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A Basic Approach on Sustained Release Drug Delivery System

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ABSTRACT

The oral route of administration is considered as the most widely accepted route because of its convenience of self administration, compactness and easy manufacturing, in which the sustain release drug delivery replaces the conventional administration of drug by delivery system. Recently, greater emphasis has been placed on controlling the rate and or site of drug release from oral formulations for the purposes of improving patient compliance and treatment efficacy, solving problems concerning targeting of a drug to a specific organ or a tissue and controlling the rate of a drug delivery to the target site. Matrix system are favored because of they are easy to formulate, and showing better patient compliance, effective etc, than ancient drug delivery, which showing many drawbacks like repeated administration, fluctuation in drug plasma level etc.; developing oral sustained release matrix tablet with constant release rate has always being beneficial to the pharmaceutical technologist. Matrix type drug delivery systems are an interesting and promising way for developing an oral controlled release system, which will maximize the pharmacological benefits and minimize the potential side effects. The matrix tablet releases the drug in continuous manner like diffusion and dissolution controlled way. Hydrophilic polymers with high gelling capacity are of particular interest in the field of matrix tablet.

Key words: Sustained release, Oral formulations, Hydrophilic polymers, Matrix tablet.

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INTRODUCTION

The oral route is the route most often used for administration of drugs. Tablets are the most popular oral formulations available in the market and are preferred by patients and physicians alike. In long-term therapy for the treatment of chronic disease conditions, conventional formulations are required to be administered in multiple doses and therefore have several disadvantages[1]. Sustained release dosage forms have been demonstrated to improve therapeutic efficiency by maintenance of a steady drug plasma concentration.[2-3]

Sustained release dosage forms are formulated in such a manner as to make the drug available over a long period following its administration. A typical sustained release system is designed to provide constant or nearly constant drug levels in plasma with reduced fluctuations via slow release over an extended period of time. In practical terms, an oral sustained release should allow a reduction in dosing frequency as compared to when the same drug is presented as a conventional dosage form. It is an established fact that the conventional immediate release drug delivery system when taken frequently in a day can maintain drug concentration levels within therapeutically effective range.[3]

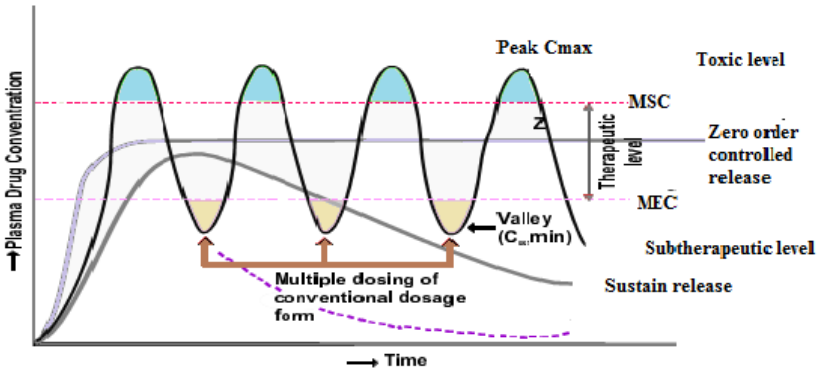

Figure 1: Hypothetical plasma drug concentration profile for immediate release, sustained release and controlled release dosage forms [4]

There are many definitions of sustained release but the simplest one is "Any drug or dosage form or medication that prolongs the therapeutic activity of drug".[4]

The United States Pharmacopoeia definition of controlled release or modified release system, as it also called, is that, the drug release characteristics of time, course and or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms. Several terms have been applied loosely and are interchanged invariably so that today there is no consistent nomenclature for the longed action products available in the market. Several terms have been utilized synonymously to describe sustained release medications. [5]

- Continuous Release (CR)
- Controlled Release (CR)
- Depot Release (DR)
- Long Term Release (LTR)
- Slow Release (SR)
- Long Acting (LA)
- Long Lasting (LL)
- Prolonged Action (PA)
- Extended Release (ER)
- Gradual Release (GR)

However, as today the most widely used terms are sustained release and controlled release.

Controlled Drug Delivery System (CDDS) is the one which delivers the drug at a predetermined rate, locally or systemically for a specified period of time.

