Available online on 15.06.2019 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Review Article

Sustained Release Drug Delivery System with the Role of Natural Polymers: A review

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ABSTRACT

An appropriately designed sustained release dosage form is opted to be a major goal in solving the problems which arises regarding the targeting of a drug to a specific organ or tissue and for controlling its rate of delivery to the target site. The development of oral sustained release system has proven to be a major challenge to formulation scientist due to their inability to restrain as well as localize the system at targeted areas of the gastrointestinal tract. Therefore the development of matrix type drug delivery system is promising option regarding the development of an oral sustained release system. There is availability of wide variety of polymers which helps the formulation scientist to develop sustained/controlled release products. The attractiveness of these dosage forms is increasing because of their awareness towards toxicity and ineffectiveness when administered by oral route in the form of tablets and capsules. Numerous advantages are provided by sustained release products over conventional dosage forms through optimizing various bio-pharmaceutics, pharmacokinetic and pharmacodynamics properties of drugs and finally leads to reduction in dosing frequency to such an extent that only once daily dose is required for therapeutic management with maximum utility of drug with reduction in both local as well as systemic side effects. They can cure or control diseased condition in shortest possible time with smallest quantity of drug to assure greater patient compliance. Polymer swelling, drug dissolution and its diffusion are the known mechanisms for drug release through polymer network.

Keywords: Oral drug delivery system, sustained release dosage form, matrix system, polymer swelling, drug diffusion.

Article Info: Received 01 May 2019; Review Completed 31 May 2019; Accepted 06 June 2019; Available online 15 June 2019

Cite this article as:

Sharma D, Dev D, Prasad DN, Hans M, Sustained Release Drug Delivery System with the Role of Natural Polymers: A review, Journal of Drug Delivery and Therapeutics. 2019; 9(3-s):913-923 **http://dx.doi.org/10.22270/jddt.v9i3-s.2859**

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INTRODUCTION

The oral drug delivery system is the most widely preferred and convenient route of drug administration. Due to high patient compliance, cost effectiveness, least sterility constraints, flexibility in the design of dosage form and ease of production causes this route to be more preferable than others. In oral administration the drugs are to be protected by unstable biological environment including drug degradation in the GIT tract and first pass metabolism in the liver after oral administration before reaching the targeted sites. Various challenges which are faced by oral drug delivery system are dissolution, permeability and solubility. Several pharmaceutical techniques have been found to stabilize and solubilize the active compounds in the GIT but they all failed to attain controlled and targeted release of oral drug as they all are capable of giving immediate and quick release. These days traditional drug delivery system has been characterized by the immediate release and repeated dosing of drug. These two factors leads to risk of dose fluctuation, this causes the need of formulation with controlled release that is capable of maintaining a constant and uniform blood levels. Drug delivery is the act or process for the administration of pharmaceutical compound in order to achieve or provide a therapeutic effect in diseased human's body. The pharmaceutical products which are made for the purpose of oral delivery mainly found in the form of immediate release type and conventional drug delivery systems, which are responsible for immediate release of drug for fast absorption. Thus Modified or Novel drug delivery systems have been formulated or manufactured for the improvement in the pharmacokinetic profiles of active pharmaceutical ingredients (APIs), patient compliance as well as causing reduction in side effects. The main objective or goal in designing these sustained release dosage form is to reduce frequency of dosing, increase the effectiveness of drug by the act of localization at the site where the drug has to act, reduce the amount of dose and to provide steady and

uniform delivery of drug. Predetermined patterns are determined already for the drug release in the gastrointestinal tract by the sustained release formulations. These formulations are well known for the continuous release of drug over extended period of time, therefore the use of hydrophilic polymer matrix is extensively used for formulating a sustained dosage form. The immediate release drug delivery system lacks dose maintenance, site target action and controlled release. The sustained release formulations acquire some swelling polymer or waxes which are the main necessities for controlling release rate [3, 5].

Drawbacks of Conventional Dosage Forms- The conventional drug delivery system is the classical methods for the delivery of the drug into the body.

1. Poor patient compliance.
2. The drug whose half- life is very short requires frequent dosing and ultimately leads to more chances of missing the dose. As the frequencies of drug administration depends on biological half-life and Mean Residual Time of drug.
3. Drug targeting is not easy to achieve.
4. To attain steady state condition becomes difficult because of the typical valley concentration appears due to frequent dosing.
5. The unavoidable fluctuations in drug level concentration may give rise to under medication or over medication due to unpredictable drug release pattern [6].
6. The fluctuations in drug levels may lead to rise of adverse effects especially with the one whose Therapeutic Index (TI) is small. And these fluctuations come whenever overmedication occurs.

Thus to overcome the drawbacks of conventional dosage form several technical advancements had led to the development of controlled and sustained drug delivery systems that could provide several number of therapeutic benefit.

SUSTAINED RELEASE DRUG DELIVERY SYSTEM

The therapy for chronic disease requires a repeated dose of the drugs to be administered. And for the drugs which possesses very short half- life are given several times a day. In order to get rid from this the development of sustained release dosage form is needed which helps in maintaining the therapeutic effective concentration of the drug over an extended period of time. The sustained release dosage form are the drug delivery system which are designed in order to provide a prolonged therapeutic effect by continuously releasing the medication over an extended period of time after the administration of a single dose of a drug of tablet. The ultimate aim of the therapy is to possess the steady state tissue level which is therapeutically effective and non-toxic for an extended period of time. The design of the proper dosage form is an important factor in achieving, providing and accomplishing this goal. The maximum drug bioavailability can be attained by tending and attempting to attain a maximum rate and extent of drug absorption. Sustained release dosage forms are considered as the best way to optimize the delivery of medication which is the utmost parameter to achieve a measure of control of the therapeutic effect and reduces the in vivo fluctuation [16].

ADVANTAGES OF CONTROLLED RELEASE DOSAGE FORMS-

Controlled release dosage forms belongs to the class of biologically active products from which the release of drug occurs in a planned, predictable as well as slower than normal manner for a prolonged period of time.

1. Controlled release dosage form results in the prolongation of drug action at a predetermined level by the maintenance of a constant, effective, drug level in the body as the kinetic pattern of peak valley which results from controlled release drug administration gets stabilized.

2. Minimization of adverse effects are seen with this dosage form due to less drug fluctuation as the release rate is already predetermined and its occurs in a constant way over an extended period of time.

3. Spatial placement of a controlled dosage form helps in the localization of drug action to a diseased organ, tissue, site and even the receptor is possible.

4. The main role of controlled release drug delivery is the achievement of target drug action by the use of carriers or chemical derivatisation to make the drug available to particular target that may be a tissue, cell or receptors.

