylcellulose | Bees' wax |
| **HPC** | Xanthan gum | Homopolymers and copolymers of acrylic acid | Hypromellose acetate succinate | Candelilla wax |
| **HPMC** | carrageenan | | Cellulose acetate | Candelilla wax |
| **HEC** | Gaur gum | | CAP | Paraffin waxes |
| **Na-CMC** | Locust bean gum | | Methacrylic acid copolymers | Cetyl alcohol |
| | Chitosan | | PVA | Stearyl alcohol |

**Mechanism Of Drug Release from Matrix System [14]**

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Many extended-release preparations are available, none working in a single drug delivery system. Drug extraction from controlled devices is by dispersing or combining a two-way or erosion-controlled system.

**Diffusion-controlled system [15]**

In this type of system, the step control level is not the dispersion rate but the dispersion of the dispersed drug using a polymeric barrier. The drug release rate never orders zero as the length of the distribution process increases over time as the insoluble matrix gradually decreases the drug. The two types of distributed control systems are:

- Matrix diffusion-controlled system.
- Reservoir devices.

In the matrix system, the tree disperses as solid particles within a matrix with holes made of a water-soluble polymer, such as polyvinyl chloride. Initially, the particles of the drug in the upper part of the release unit will dissolve, and the drug will be released immediately. After that, the wood particles at a straight distance from the top of the extracted team will be dispersed and removed by scattering holes to the outside of the release unit. This process pursues the interface between the bath solution and the solid wood that goes inside.

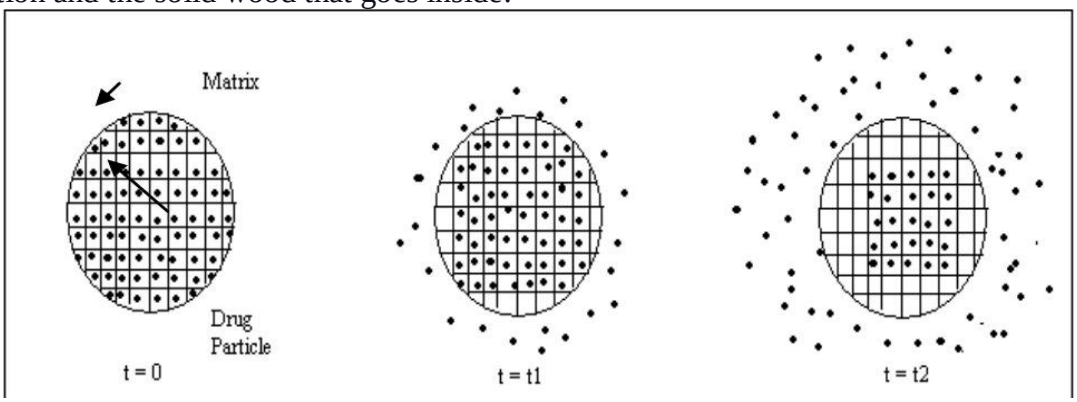


**Fig. 2:** Schematic for the mechanism of drug release from a diffusion-based matrix tablet. Obviously, for this system to be diffusion controlled, the rate of dissolution of drug particles within the matrix must be faster than the diffusion rate of the dissolved drug leaving the matrix.

**Dissolution Controlled system**

A tree with a low degradation rate will show supporting properties, as the release of the drug will be determined by the level of dissolution. It seems possible to adjust the increased product release by reducing the elimination rate of highly soluble drugs in water. it can be done by

• Preparation of suitable salt or from it.

• Cover the tree with a slightly soluble melt control.

• Applying the drug to the tablet with the carrier–matrix dissolution. (To drug withdrawal rates continue to decline over time) **[16].**

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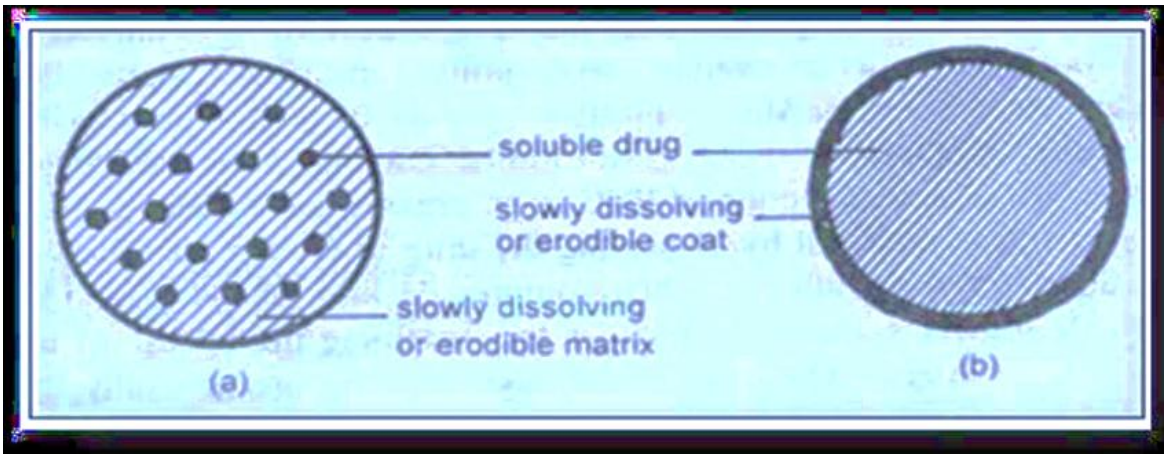