Targeted Drug Delivery System (TDDS) is the one which deliver the drug only to its site of action and not to non-target organs or tissues.

Sustained Drug Delivery System (SRDD) is the dosage form or medication that prolongs the therapeutic activity of drug.[3]

Controlled release system differs from sustained release system which simply prolongs the drug release and hence plasma drug levels for a long period of time.[6]

Difference between Sustained Release and Controlled-release Medications:

Controlled-release systems also offer a sustained-release profile but, in contrast to sustained-release forms, controlled-release systems are designed to lead to predictably constant plasma concentrations, independently of the biological environment of the application site. This means that they are actually controlling the drug concentration in the body, not just the release of the drug from the dosage form, as is the case in a sustained-release system. Another difference between sustained and controlled-release dosage forms is that the former are basically restricted to oral dosage forms whilst controlled-release systems are used in a variety of administration routes, including transdermal, oral and vaginal administration.[7]

Advantages of sustained drug delivery system: [8, 9]

1. Reduced fluctuation in circulating drug plasma levels
2. Increased patient convenience and compliance
3. Avoidance of night time dosing
4. More uniform effect

5. Maximum utilization of drug
6. Reduction in GI irritation and other side effects
7. Reduction in cost and toxicity
8. Improve bioavailability of some drugs
9. Reduction in dosing frequency

Disadvantages of controlled drug delivery system: [8, 9]

1. Decreased systemic availability in comparison to immediate release conventional dosage form. This may be due to,
   - Incomplete release,
   - Increased first-pass metabolism, Increased instability,
   - Insufficient residence time for complete release,
   - Site specific absorption, p^H dependent solubility, etc.
2. Poor *in vitro-in vivo* correlation.
3. Possibility of dose dumping.
4. Retrieval of drug is difficult in case of toxicity, poisoning, or hypersensitivity reactions.
5. Higher cost of formulation.

CRITERIA FOR DRUG PROPOSED TO BE FORMULATED IN SUSTAINED RELEASE DOSAGE FORMS:

During formulation of a sustained release product some factors or properties of drug are consider such as the physical, chemical and biological properties of the drug, and other factors as the patient disease state, and technological limitations in fabrication of the final dosage form. Depending on the drug, disease state, route of administration, all of these factors must be considered.

Physicochemical Properties:

a. Dose size:

Limitation of dose of drug is a major factor to be considered in the formulation SRDF**.** If dose is greater than 0.5g it is a poor candidate for a sustained release system since the product size will be exceptionally large.

b. Aqueous solubility and pka:

For drugs with low water solubility having Absorption is dissolution rate limited, they will be difficult to incorporate in sustained release mechanism. A drug with good aqueous solubility is suitable.

c. Partition coefficient:

Drugs that are highly lipid soluble or very water-soluble i.e. extremes in partition coefficient, will show either low flux in tissue or rapid flux followed by accumulation in the tissues, having greater bioavailability. In case of compounds with very low partition coefficient, it is very difficult for them to penetrate the membrane, resulting in poor bioavailability.

f. Drug protein binding:

The drug protein binding plays significant role, retention of drug in the vascular space is governed by the degree of its protein binding. Drugs that exhibit high degree of protein binding there by prolong the elimination half-life of the drug. Such drugs do not require SR dosage form.[10]

e. Drug stability:

As sustained release systems are designed to release their contents over much of the length of GI tract, drugs, which are unstable in environment of intestine, are poor candidates for sustained release. Stability to the GI pH, enzymes and normal microbial flora, metabolizing effect of the colonic bacteria is essential.[11]

Biological properties:

a. Absorption:

Drugs that are slowly absorbed or absorbed with variable absorption rate are poor candidates for sustained release systems. Drug release from dosage form is a rate limiting step. Drugs that absorb by active transport system and also drug showing there therapeutic action in stomach are unsuitable candidate for formulation of sustain release dosage form

b. Distribution:

Drugs with high apparent volume of distribution, which in turn influences rate of elimination, are poor candidates.

c. Metabolism:

Drug which undergo extensive first pass metabolism or the drug undergo significantly metabolism before absorption are unsuitable candidate for SRDF. The metabolism of a drug can either inactive an active drug or convert an inactive drug to active. Complex metabolic pattern would make SRDF much more difficult.