5. It is a suitable delivery system for drugs which are having a short biological half-life (3-4 hours) and which rapidly eliminate from the body.

6. Reduction in drug toxicity occurs with this dosage form.

Improvement in drug bioavailability is seen because of spatial control [3, 7].

RATIONAL OF SUSTAINED RELEASE DOSAGE FORM

The basic rational of sustained release dosage form is to extend the duration of action of the drug ,to minimize the fluctuations in plasma level ,improved drug utilization ,less adverse effects., to reduce the frequency of the dosing and thus providing the uniform drug delivery. The main target by which sustained release delayed drug delivery system are able to show their well-defined action is by altering the pharmacokinetics and pharmacodynamics of pharmacologically active drug moieties by using novel drug delivery system or by doing the modification of molecular structure and physiological parameters inherent in a selected route of drug administration. The sustained drug delivery occurs when a polymer is combined with a drug or active agent such a way that the release from the bulk material is pre-designed and its release is also predetermined by the use of film forming polymer and enteric depending on its use respectively. Controlled and Sustained Release both are used in consistent and confusing manner. Both are used to represent separate drug delivery process. As the sustained release constitutes any dosage form that provides medication over an extended period of time and it shows that the system is able to provide some actual therapeutic control and that can be of a temporal, spatial nature or both. Sustained release system generally don't attain zero order type release but they try to mimic zero order release by providing drug in a slow first order [9,17].

OVERALL FUNCTION OF SUSTAINED DOSAGE FORM-

Sustained release systems can be used to protect the drug from degradation in the acidic environment i.e. low pH environment of the stomach from irritation by the drug. In such circumstances the drug release should be delayed until

and unless it reaches the small intestine. In order to achieve this mission the use of polymers are needed as an important measure to control the release and as film forming agent. The dosage form (For example – a tablet or the granules before tableting) can be coated with an appropriate polymer. The polymer dissolves as a dependent function of pH that is when the dosage form travels from the low pH environment which is found in the stomach to the higher basic pH environment of the small intestine. As the small intestine is having large surface area because of the presence of microvilli and it is the only the site of area where polymer coat dissolves. The use of Microencapsulation *is* the technique by which coating can be applied in a proper way to enhance the formulation of sustained release dosage form. Microencapsulation is the means of applying thin coatings to small particles of solids or droplets and dispersions. It is differentiated and different from macro coating in the means that the former involves the coating of particles ranging from several tenths of a micron to 5000 microns in size. It is the means of converting liquids to solids capable of changing colloidal and surface properties as well as controlling the release characteristics of coated materials. Along with this property they are also capable of masking the taste of tablets, powders, suspensions etc.

Various techniques used for this purpose are Air suspension, Coacervation phase separation, Spray Drying and Spray Congealing [8]

As the basic aim of sustained release dosage form is to achieve and maintain therapeutic blood level in a target system for an extended period of time at a constant level. This attempt usually tries to follow the zero order release from the dosage form. Zero order release comprises the drug release from its dosage form that is independent of the amount of the drug in the delivery system i.e. it does not depend on concentration and release is in constant manner. Sustained release systems in general do not attain this type of release and try to follow and mimic zero order release by continuously releasing the drug in a slow first order manner (i.e. concentration dependent) [11, 17].

METHOD OF FORMULATION [6, 8]

Sustained release dosage form may contain-

- Maintenance Dose
- Loading Dose

Sustained release dosage form includes all drug delivery systems that achieve slow release of drug over an extended period of time. Basically a sustained release oral dosage form is designed to rapidly release pre-determined fraction of the total dose (loading dose) into gastrointestinal tract, which will produce the desired pharmacological response as promptly as possible and the remaining fraction of the total dose (maintenance dose) is then released at a controlled rate to maintain the steady state. The controlled release of the drug product is designed so that the release rate of maintenance dose is equal to the elimination rate. The constant blood levels can be achieved from controlled release system and the prolonged release of the dosage form reduces the fluctuation in plasma by slowing down its absorption rate so that its slower drug release rate can be achieved as well as can be maintained. The Maintenance dose also called as slowly available portion which will release the drug slowly and will maintain the therapeutic level for an extended period of time. The Loading dose is the immediately available portion which help in obtaining the therapeutic level quickly after administration. If the drug at the absorption site is to remain at constant rate then the rate of release of the drug from the maintenance dose should follow zero order rate. Zero order means the drug release is independent of initial concentration or amount of drug. The release of drug from the loading dose should follow first order rate release i.e. dependent on initial concentration of the drug [6, 8].

CLASSIFICATION OF SUSTAINED RELEASE DOSAGE FORM

Sustained release drug delivery system can be considered as an effective advance toward solving the problem concerning drugs have a short half-life are eliminated quickly from blood circulation require frequent dosing. In order to avoid this problem oral sustained release formulations have been developed in an attempt to release the drug slowly into the g.i.t and maintain a constant drug concentration for long period of time. The Sustained release is a type of dosage form that releases the drug at a predetermined rate in order to maintain the constant drug concentration for a specific period of time with the minimum side effects. The sustained release dosage form can be classified as such [7- 10].

Continuous release system

These are the systems which releases the drug for a prolonged period of time along the entire length of GIT tract with the normal transit of the dosage form. The various systems under this category is-

(A). Diffusion sustained release system

(B). Dissolution sustained release system

(C). Dissolution and diffusion sustained release system

(D). Ion Exchange resin- drug complex

(E). pH dependent formulation

(A). Diffusion sustained release system [11, 16]

Diffusion systems are characterized by the release rate of a drug which is being dependent on its diffusion through an inert membrane barrier. In this type of systems the diffusion of dissolved drug occurs through a polymeric barrier which is a rate limiting step. The drug release can never occur at zero order. The diffusional path length of drug increases with time as the insoluble matrix gradually gets depleted of the drug. In these systems there is a water insoluble polymer which is responsible for the control of flow of water and the subsequent release of dissolved drug from the dosage form. Diffusion occurs when a drug passes through a polymer that forms the controlled release device. The diffusion can occur through the pores in the polymer matrix or by passing between the polymer chains. In this case the diffusion of the drug molecules serves the basis of these controlled drug delivery system. Diffusion process is defined as the movement of the molecules of drug from a region of higher concentration to a region of lower concentration. The diffusion controlled system are formulated either by these two methods i.e. Encapsulating the drug particles in a polymeric membrane or by dispersing the drug in a polymeric membrane.

Types of Diffusion sustained release systems

- Reservoir devices
- Matrix devices
- Erosion controlled devices [13].