**Fig. 3.** Schematic representation of dissolution-controlled release systems (a) matrix system and (b) coated/encapsulated system.

**Erosion controlled systems**

In an extended erosion-controlled release system, the drug release rate does control by the erosion of the matrix in which the drug disperses. The drug is then diluted with gastric juice and mixed (if the drug dissolves in the matrix) or distributed in (if the medication does suspend in the matrix) fluid. This drug withdrawal program is simplistic, as the erosion process may involve a different approach to drug withdrawal. For example, a tree may be free from erosion and distribution within the matrix. However, drug withdrawal may generally limit zero-order to a significant portion of the total release time. The eroding matrix can make of different materials. One example is lipids or waxes, where the drug does disperse. Another example is a polymer, a gel that comes in contact with water (**e.g., Hydroxyethylcellulose**). The gel will then erode and release the dissolved or dispersed substance into the gel **[17-19]**.

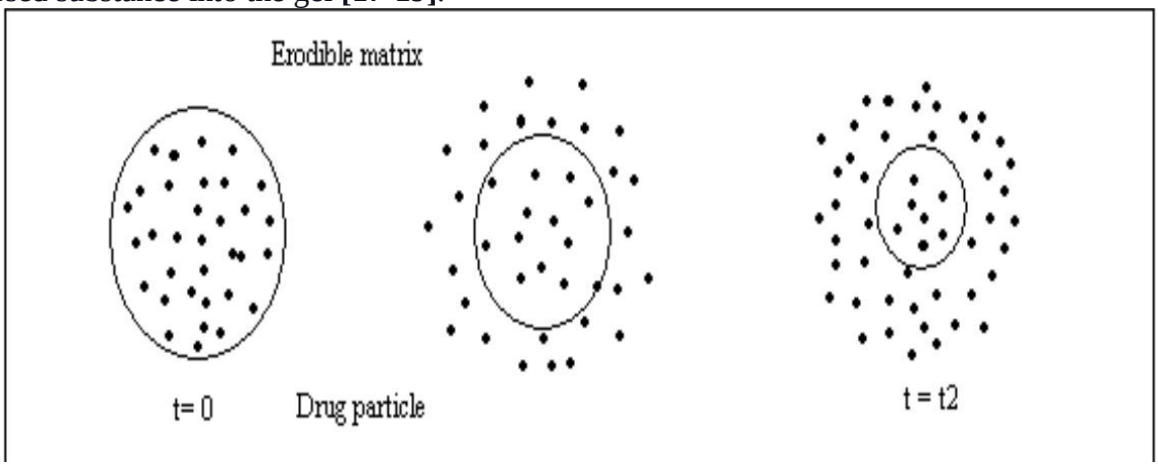


**Fig. 4:** Schematic illustration of the mechanism of drug release from an erosion tablet

## CONCLUSION

SRDDS is usually frightened by an effective drug Discovery to obtain the highest dose and dosage of the drug Absorption; however, it controls drug action by construction and means controlling the bioavailability to lower the drug Absorption rates. Oral dosage forms indicate one of these Leading areas of the ongoing drug delivery system (SRDDS). S.R. builds help increase the Efficiency of volume and ease of use due to common drugs to manage. SRDDS may be used to deliver drugs at a continuous rate over 24 hours. The volume form composition is an excellent way to provide medication to control treatment—the effect on the surface of uncertain Vivo variables The place where the drug release occurred. The current overview also provides insight into the technology of various trading platforms, drug conditions Selection, development of novel research, and SRDDS

patents. In the future, the design of oral S.R. products will use to get what all want, the level of access to the drug in the form of continuous action dose. They include increasing the particle size, embedding the Medicine in a matrix, a drug cover, or an amount containing a drug or microencapsulation to form drug structures with Substances such as ion exchange resins. S.R. format is easy Improvement and more effective when antibiotics are introduced in the same absurd use that is likely to result in resistance. Own effort will find a new application or system soon.

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