d. Duration of action:

The biological half-life and hence duration of action plays a major role. Drugs with half-life between 2-7 hrs are good candidates for SRDF. Drugs with biological half-life less than 2 hrs

should not be used such as Furosemide. At the other extreme a drug with half-life of greater than 8 hrs has inherently sustained action. Table 1

Table 1: Duration of Actions of Some Drugs

Drug	Half life
Metoprolol succinate	3-7 hr
Salbutamol	4-6 hr
Diltiazem	3-6 hr

e. Therapeutic index:

Drugs with narrow therapeutic index are unsuitable for incorporation in sustained release formulations. A drug with narrow therapeutic index needs frequent drug administration.[10, 12.]

Classification of oral controlled drug delivery system:

Oral controlled drug delivery systems can be divided into following class based on their mechanism of release the drug,

A. Diffusion controlled extended release

- Reservoir system
- Matrix system

B. Dissolution controlled extended release

C. Osmotic controlled extended release formulations:

D. Ion exchange resin

E. pH– Independent formulations

F. Gastroretentive systems.[14]

TECHNIQUES FOR PREPARING SRDF FORMULATIONS:

Different methods used are:

A. Based on drug modification:

i. Complex formation

The rate of dissolution of solid complex in biological fluids and rate of dissociation of complex in the solution are considered and they depend upon pH and composition of gastric and intestinal fluids.

ii. Drug-adsorbate preparation:

In this, the drug is insoluble. Drug availability is determined by rate of disabsorption.

iii. Pro drug synthesis:

They are inactive and need enzymatic hydrolysis for regeneration. Solubility, absorption rate of prodrug must be lower than parent drug.

iv. Ion exchange resins:

They are water insoluble, cross linked polymers containing salt forming groups. The drug is bound to the resin by using chromatographic column or by prolonged contact. Drug release from this complex depends on pH & property of resin. Drug that is attached to the resin is released by exchanging with the ions present in the GIT.

Example: Biphetamine.

B. Based on dosage form modification.

i. Microencapsulation:

It is a process in which tiny particles are surrounded by uniform coating (microcapsule) or held in a matrix of polymer (microsphere.) Spray drying is used which involves rapid evaporation of the solvent from the drug surface.

ii. Barrier coating:

In this one quarter of the granules are in non sustained form for sudden drug release, remaining part is coated for sustained release. Both these granules are filled in hard gelatin capsule or compressed in a tablet, and the release mechanism is by diffusion. Coating material used are fats, waxes.[15]

Matrix tablets:

One of the easy approaches to the manufacture of controlled release dosage forms involves the direct compression of blend of drug, retardant material and additives to formulate a tablet in which the drug is embedded in a matrix of the retardant. Alternatively drug and retardant blend may be granulated prior to compression.[14]

Matrix systems are widely used for the purpose of sustained release. It is the release system which prolongs and controls the release of the drug that is dissolved or dispersed. In fact, a matrix is defined as a well-mixed composite of one or more drugs with gelling agent i.e. hydrophilic polymers. By the sustained release method therapeutically effective concentration can be achieved in the systemic circulation over an extended period of time, thus achieving better compliance of patients. Numerous SR oral dosage forms such as membrane controlled system, matrices with water soluble/insoluble polymers or waxes and osmotic systems have been developed, intense research has recently focused on the designation of SR systems for poorly water soluble drugs.[16]

The term “matrix” indicates the three dimensional network containing the drug and other substances such as solvents and excipients required for the specific preparation. Matrix drug delivery systems release the drug in continuous manner. These release the drug by both dissolution controlled as well as diffusion controlled mechanisms.

Advantages of matrix tablets: [17]

1. Very easy to manufacture or fabricate in a wide range of shape.
2. Versatile and effective and has low cost.
4. Can be made to release high molecular weight compounds.
5. Suitable for both non degradable and degradable systems.
6. No danger of dose dumping in case of rupture.
7. Can be fabricated in a wide range of sizes and shapes.

Limitations of matrix tablets: [18]

1. The remaining matrix must be removed after the drug has been released.
2. The drug release rates vary with the square root of time.
3. Achievement of zero order release is difficult.
4. Not all drugs can be blended with a given polymeric matrix.