Reservior Devices- In this type of system, water insoluble polymeric material encases a core of drug. The drug will get partition into the membrane and exchange with the fluid

surrounding the particle or tablet.The active drug agent will get released into the surrounding media environment by diffusion process through the rate limiting membrane. In the reservoir devices the drug delivery rate remains fairly constant. The additional drug will again enter the polymeric membrane then diffuses into the periphery and gets exchanged with the surrounding media. The drug release from this system takes place by diffusion process.

Matrix Devices- A matrix system consists of active and inactive ingredients that are homogeneously dispersed and mixed in the dosage form. The drug is dispersed as the solid particles within a porous matrix formed of a water-insoluble polymer. The drug particles which are located at the surface of the release unit will be dissolved firstly and will release the drug release rapidly. Thereafter, drug particles at a successively increasing distance from the surface of the release unit will be dissolved and will release by the diffusion in the pores to the exterior of the release unit. Matrix can also be defined as well mixed composite of one or more drugs with gelling agent's i.e. hydrophilic polymers. Matrix systems are widely used for sustaining the release rate. It is the release rate which prolongs and controls the release of the drug. Release from matrix type formulation is governed by Fick's first law of diffusion [7-10].

Advantages of Matrix System

Unlike reservoir and osmotic systems, products based on matrix design can be manufactured by using conventional processes and its equipment's. Secondly, development cost and time associated with the matrix system generally are viewed as variables, and no additional capital investment is required. A matrix system is capable for accommodation of both low plus high drug loading and active ingredients by providing a wide range of physical as well as chemical properties [2-5].

These diffusion controlled systems are the type of rate programmed drug delivery system from which the drug release has been programmed at specific rate profiles. In these systems the rate controlling step is not the dissolution rate of drug or release controlling element but it is the diffusion of dissolved drug molecules through the rate controlling element. The rate controlling element in such types of the systems are insoluble, non-erodible and non-degradable and therefore these are porous in their nature and allows the diffusion of dissolved drug. Thus they can be classify according to the mechanism by which their rate controlling element controls drug diffusion and these are divided two categories –

Porous matrix controlled systems

In these systems the rate controlling element is either a water swell able material i.e. hydrophilic polymers or gums such as guar gum, xanthan gum, high viscosity grades of hydroxypropyl methylcellulose (HPMC) and hydroxypropyl cellulose, alginates etc. or the non-swell able water insoluble polymer such as Ethyl cellulose. Various polymers are used for the maintenance of these systems which are listed below.

Properties of basic polymers used [8]

- **HPMC** is considered as an ideal polymer for film coating but when used alone it has the tendency to bridge or fill the debossed tablet surfaces. The mixture of HPMC with other polymers or plasticizers is used to eliminate bridging and filling problems. It is also used in glossing solutions (Chauhan *et al.,* 2012).
- **Ethyl cellulose** is completely insoluble in water and gastrointestinal fluids and therefore it cannot be used alone for tablet coating. It is generally combined with water soluble additives e.g. HPMC in order to prepare films which is having reduced water solubility properties. The combination of ethyl cellulose with water soluble additives are most widely used for the preparation of sustained release tablets.
- **Povidone** is a synthetic polymer consisting of linear 1-vinyl-2 pyrrolidinone groups. The degree of polymerization results in various molecular weight range. Povidone is usually available in four viscosity grades which are identified by their K values such as K-15, K-30, K-60 and K-90. The average molecular weight of these are 10,000, 40,000, 160,000 and 360,000. The most important use of it as a tablet binder and in a tablet coating. It can be cross-linked with the other materials to produce films with enteric properties.

Porous membrane controlled systems

These are those systems in which the rate controlling element is non-swell able water insoluble polymer such as ethyl cellulose or polymethacrylate which can control the drug release through the micro pores present in the membrane or matrix structure. In Matrix systems the drug active agent is present as a dispersion within the polymer matrix and they are usually formed by the compression of a polymer and drug mixture or by dissolution or melting [12.13].

Drug release properties from monolithic devices

From an engineering point of view, the term "matrix" indicates a three-dimensional network, more often polymeric, fabricated for a particular application and containing an active agent (drug) and other substances such as solvents and excipients. There are three methods for the preparation of polymer monolithic systems. The first one is based on mixing the drug, as a thin powder, with the prepolymer and subsequently placing the whole mixture in the polymerization reactor. A matrix can be prepared in advance and then it is made to put in contact with a highly concentrated drug solution so that swelling of the matrix can occur. The solvent is then removed by a physical treatment. The second approach depends on mechanic-chemical activation, by which the loading of a drug is made into a polymeric carrier, thus helps in the avoiding the use of those solvents whose elimination is a very expensive and delicate operation. Supercritical fluid techniques is also used for drug loading in the matrices. The supercritical fluids are supposed to be dense as liquid but viscous as gas, and easily swell the matrix (bringing the drug inside the matrix or extracting solvents) and can be easily removed by decreasing pressure. These supercritical fluids are used when drug is not showing compatible with other polymers for the loading purpose. The simplest way for making or developing a monolithic system is to compress, the proper ratio of the polymer, drug and the excipients [15, 16].

CLASSIFICATION OF MATRIX TABLETS-

(a) On the Basis of Retardant Material Used:

Matrix tablets can be divided in to five types-

1. Hydrophobic Matrices (Plastic matrices) –

The idea of using hydrophobic or inert materials as matrix materials was first introduced in 1959. It is the method of obtaining sustained release effect from an oral dosage form in which the drug is mixed with an inert or hydrophobic polymer and then compressed into a tablet. Sustained release is produced due to the concept that the dissolving drug has diffused through a network of channels that are present between compacted polymer particles. Examples of

materials that are used as an inert or hydrophobic matrices include polyethylene, polyvinyl chloride, ethyl cellulose and acrylate polymers and their copolymers. The rate-controlling step in these formulations systems is liquid penetration into the matrix. Hydrophobic matrix tablets are the most frequently and largely used as sustained release oral dosage forms intended for oral administration in which the very possible mechanism of release of drug from tablet matrix is diffusion. Hydrophobic matrix systems are mainly formulated by the use of waxes and can be suitable for drugs which have a high solubility. Wax based matrices have been explored to ascertain the factors that would affect the release of drug. Hydrophobic systems are the only systems where the use of polymer is not essential to provide the controlled release however the use of insoluble polymers can be used. The primary rate controlling elements of hydrophobic matrix are found to be water insoluble in nature. The required ingredients mainly are waxes glycerides fatty acids and the above mentioned polymers [11].

The drug release has been successfully modulated by the use of hydrophobic matrices as these matrices are based on waxes which can modify release rate by increasing the amount of drug or wax concentration, make the system also capable for incorporating hydrophilic polymers which helps in the enhancement of drug release by getting swell. On coming in contact with water a hydrophilic matrix increases in size due to the fact of entry of the solvent. Then this causes the polymer to swell up forming a barrier to drug release. The drug particles would then move through this gel layer by diffusion or erosion of the gel eventually allows the drug to get released. This type of systems are the type of monolithic matrix system which allows the drug to be encapsulated or dispersed in a matrix. To modulate the drug release it is necessary to add or incorporate the soluble ingredients such as lactose in the formulation. Diffusion of active ingredient from the system is the release characteristic of drug. The diffusion of the active ingredient from the system is the release mechanism, can be best explained by Higuchi equation which is also known as square root of time release kinetic. The square root of time release profile is thought to be with a porous monolith, where the release rate from such system is proportional to the drug loading. Additionally the hydrophobic matrix systems are not suitable and compatible for insoluble drug as the concentration gradient is too low for the adequate release of the drug to occur. While considering the formulation design, incomplete release of drug within the gastrointestinal tract time proves to be a potential risk and need to be focused and taken into account during the process of development [4-7].

2. Hydrophilic Matrices

Hydrophilic matrix tablets are the most frequently used sustained release oral dosage forms intended for oral administration. The primary rate limiting step is that the polymers would swell when it comes into contact with water and forms a gel layer on the surface of the system. When the release medium is thermodynamically compatible with a polymer then the solvent gets penetrated into the free spaces present between the chains of the macromolecules. The polymer undergoes a relaxation process due to the stress of the penetrated solvent. This relaxation process causes the polymer chains to become more flexible and the matrix swells as well as it also allows the encapsulated drug to diffuse more rapidly out of matrix. Hydrophilic matrix can be formulated by the method of wet granulation of the drug and hydrophilic matrix materials or by the use of the direct compression of the blended mixture of active ingredient with certain hydrophilic carriers. The hydrophilic matrices offer several advantages such as ease of the manufacture, cost effectiveness, uniformity of matrix tablets and broad regulatory acceptance. The best choice regarding the use of the hydrophilic polymers in matrix tablet is its capability for matrix building material with fast polymer hydration capability. An insufficiency in the polymer hydration rate may cause premature diffusion of the drug and easy disintegration of the tablet because of the faster penetration of water. But on the other hand the drug release process could take more time to diffuse out of the matrix as matrix swelling lengthens the diffusion path. Various factors which can determine the drug release from the dissolvable matrix are [12, 13].

- Swelling
- Diffusion
- Polymer dissolution [11].

This polymer dissolution is another important factor which has to be taken into consideration from this hydrophilic matrix and can modulate the drug delivery rate. In the most drug release kinetics the two predominant factors for specific type of polymers are the swelling and dissolution. The presence of water decreases the glass transition temperature which in turn gives rise to the transformation of glassy polymer to rubbery phase i.e. gel layer [11, 13].

Glass Transition Temperature- The glass transition temperature is an important property while considering polymers for a particular use. It is the temperature below which the physical properties of polymers changes into those of glassy or a crystalline state. Above which they behave like rubbery materials. As in hydrophilic matrix the use of HPMC is done to provide swell able properties. The glass transition temperature for HPMC is from 184 degree Celsius to below 37 degree Celsius. The presence of water decreases the glass transition temperature thus giving the rise to rubbery phase of polymer that is the gel layer. Favoring of the transportation of dissolved drug is developed by the enhanced motility of the polymeric chain. The Swelling or the volume increase of the matrix is determined by the polymer relaxation mechanism. The main polymers which are used in the preparation of hydrophilic matrices are Hydroxypropyl methylcellulose, hydroxypropyl cellulose, carbopol, alginates and xanthan gum [10, 11].

The hydrophilic matrices has most widely gained acceptance in the use of sustained drug delivery because of their cost effectiveness, flexible nature and it is also accepted on regulatory basis. Formulation of the drugs in the gelatinous capsules uses hydrophilic polymers which has high gelling capacities which are used as base excipients are of particular concern in the field of sustained release. Thus Matrix can be defined as well mixed composite of one or more drugs with the use of gelling agent i.e. hydrophilic polymer and therefore these systems are called as swell able sustained release systems.

3. Fat-wax matrix tablet

The drug can be incorporated into fat wax granules by the method of the spray congealing in the air, blend congealing in an aqueous media with or without the need of the surfactant and spray drying techniques. By the technique of bulk congealing method, a suspension of drug and melted fat wax is allowed to solidify and then it is allowed for comminuted in order to obtain the sustained-release granulations. The mixture of active ingredients, waxy materials and other additives can also be converted into granules by compacting with the use of roller compactor and then heating in a suitable mixture such as fluidized – bed and

steam jacketed blender or granulating it with a solution of waxy material or other binders. Hydrolysis, leaching and dissolution of fats under the influence of enzymes serve as the important characteristics tool for the drug release which is embedded into the melt of fats and waxes. These matrices prepared by the lipid waxes and other related materials. Drug release from such matrices can also follow the both pore diffusion and erosion. Release characteristics are therefore said to be more sensitive to digestive fluid composition than to totally insoluble polymer matrix. Carnauba wax in combination with stearyl alcohol or stearic acid has been commonly used for the retardant base of many sustained release [10, 11].

4. Biodegradable matrices

These matrices consist of the polymers which are composed of monomers that linked to one another with the help of the functional groups and pursue an unstable linkage in the backbone. It is degraded or eroded biologically by the help of enzymes which are produced in the living cells or by non – enzymatic process into the formation of oligomers and monomers that can be easily metabolized or excreted from the body. Examples includes the natural polymers such as proteins, polysaccharides, modified natural polymers and synthetic polymers such as aliphatic polyesters, poly anhydrides, polycaprolactone etc.

5. Mineral matrices

These type of matrices are consist of polymers which are obtained and found from various species of seaweeds. Example include alginic acid which is a hydrophilic carbohydrate obtained from species of brown seaweeds with the use of dilute alkali [10, 11].

Mechanism of drug release from the matrix system

The drug in the outside layer is exposed to the bathing 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 which is 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 occur at much faster than the diffusion rate of dissolved drug leaving the matrix. In a hydrophilic matrix, there are two opposite mechanisms are responsible for the drug release: Fickian diffusional release and relaxation release. Diffusion is not the only way by which a drug is released from the matrix; the erosion of the matrix following polymer relaxation contributes to the overall release. (a).The swelling front- As the water enters into the matrix, the polymer undergoes passage from the crystalline state to a hydrated or gelified state.