CLASSIFICATION OF MATRIX TABLETS:

I. On the basis of polymer or the retardant material used:

i. Plastic matrix tablet (hydrophobic matrices):

Controlled release tablets based upon an inert compressed plastic matrix have been used extensively. Release is usually delayed because the dissolved drug has to diffuse through capillary network between the compacted polymer particles. Plastic matrix tablets, in which the active ingredient is embedded in a tablet with coherent and porous skeletal structure, can be easily prepared by direct compression of drug with plastic materials provided the plastic material can be comminute or granulated to desired particle size to facilitate mixing with the drug particle. The concept of using hydrophobic or inert materials as matrix materials was first introduced in 1959.

ii. Hydrophilic matrix tablet:

The matrix can be formulated by direct compression of the blend of active ingredient and certain hydrophilic carriers or from a wet granulation containing the drug and hydrophilic matrix materials. The hydrophilic matrix requires water to activate the release mechanism having different advantages, including very easy of manufacture and excellent uniformity of matrix tablets. Upon immersion in drug release is controlled by a gel diffusion barrier that is formed and tablet erosion. The effect of formulation and processing variables on drug release behaviour from compressed hydrophilic matrices has been studied by number of investigators. The matrix building material with fast polymer hydration capability is the best choice to use in a hydrophilic matrix tablet formulation. An inadequate polymer hydration rate may cause premature diffusion

of the drug and disintegration of the tablet owing to fast penetration of water. It is particularly true for formulation of water soluble drug. The polymers used in the preparation of hydrophilic matrices are divided into following different groups as follow,

Cellulose derivatives:

- Sodium carboxy methyl cellulose
- Hydroxyethylcellulose,
- Hydroxypropylmethylcellulose (HPMC) and
- Methyl cellulose 400 and 4000 cps.

Non-cellulose natural or semi synthetic polymers:

- Chitosan, Galactose and Modified starches,
- Molasses, Polysaccharides of mannose and
- Agar-agar, Carob Gum, Alginates.

Polymers of acrylic acid:

- Carbopol 934 the most used variety.

Other hydrophilic materials

- Alginic acid,
- Natural gums,
- Gelatin.

iii. Fat-wax matrix tablet:

The drug can be incorporated into fat wax granulations by spray congealing in air, blend congealing in an aqueous media with or without the aid of surfactant and spray-drying techniques. In the bulk congealing method, a suspension of drug and melted fat-wax is allowed to solidify and is then comminute for controlled-release granulations. The mixture of active ingredients, waxy materials and fillers also can be converted into granules by compacting with roller compactor, heating in a suitable mixture such as fluidized-bed and steam jacketed blender or granulating with a solution of waxy material or other binders. The drug embedded into a melt of fats and waxes is released by leaching and/ or hydrolysis as well as dissolution of fats under the influence of enzymes and pH change in the GIT. The addition of surfactants to the formulation can also influence both the drug release rate and the proportion of total drug that can be incorporated into a matrix.

iv. Bio-degradable matrices:

These consist of the polymers which comprised of monomers linked to one another through functional groups and have unstable linkage in the backbone. It is biologically degraded or

eroded by enzymes generated by surrounding living cells or by non enzymatic process into olegomers and monomers that can be metabolised or excreted. Examples are natural polymers such as proteins, polysaccharides and modified natural polymers, synthetic polymers such as aliphatic poly (esters) and poly anhydrides.

v. Mineral matrices:

They are consisting of polymers which are obtained from various species of seaweeds. Example is Alginic acid which is a hydrophilic carbohydrate obtained from species of brown seaweeds by the use of dilute alkali.[17, 19.]

II. Classification on the basis of their porosity:

1. Micro porous system:

Diffusion in this type of system occurs essentially through pores. For micro porous systems, pore size ranges between 50-200 A°, which is slightly larger than diffusing molecules size.

2. Macro porous systems:

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

3. 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. [20]

Polymers used in the matrix:

Polymers are large chain macromolecules containing a variety of functional groups. Blended with other low- and high-molecular-weight materials, they can be tailored for variety of applications. Polymers are widely used in pharmaceutical dosage forms and food products, which include both synthetic as well as natural polymeric materials. The materials most widely used in preparing matrix systems include both hydrophilic and hydrophobic polymers. It is usually supplied in micronized forms because small particle size is critical to the rapid formation of gelatinous layer on the tablet surface. [21]

Hydrophilic polymers:

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

Hydrophobic polymers:

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

Waxes:

Carnauba wax, bees wax, candelilla wax, micro crystalline wax, ozokerite wax, paraffin waxes and low molecular weight polyethylene.