(b).The erosion front or dissolution front-This point separates the gelified zone from the matrix of the solvent.

c). Diffusion front (solid drug–drug solution boundary) - This is located between the swelling and erosion fronts and is responsible for the separation of the zone of the gelified matrix which is containing the drug dissolved in the medium from the zone of the matrix containing the undissolved solid drug [5-7].

The relative contribution of every component reflects their role to the total release and it is primarily dependent relative on the properties of a given drug. For example, the release of a sparingly soluble drug from hydrophilic matrices follows the immediate absorption of water and therapeutic activity of drug by a swelling-controlled diffusion mechanism. When the water penetrates into a glassy polymeric form of the compound matrix, the polymer swells and its glass transition temperature is lowered. At the constant time the dissolved drug diffuses through this swollen rubbery region into the external dissolution releasing medium. This type of diffusion and swelling does not basically follows this Fickian diffusion mechanism. Solvent diffusion into polymers is central to their performance in the controlled delivery pharmaceutical products. HPMC is a polymer commonly used in the production of tablets to control the release of the drug. A layer of hydrogel is formed by polymer hydration and chain relaxation when the tablet coating is in contact with water. This layer represents a barrier that retards processes of further water uptake and of drug release. Swelling-controlled systems basically composed of a uniformly dispersed or distributed drug within a biodegradable and swell able polymer. These swell able polymers are hydrophilic in nature so that when in contact with water, the latter is absorbed into the polymer, thereby swelling the polymer matrix. The swelling helps in loosening the polymer entanglement leading to disentanglement of the polymer. The polymer matrix swelling leads to the formation of a rubbery region, in which there is better drug mobility due to lower polymer concentration. This helps in the enhancement of release characteristics of the drug which not only depends on the diffusion rate of the drug but also on the polymer disentanglement and dissolution processes [12, 15].

Erosion controlled devices- The biodegradable polymers are mixed with drug or active agents in this system. With the access of natural biological processes the materials undergo degradation and the release of drug occurs at the constant rate. Hydrolysis plays a pivotal role in the degradation of biodegradable polymer chains into biologically acceptable smaller compounds. The release of drugs is mainly controlled by the controlling rate of the polymer matrix.

Erosion is mainly defined as the physical disintegration of a polymer matrix coating by the result of degradation and it can be characterized by the loss of polymer material from the surface generally in the physical state. The main causes of the degradation or hydrolysis of the polymer chains which are entangled are the osmotic pressure, hydrodynamic pressure i.e. the pressure exerted by excipients that imbibe water and undergoes swelling, enzymes, change in pH and finally causes fragmentation [12, 15].

Depending on the erosion mechanism polymers can undergo two types of erosion

Surface erosion -The erosion occurs from the surface layers of the device and the gradual decrease in the size of the device occurs but the bulk phase of the system remains unchanged and undegraded. This process is also called as the heterogeneous erosion because the difference in the erosion rate between the surface and the center of the matrix occurs [12].

Bulk erosion – The erosion occurs throughout the bulk of polymer and therefore this process is also known as homogenous erosion. Bulk erosion occurs when the water penetration is readily to occur or is easily able to penetrate the matrix of the system [15].

(B). Dissolution Sustained System

A drug with a slow dissolution rate will effectively show the sustaining properties as the release of the drug will get limited by the rate of dissolution. Sustained release preparation of drugs can be formulated by making their rate of dissolution to be lowered or decreased. The approaches to achieve this sustained effect includes the preparation of the appropriate salts or derivatives and coating the drugs with

slowly dissolving materials called polymers or incorporating it into a tablet with the use of a slowly dissolving carrier. These systems are most commonly used in the formulation of enteric coated dosage forms. To protect the stomach from the effects of drugs such as aspirin, a coating that gets dissolved in the alkaline media is commonly employed. This results in the inhibition of the release of drug from the device until it reaches the site of higher pH of the intestine. In most of the circumstances an enteric coated dosage forms are not truly showing sustaining effect but still serve as a useful function in directing release of the drug to a special site [6, 15].

Types of dissolution sustained release drug delivery system

Reservoir type- The drug is coated with a given thickness of the coating, which gets slowly dissolved in the contents or substances of gastrointestinal tract. By doing alternation of the layers of drug with the rate controlling elements, a pulsed delivery can be achieved. If the outer layer is quickly releasing bolus dose of the drug then initial levels of the drug in the body can be quickly established with pulsed intervals. An alternative method is to administer the drug as a group of beads that acquires the coating of different thickness. As the beads have different coating thickness therefore their release takes place in a progressive manner **Matrix Type-** These are common type of dissolution sustained dosage form. Here the drug can be either in the form of the impregnated sphere or a drug impregnated tablet which will be subjected to slow erosion. Two types of dissolution sustained pulsed delivery systems.

- The Single bead type device with alternating drug and rate-controlling layer.
- The Beads containing drug with different thickness of dissolving coats.

Amongst the sustained release formulations the hydrophilic matrix technology is the most widely used and preferred drug delivery system due to following advantages-

- It provide desired release profiles for a wide therapeutic drug category, dose and solubility [1, 2].
- It is simple and cost effective manufacturing using existing tableting unit operation equipment. Occupies broad regulatory and patient acceptance.
- The ease of modulating drug release is possibly guaranteed through level and with the choice of polymeric systems and function coatings.

(C). Dissolution and diffusion sustained release system

In these systems the rate of drug release is controlled by the dissolution of drug as dissolution are responsible for the creation of the pores in the partially soluble membrane. The pores which are formed by this process of dissolution allows the entry of aqueous medium into the core which is composed of drug. Thus drug dissolution is the main enforcement factor for the diffusion of dissolved drug out of the system. These systems are combination of two or more processes. The use of non-swell able and swell able polymers used for the development of this system as they are composed of reservoir and matrix system. The non-swell able polymers used for this purpose are Ethyl cellulose and polymethacrylate as these systems are capable of controlling the release of drug owing to their factors such as thickness, insolubility or slow dissolution or porosity. The best example for the swelling purpose is hydroxyl propyl cellulose (HPMC) polymers as they are capable of forming hydration barrier for the constant release of drug [1, 2].

Mechanism of drug release from dissolution controlled system

The drug with slow dissolution rate can show the sustaining properties as the discharge of the drug will be limited by the rate of dissolution. In reality it is possible to prepare extended release products by decreasing the dissolution rate of drugs that are highly water soluble. Coating of the drug with a gradually dissolving material – encapsulation dissolution. Incorporation of the drug as a tablet in a slowly dissolving carrier matrix can help the dissolution to get manage. But the major disadvantage is that the drug release rate continuously decreases with time. The dissolution method can be depicted as the diffusion-layer-controlled. The rate of diffusion from the solid surface to the bulk of the solution through an unstirred liquid film is considered to be rate-determining step. The dissolution release rate occurs at steady-state can be well described by the Noyes-Whitney equation [8].

(D). Ion- Exchange resin drug delivery system

Ion-exchange systems make use of resins composed of water-insoluble cross-linked polymers. These used polymers are constituted of the salt-forming functional groups in repeating positions on the polymer chain. The drug is bound to the resin and gets released by exchanging with appropriately charged ions in contact with the ion-exchange groups.

Anion Exchangers - Resin+ - Drug- + Cl- goes to Resin+- Cl- + Drug-

Cation Exchangers - Resin-- Drug+ + Na+ goes to Resin- - Na+ + Drug+

The ion exchange resins are mostly cross linked water insoluble polymers which are carrying functional groups present in their ionisable form. The resins are used in numerous pharmaceutical applications mainly for the establishment of controlled release dosage form and taste masking systems. The resin forms the irreversible complex with ionisable drugs and resin bound drug has to be removed when appropriate ions are already in contact with ion exchanged groups. In addition to these functions resins are employed as they are capable to disintegrate because they are having ability to swell. The rate of drug diffusion out of the resin is controlled by three factors-

- Area of the diffusion which the drug has to travel for absorption.
- The path length of diffusion.
- Rigidity of the resin which is the major factor in the amount of cross-linking agent used to prepare the resin. For the better release mechanism from this system is to apply coating on the ion-exchange resin with the use of hydrophobic rate-limiting polymer i.e. by the use of microencapsulation process [10, 14].

(E). pH-independent formulation

As most of the drugs are either weak acids or weak bases the release from sustained release (SR) formulations is pH-dependent. But the addition of the buffers such as salts of amino acids, citric acid, phthalic acid, phosphoric acid or tartaric acid can be added to the formulation in order to help to maintain a constant pH therefore rendering pH-independent drug release. A buffered sustained release formulation can be prepared or formulated by mixing a basic or acidic drug with one or more buffering agent, granulating

with the use of an appropriate pharmaceutical excipients and coating with polymer that is permeable to gastrointestinal fluid. When this fluid penetrates through the membrane then the buffering agents adjust the fluid which comes inside in the polymer coating to suitable constant pH thereby rendering a constant rate of drug release [14].

Role of polymers in sustained dosage form-

The use of polymers is inseparable part of sustained dosage form. The first polymeric devices developed for controlled drug release system was done in 1960. The polymer based controlled drug delivery systems are generally classified as Reservoir Membrane Devices and Matrix Monolithic Devices .In both of these the drug release is controlled by the polymeric membrane that surrounds the drug moiety. These polymeric membranes can be sub categorized into nonporous, micro porous, hydrophobic, hydrophilic substances like hydrogels and water swollen polymers. Various kinds of cellulose materials are developed for this purpose enhancement like cellulose triacetate, polycarbonate and polypropylene. These polymers help in the formation of membranes with the diameters of the order 1.5×10^{-3} µm to several microns. In transdermal drug therapy the use of polyacrylate, vinyl polymers, polyurethane and cellulose derivatives are used commonly. Both acrylic and cellulosic polymers are used as film forming agents which allow the formation of tough protective coatings. The availability of chitosan as a film forming agent permits it wide use in the formulation of film dosage form. Before casting into films chitosan can be dissolved in organic acids such as lactic acid and acetic acid. For the direct compression tableting process Starch acetate (SA) polymer has been discovered as a novel and multifunctional excipient. Materials such as fibrinogen, fibrin and collagen have been investigated as suitable carriers for novel drug delivery system. In the terms of non-toxicity and biocompatibility to most tissues the collagen has efficient structural, physical, chemical and immunological properties that can be easily altered. The drug release rate is influenced by factors such as diffusion across the membrane, tablet coating so that polymer doesn't undergo two factors during its lifetime i.e. dissolution and degradation [11, 13].

THE MECHANISM OF SWELLING, EROSION AND DRUG RELEASE FROM HYDROPHILIC POLYMERS

The three steps which are involved in the drug release from hydrophilic polymers are the following as the present research study and thesis work also deals with the usage of these polymers-

(1). Polymer Swelling

(2). Drug dissolution

(3). Matrix Erosion

When the drug loaded with swell able cellulose ethers based on hydrophilic matrices are exposed to dissolution fluid then the steep water concentration gradients are developed between the dissolution fluid and the outermost surface of matrix tablet. This lead to the water imbibition into the polymer matrix network. When the dry matrix tablets are introduced into the liquid system the diffusion coefficient tends to be very low as compared to the highly swollen gels where it is of the same magnitude as pure water. Thus the liquid acts as a plasticizer and the glass transition temperature reduces from 154 – 184 °C to around the system temperature 37 °C. As the glass transition temperature becomes equal to the temperature of the system the polymer chains starts to undergo relaxation and finally takes the suitable form of disentanglement therefore increasing the molecular surface area. This phenomena of the polymer chain relaxation is called as the Swelling. Swelling plays an important role in the release of drug.

Polymer Swelling- When the polymer chain undergoes disentanglement after their glass transition temperature becomes equal to the temperature of system then the swelling of the polymer occurs which results in the increase of the molecular surface area. At this point the continuous inward ingression of liquid causes breakage of the hydrogen bonds formed during tablet compaction and can lead to the development of new hydrogen bonds accommodating water molecules. Thus the reduction in transition temperature and the formation of new hydrogen bonds leads to the swelling of polymer chains. As a result, a thick gelatinous layer forms on the surface of matrix tablets commonly known as a gel layer as MC/HPMC pass from the amorphous glassy state to the rubbery state and forms the gel like layer [2, 5].

The transition temperature of HPMC can become lowered up to 40 degrees Celsius by the reduction of hydroxyl propyl molar substitution. At the lower temperature the polymer chains undergo hydration and become dehydrated as the temperature increases. Therefore the glass transition temperature gives information about the nature of the polymer and it is defined as the temperature when a thermoset polymer goes from an amorphous rigid state to a more flexible state. The normal state of polymers usually occurs in the amorphous solid form at the room temperature. In case of HPMC the glass transition temperature increases as the methoxyl and hydroxypropyl content ratio decreases and causes loss of hydrogen bonding network between cellulose. And finally it leads the polymer molecules to get locked into rigid amorphous structure due to short chin length and molecular chains do not have enough energy present in them to make them to move around. But as the glass transition temperature decreases there is a formation of new hydrogen bonds which results in swelling of the polymer chains and eventually leads to increase in surface area.