Insoluble polymers:

Ammoniomethacrylate co-polymers (Eudragit RL100, PO, RS100, PO), ethyl cellulose, cellulose acetate butyrate, cellulose acetate propionate and latex dispersion of meth acrylic ester copolymers.[22]

Mechanism of drug release from matrix tablet:

Drug present in the outer layer exposed to the *aqueous* solution is dissolved first and then diffuses out of the matrix. This process continues with the interface between the bathing solution and the solid drug moving toward the interior. It follows that for this system to be diffusion controlled, the rate of dissolution of drug particles within the matrix must be much faster than the diffusion rate of dissolved drug leaving the matrix. This system involves the following assumptions:

a) A pseudo-steady state is maintained during drug release,

b) The diameter of the drug particles is less than the average distance of drug diffusion through the matrix,

c) The bathing solution provides sink conditions at all times. [23, 24]

EVALUATION OF MATRIX TABLETS:

A. Pre compression characterization: [25]

i. Angle of Repose:

Angle of repose is defined as the maximum angle possible between the surface of pile of powder and horizontal plane. The angle of repose was calculated by substituting the values of the base radius ‘r’ and pile height ‘h’ in the following equation:

$$\text{Tan}\theta = h/r$$

Where, h = Pile Height, r = Radius of Pile

ii. Bulk Density:

For bulk density determination a weigh quantity of the powder material is introduce into a graduated measuring cylinder and volume of powder is determine. The bulk density was calculated by the following formula,

Bulk Density =Weight of samples in grams /Volume occupied by the sample

iii. Tapped Density:

Weighed quantity of the granular powder is introduced into a graduated measuring cylinder and is tapped mechanically, manually or using other method. Tapped density was calculate by the

following formula,

Tapped Density = Weight of samples in grams/Volume occupied by the sample

iv. Carr's Index:

One of the important measures that can be obtained from bulk and tapped density determinations is the percent compressibility or the Carr's index I, which is determined by the following equation**,**

$$\text{Compressibility Index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

v. Hausner's Ratio:

Hausner's ratio is related to interparticle friction and as such used to predict powder flow properties.

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

B. Post Compression Characterization:[26]

a. Hardness:

The resistance of tablets to shipping or breakage under conditions of storage, transportation and handling before usage depends on its hardness. The hardness of tablet was measured by Monsanto hardness tester and also can be measured by other tester like Pfizer tester, Strong cob tester. The hardness was measured in terms of kg/cm^2.

b. Thickness:

Thickness and diameter of tablets were important for uniformity of tablet size. Thickness and diameter were measured using Micrometer screw.

c. Friability:

Friability is the measure of tablet strength. Roche friabilator was used for testing the friability. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 minutes, the tablets were weighed and the percentage loss in tablet weight was determined.

% loss =Initial weight of tablets – Final weight of tablets/Initial weight of tablets*100

Table 2: Specifications For Tablets As Per Pharmacopoeia of India

Sr No.	Average Weight of Tablet	% Deviation
1	80 mg or less	10
2	More than 80 mg but less than 250 mg	7.5
3	250mg or more	5

d. Uniformity of Weight:

Weigh 20 tablets at random and calculate the average weight. Not more than two of the

individual weights deviate from the average weight by more than the percentage shown and none deviates by more than twice that percentage.

e. *In-vitro* Dissolution Studies:

In vitro drug release profile of matrix tablet is determined with the help of USP dissolution apparatus. In general, a single matrix tablet is placed in dissolution flask which contain 900 ml dissolution medium. The flask is maintained at 37º ± 0.5º C by a constant temperature bath.