On the basis of the development of the gel layer the matrix tablet gets divide into three distinguishable regions-

1). Erosion Front- It is the highly swollen outer region which consist of the highest amount of water molecules but is considered to be weak in terms of the mechanical strength. And this layer acts as a diffusion barrier which serves the function of prevention of water penetration into the other two regions.

2). Dissolution Front- It is the middle region and is considered to be moderately swollen and has relatively more strength than the outer one.

3). Swelling Front- It is the innermost region and forms the core of the tablet which remains dry and has the capacity to maintain its glassy state for a longer period of time

4). Penetration Front- This layer exists between the dissolution and swelling front and is responsible for adding further complexity to the system.

The gel layer grows continuously time as the water penetrates into the matrix tablet. The polymer chains present on the surface of matrix tablet hydrate quickly as compared to those which are present inside the core and contact with the liquid causes chain relaxation (swelling) which causes the erosion of the matrix. Instantaneously, the outermost layer becomes fully hydrated and relaxation occurs which causes the disentanglement of polymeric chains which means breakage of the polymeric network which is responsible for the sustaining action of the drug.

Consequently the matrices start to dissolve from their surface as water continuously permeates towards the core. The relative rates of liquid uptake and erosion of a polymer matrix play a critical role in controlling the rate of drug release. The swelling, matrix erosion, drug release mechanisms are dependent on the concentration, degree of substitution and the polymer chain length of HPMC. It has the capacity to hydrate quickly to form a gel layer before the drug entrapped in the tablet matrix can dissolve. The

Two processes which are involved in the dissolution of hydrophilic matrix tablets which can further lead to polymer erosion are the following-

- Disentanglement of the polymer chains which are present at the surface of matrix tablets.
- Second step involves the subsequent transport of the core drug into the surrounding medium or bulk solution after disentanglement.

The physical entanglement of the polymer chains makes the polymer as well as the drug core to get rid or to become safer from the dissolution process itself. But with the passage of the time as the polymer remains no longer stronger and reduces its structural integrity the dissolution of the polymer which is present at the outer surface takes place by the bulk dilution medium present in the surrounding [13,17].

Both MC and HPMC are water soluble and as the water penetrates into the hydrophilic matrix, the polymer chains become hydrated and they start to disentangle from the matrix because MC and HPMC contains the linear hydrophilic polymeric chains which do not chemically cross-link but instead of it forms the gelatinous layer on the surface of the tablets that is vulnerable to matrix erosion. At high polymer concentrations, the linear polymer chains entangle to form a physically cross-linked structure, which finally erodes and resulting in the liberation of polymer and drug molecules. However, the rate of polymer erosion is dependent on the viscosity of the MC/HPMC grade which are used in the formulation. Tablets which are fabricated from a high molecular weight and viscosity grade MC/HPMC show more resistance to polymer erosion than the low molecular weight and low viscosity grades.

VARIOUS FACTORS AFFECTING DRUG RELEASE FROM THE POLYMER MATRIX LAYER [10, 16]

The drug release kinetics are affected by various kinds of factors described as such as polymer swelling, drug diffusion/ dissolution, polymer erosion, drug distribution inside the matrix and the geometry of the system in which it is arranged i.e. cylinder or sphere shape. Besides these factors drug/polymer ratio also plays an important role in affecting these release characteristics.

(A). Drug solubility

The water solubility of drug and molecular size is an important factor which plays an important role in the release of drug from swelling and erosion controlled polymeric matrices. For drugs which are having reasonable aqueous solubility, in these cases release of water soluble drugs occurs by dissolution in infiltrating medium and the release of poorly water soluble drug occurs by both dissolution of drug and dissolution of drug particles through erosion of the matrix tablet [16].

(B). Polymer hydration

It is essential to study polymer hydration/swelling process to know the maximum number of polymers and polymeric combinations. The more important step in polymer dissolution include absorption/adsorption of water in more accessible places, rupture of polymer-polymer linking's with the simultaneous forming of water-polymer linking's, separation of polymeric chains, swelling and finally dispersion of polymeric chain in dissolution medium [17].

(C). Polymer diffusivity

The diffusion of small molecules from polymer structure is considered to be energy activated process in which the movement of diffusant molecules occurs from a successive series of equilibrium position when sufficient amount of energy of activation for diffusion has been obtained by the diffusant molecules and in turn this depends on length of polymer chain segment, cross linking and crystallinity of polymer. The release of drug may be attributed to the mainly two factors [6, 13].

(1). Polymer viscosity- As it is a simple phenomenon that increasing molecular weight or viscosity of the polymer causes increase in the gel layer viscosity, which is formed when water hydrates the drug matrix system when it comes in contact with the dissolution medium in the GIT layer.

(2). Polymer concentration- An increase in the polymer concentration causes an increase in the viscosity of gel layer and further causes increase in the diffusional pathway of the drug. This could cause a decrease in the effective diffusion coefficient of the drug and finally leads to reduction in the drug release. And this is the utmost reason which serves as an important pathway for the sustained effect of the drug [13].

(D). Thickness of hydrodynamic diffusion layer

The drug release profile is a function of the variation in thickness of the hydrodynamic diffusion layer on the surface of matrix type delivery devices. As the thickness of hydrodynamic diffusion layer increases the magnitude of drug release value also decreases proportionality [10, 16].

(E). Drug loading dose

The release kinetics is significantly affected by loading dose of the drug. The effect of the initial drug loading of the tablets on the resulting release kinetics thought to be more complex in the case of poorly water soluble drugs. With increasing initial drug loading the relative release rate first decreases and then increases, whereas, absolute release rate monotonically increases. In case of the freely water soluble drugs the porosity of matrix upon the principle of drug depletion increases with increasing initial drug loading [10, 16].

(F). Surface Area

Both the in vitro and in vivo rate of the drug release are observed to be dependent upon the surface area of dosage form. The release rate of drug from small tablet is faster as compared to large cylindrical tablets [16].

(G). Effect of diluent-

The effect of diluent or filler is totally dependent on the nature of diluent. Water soluble diluents like lactose cause marked increase in drug release rate and release mechanism is also shifted towards Fickian diffusion and therefore they are added with the hydrophobic matrices tablets. But while in the case of the insoluble diluents like dicalcium phosphate reduce the Fickian diffusion and increase the relaxation (erosion) rate of matrix. The reason behind this is that water soluble filler in matrices stimulate the water penetration in to inner part of matrix because of its hydrophilic nature which leads to increased drug release rate [10, 16].

ROLE OF NATURAL GUMS IN CONTROLLED RELEASE DOSAGE FORMS

Due to great need and demand in drug delivery systems the excipients are included in novel dosage forms to fulfil required functions regarding the dosage form and these gums directly or indirectly influences or affects the rate and extent of drug release as well as their absorption in the GIT. Therefore the plant based and natural products demand the replacement of synthetic additives with these natural gums. Today, the whole world's interest is lying in these natural drugs and excipients. These natural materials have many benefits over synthetic ones because these are chemically inert, nontoxic, less expensive and biodegradable [4, 8].

1).Tamarind Seeds

Tamarind xyloglucan is found in the endosperm of the seed of the tamarind tree, Tamarindus indicia (family Fabaceae). The polysaccharide which is obtained from tamarind seeds has found use in formulating matrix tablets by the wet granulation technique and they were evaluated for its drug release characteristics. The different concentrations of the polymer were used for the preparation of tablets. Increase in polymer content causes the decreased release of drug. These polysaccharides serve as a biodegradable carrier for colon specific dosage forms. It was found that the matrix tablets which were formulated by using tamarind gum were able to carry most of the drug to the colon and restrict the release in upper GIT [4, 8].

2).Hibiscus Mucilage

The fresh leaves of Hibiscus rosa-sinensis are responsible for the extraction of mucilage which is responsible for sustained action. (Family: Malvaceae). Mucilage of Hibiscus rosa-sinensis contains various chemical constituents such as L-rhamnose, D-galactose, D-galacturonic acid, and D-glucuronic acid. The use of its mucilage has been reported for the development of sustained release tablets [4, 13].

3).Fenugreek Mucilage

Mucilage is found from the seeds of Trigonella foenum-graceum (family: Leguminosae).Seeds are responsible for containing a high percentage of mucilage which do not dissolve in water but form viscous and tacky mass which undergoes swelling when exposed to fluids. Gum contains various chemical constituents' mannose, galactose, and xylose which are responsible for prolonged action of drug. The mucilage which is obtained from fenugreek was found to be better release retarding agent as compared to hypromellose at equivalent content [4, 13].

4).Neem Gum

Neem gum is obtained from the trees of Azadirachta indica whose family is Meliaceae. The gum comprises of various constituents such as mannose, glucosamine, arabinose, galactose, fucose, xylose, and glucose. Studies were performed on the neem gum for the evaluation of its binding property as well for sustained release property. Results indicated that as the proportion of Azadirachta indica fruit mucilage increases, the overall time for the release of drug from the matrix tablet also gets increased [4].

5).Aloe Vera Mucilage

Aloe mucilage is produced from the leaves of Aloe barbadensis which belongs to family Liliaceae. It contains arabinan, arabinorhamnogalactan, galactogalacturan, glucogalactomannan, galactoglucoarabinomannan and glucuronic acid containing polysaccharides which show good response in extended release dosage form. A controlled delivery system of glibenclamide, anti-diabetic drug was studied using aloe mucilage. The swelling behaviors with in vitro release rate characteristics were also undergone investigation. The dissolution study proved that the dried Aloe barbadensis leaves dried mucilage can be satisfactorily used as a matrix forming material for the controlled release of glibenclamide matrix tablets [4].

6).Guar gum

Guar gum is obtained from the seeds endosperm of the legume plant known as Cyamopsis tetragonolobus. It is chemically composed of sugars as it is belongs to a variety of polysaccharides namely mannose and galactose. Guar gum is found to be more soluble than locust bean gum and founds to be better emulsifier than it as it is composed of more galactose branch points. Its degradation occurs extremes of temperature as well as pH such as pH 3 at 50°C. Stability of guar gum is found in the solution over pH range of 5-7. The strong acids are responsible for its degradation, hydrolysis and loss of viscosity. Higher concentration of alkalies also causes reduction in viscosity of guar gum. It is widely used for the purpose of thickener in cosmetics, pharmaceutical dosage forms. In an attempt made for the sustained release tablets of furosemide, combination of pectin, xanthan gum and guar gum were used for it. In vitro release of drug in phosphate buffer of pH 7.4 was performed and extended action of drug was found up to fifteen hours. In addition to this sustained action, guar gum is investigated as carrier for Indomethacin tablets for the purpose of colon specific drug delivery system [4, 13].

7). Karaya Gum

It is found in the form of dried gummy exudates which are found to obtain from the tree Sterculia urens, family Sterculiaceae. This gum has low solubility in water but found to swell many times of its original volume. The sustained release matrix tablet of water soluble Tramadol hydrochloride was formulated using various polymers like karaya gum and carrageenan. After the evaluation of various physical parameters the in vitro dissolution data was studied in phosphate buffer of pH 6.8, the extended release of drug was found to be up to 12 hours [4].

CONCLUSION

Among the various routes of drug delivery the oral route is most preferred route for drug administration. The conventional dosage form offers few limitations which can successfully be resolved by doing modifications in the existing dosage form. Modified dosage forms provide helps in the maintaince of constant plasma drug concentration as well retards the release rate of drug for the long period of time. By optimizing or doing modifications with the help of polymers the various pharmacokinetics and pharmacodynamics parameters can be altered to provide sustained action. The polymers are said to be backbone of the pharmaceutical drug delivery system because they control the release of drug from the device by the act of diffusion, degradation and polymer swelling. The attractiveness towards natural gums is increasing day by day because they are non-toxic, biodegradable, biocompatible and readily available. Several polymers are found to be of plant origin which are satisfactorily investigated and used as excipients in the design and formulation of sustained release dosage form. These natural polysaccharides offers excellent potential as the carrier materials found in the matrix type sustained drug delivery system such as beads, tablets, cross linked hydrogels etc. These polymers are also widely used for film forming activities around tablet core, which leads to provide

sustained action of drug. Thus it is concluded that it is the use of polymers only which modified the release of drug and provides predetermined action of the drug for extended period of time by eliminating repeated dosing and finally provides reduction in the fluctuations of plasma peak profile of drug which ultimately leads to patient compliance as only one dose of sustained drug is enough for providing therapeutic benefit.

ACKNOWLEDGEMENTS

I, myself Diksha Sharma wants to firstly thank Almighty God and my parents for their immense support during the writing of review article. I would like to put my gratitude to the co-authors who helped a lot during this review article work. Special thanks to our Head of Pharmaceutics Department, Mr. Dhruv Dev who helped a lot with the understanding of concepts which arises during the review article.

CONFLICT OF INTEREST

A special vote of thanks as a token of helping hands was given to co- authors. But during the submission of this manuscript, not any kind of financial or personal help was taken. During the review article work, it was kept in mind that nobody intentions are disturbed. Thus after the publication of this review article, not any kind of conflict of interest will be seen at any step. As this review article work is of my keen interest, hard work and efforts.

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