Description about Natural and Synthetic Polymer Used in Sustained Release Dosage Form:

A. Natural polymer:

i. Xanthan gum:

Xanthan gum, a high molecular weight, water soluble, anionic-bacterial heteropolysaccharide, used as a rheology modifier is derived a result of microbial fermentation of glucose from the bacterial coat of *Xanthomonas campestris*. It is a hydrophilic polymer, biocompatible and inert which along with retarding the drug release provides the time dependent release kinetics.[27]

Pentoxifylline-controlled release tablets are prepared using xanthan gum and found that, the drug release rate decreased on increasing the concentration of xanthan gum in the prepared formulation, as reflected from the increase in the mean dissolution time. Also prepared propranolol hydrochloride-loaded matrix tablets using guar gum, xanthan gum, and hydroxypropylmethylcellulose (HPMC) as rate-retarding polymers and prepared tablets are evaluated for drug release in simulated gastric and intestinal media.[28, 29.]

ii. Pectin:

Pectin has been shown to be effective medium in controlling the release of the drug within the gastrointestinal tract. It been used as an adsorbant and bulk forming agent and it is present in multi-ingredient preparations for the management of diarrhea, constipation and obesity. It is also used as an emulsion stabilizer.

Experimentally, pectin has been used in gel formulations for the oral sustained delivery of Ambroxol. It has also been used in colon biodegradable pectin matrix with a pH sensitive polymeric coating, which retards the onset of drug release, overcoming the problems of pectin solubility in upper gastrointestinal tract. Pectin has been used as a component in the preparation of mixed polymer microsphere system with the intention of producing controlled drug release.[30]

iii. Guar gum:

In addition to the use of guar gum in food and pharmaceuticals, its utility in combination with other excipients has been reported. Guar gum hydrates and swells rapidly in aqueous media to form viscous dispersions or gel layer on the tablet surface. Consequently, drug releases out from

the guar gum tablet in a sustained release manner, achieving the desired kinetics. Currently guar gum introduced into new emerging area especially therapeutic and medicinal role as hypocholesterolemic and hypoglycemic agent. Guar gum is suitably inexpensive, commercially available and green (of natural origin) polymers for use as stabilizing agents for iron nanoparticles. It is most effective polymer for long-term stabilization of the nanoparticles.[31]

iv. Karaya gum:

Gum Karaya is a vegetable gum produced as an exudates by trees of the genus *Sterculia*. Gum Karaya is a dried gummy exudates obtained from the tree *Sterculia urens (*Sterculiaceae). The use of naturally occurring biocompatible polymeric materials has been the focus of recent research activity in the design of dosage forms for oral controlled release administration. Directly compress matrices is produced containing of karaya gum as a release-controlling agent. These swellable hydrophilic natural gums were used to control the release of varying proportions of two model drugs, caffeine and diclofenac sodium, which have different solubility in aqueous medium. Gum erosion, hydration and drug release studies were carried out using a dissolution apparatus (basket method) at two agitation speeds. Karaya gum displayed a much lower hydration capacity and a higher rate of erosion, markedly affected by agitation speed. The study concluded that Karaya gums produced near zero order drug release with the erosion mechanism playing a dominant role.[32]

v. Gum acacia:

Gum acacia or gum arabic is the dried gummy exudates obtained from the stem and branches of *Acacia senegal* (Linne) and other related species of acacia (Family Leguminosae). The gum has been recognized as an acidic polysaccharide containing D-galactose, L-arabinose, L-rhamnose, and D-glucuronic acid. Acacia is mainly used in oral and topical pharmaceutical formulations as a suspending and emulsifying agent, often in combination with tragacanth. It is also used in the preparation of pastilles and lozenges and as a tablet binder.

Gum Arabic was used as an osmotic, suspending and expanding agent in the preparation of a monolithic osmotic tablet system (MOTS) with two orifices on both side surfaces. Water-insoluble naproxen was selected as the model drug. The optimal MOTS found to be able to deliver naproxen at a rate of approximately zero order up to 12 h in pH 6.8. Cumulative release at 12 h is 81%, and is independent of environment media and stirring rate. Therefore, these MOTS can be used in the oral drug-controlled delivery field, especially for water-insoluble drugs.[33, 34]

vi. Alginates:

Alginates are natural polysaccharide polymers isolated from the brown sea weed (Phaeophyceae). Alginic acid can be converted into its salts, of which sodium alginate is the major form currently used. Alginates offer various applications in drug delivery, such as in matrix type alginate gel beads, in liposomes, in modulating gastrointestinal transit time, for local applications and to deliver the biomolecules in tissue engineering applications**.** [35] Alginates have proven to be effective for the symptoms of malignant wounds. Bleeding in malignant wounds is caused by the absence of platelets and the abundance of friable capillaries. Because bleeding occurs easily, it is essential that dressings do not adhere or cause trauma. Alginates are ideal for bleeding wounds as they have haemostatic properties.[36, 37]

vii. Tragacanth:

This gum is obtained from the branches of *Astragalus gummifer*, Family Leguminosae. Tragacanth when used as the carrier in the formulation of 1- and 3-layer matrices produced satisfactory release prolongation either alone or in combination with other polymers.[38]

viii. Ispaghula:

Psyllium or Ispaghula (*Plantago ovata*) is the common name used for several members of the plant genus *Plantago* whose seeds are used commercially for the production of mucilage. It is mainly used as natural retardant material.[39]

B. Synthetic:

i. Polymethacrylates:

Polymethacrylates are synthetic cationic and anionic polymers of dimethylaminoethyl methacrylates, methacrylic acid, and methacrylic acid esters in varying ratios. Several different types are commercially available and may be obtained as the dry powder, as an aqueous dispersion, or as an organic solution.

ii. Ethyl cellulose:

The main use of ethylcellulose in oral formulations is as a hydrophobic coating agent for tablets and granules. Ethylcellulose coatings are used to modify the release of a drug, to mask an unpleasant taste, or to improve the stability of a formulation, can be used on its own to produce water-insoluble films, High-viscosity grades of ethylcellulose are used in drug microencapsulation. In topical formulations, ethylcellulose is used as a thickening agent in creams, lotions, or gels, as a stabilizer for emulsions.[40]

iii. Carbopol:

Carbopol is a water soluble vinyl polymer, used as an emulsifying, stabilizing, suspending, thickening and gelling agent in many industries. Carbopol® is available in several different

grades Carbopol, Pemulen and Noveon polymers are powders averaging two to seven microns in diameter. They are produced from primary polymer particles of about 0.2 micron diameter. Each primary particle can be viewed as a network structure of polymer chains interconnected by crosslink. Without the crosslink, the primary particle would be a collection of linear polymer chains intertwined but not chemically bonded.[41]

iv. Hydroxy Propyl Methyl Cellulose: [40]

It is odorless and tasteless, white or creamy white colour, fibrous or granular powder. It is suspending, viscosity enhancing and film forming agent. HPMC, with its varieties dependent upon viscosity and proportion between its substituent, is most widely used in hydrophilic matrix sustaining release tablets and other type of controlled release pharmaceutical dosage forms, because of its characteristic namely non-toxic nature, its capacity to incorporate active. The K4M formulation showed a slightly higher drug release rate than that of K15M and K100M. The release profiles from the K15M and K100M were nearly same, so the viscosity of 15000 cps was suggested as the limit, above which the release rate remains unaffected. On the basis of viscosity HPMC classify as,

Viscosity (2% aqueous solution)

HPMC K100 LV**:**	100 cps
HPMC K4M**:**	4,000 cps
HPMC K15 **:**	15,000 cps
HPMC K100M **:**	1, 00,000 cps

Table 3: Different Drugs & Polymers For Sustained Release Matrix Tablet

Drugs	Polymer
Metoprolol succinate	HPMC K4M, Guar gum
Metoclopramide Hydrochloride	HPMC,CMC
Tramadol Hydrochloride	EC, HPMC K100M
Aceclofenac	Guar gum, Xanthan gum
Metformine Hydrochloride	HPMC K100M
Itopride	Sodium alginate, Pectin
Ambroxol Hydrochloride	HEC, HPMC

CONCLUSION:

Sustained release drug delivery system plays an important role to provide constant or nearly constant drug levels in plasma with reduced fluctuations, improved patient compliance and is beneficial than conventional dosage form. In sustain release drug delivery system matrix tablet beneficial than other release pattern, as sustain release matrix tablet deliver the drug in continuous manner which minimizes toxicity and other disadvantages associated with

conventional system. In sustain release delivery system both natural and synthetic polymer having hydrophilic and hydrophobic nature can be used, which prolong the time of release of active material from dosage form. This type of dosage form is easy to optimize and very easy to fabricate than other dosage form.

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