"Evaluation of Some Natural Polymers as Pharmaceutical Excipient For Sustained Drug Delivery System"

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ABSTRACT:

The use of natural polymer as excipients in pharmaceutical sector is expanding day by day. Low cost, safety issues, availability, bio-degradable are the main causes that make them differ from other sources. Natural sources have wide range of varieties and characteristics. Excipients facilitate the formulation design and perform a wide range of functions to obtain desired properties for the finished drug product. Polysaccharide hydrocolloids including mucilages, gums and glucans are abundant in nature and commonly found in many higher plants. Currently, various plant polysaccharides have been studied for their diverse applications as excipients like binders, granulating agents, disintegrants, emulsifiers, suspending agents, gelling agents, mucoadhesive agents, matrix-formers, release retardants, enteric resistants, these polysaccharides constitute a structurally diverse class of biological macromolecules with a broad range of physicochemical properties which are widely used for various applications in pharmacy and medicine.

Key Words: Excipients, Modification, Natural Polymer, Sustained Drug Release.Gums and Mucilages

1. INTRODUCTION

Oral controlled drug delivery system represents the most popular form of controlled drug delivery systems for the obvious advantage of oral route of drug administration. Such systems release the drug with constant or variable release rates. The oral controlled release system shows a typical pattern of drug release in which the drug concentration is maintained in the therapeutic window for a prolong period of time, thereby ensuring sustained therapeutic action.oral drug delivery system is the most widely utilized route of administration when compared to all other routes. Tablets and capsules represent preferred class of products for oral administration due to their ease of administration, high patient compliance, least sterility constraints and flexibility in the design of the dosage form. The conventional dosage form causes the fluctuation of drug concentration in blood and tissues which may lead to insufficient drug concentration in the blood and thus multiple dosing may be required. To overcome this problem, sustained release dosage forms are developed in order to control the amount of drug releasing in the systemic circulation and to maintain steady state plasma drug concentration.

1.1 Sustain Release Drug Delivery

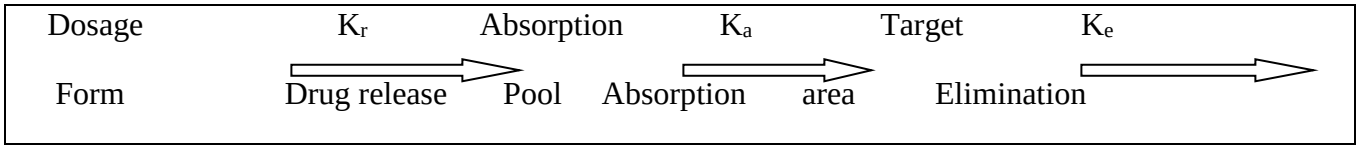
Sustain release provides most desirable dosing regimen and it alleviate the variability involved in the administration of multiple doses per day. Simple definition of sustained release drug system is “any drug or dosage form modification that prolongs the therapeutic activity of the drug” called as sustain release drug system. Ideally a sustained release oral doses form is design to release rapidly some pre determined fraction of the total dose(Loading dose), is an amount of drug, which will produce the desired pharmacological response as promptly as possible and the remaining fraction of the total dose(maintenance dose) is then release at a constant rate. The rate of the drug absorption from the entire maintenance dose in to the body should equal to the rate of the drug removal from the body by all the processes over the time for which the desired intensity of pharmacological response is required.

In recent years, natural polysaccharides are growing rapidly importance in the new formulation development of the controlled released dosage form as they are much safer than synthetic. Interest in gums and mucilage’s used in pharmaceutical industry as an excipient in various formulations for various roles such as binder, matrix former, emulsifying agent, suspending agent, floating agent, Mucoadhesive etc.

Ideally two main objectives exist for these systems:

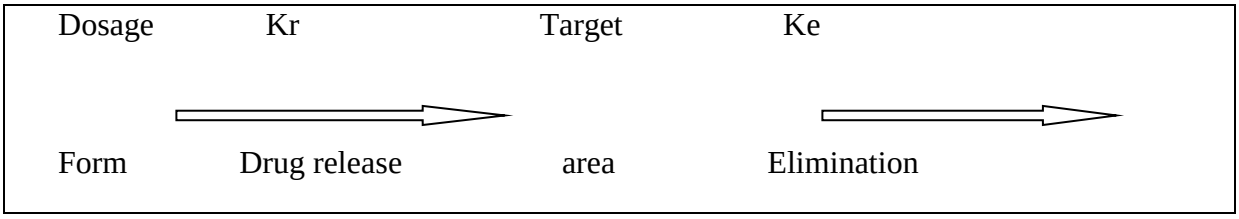
1) **Spatial** drug delivery, which is related to the control over the location of drug release.
2) **Temporal** drug delivery, in which the drug is deliver over an extended period of time during treatment
3) **Principle of sustained release drug delivery**

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



The absorption pool represents a solution of the drug at the site of absorption, and the term Kr, Ka and Ke are first order rate constant for drug release, absorption and overall elimination respectively. Immediate drug release from a conventional dosage forms implies that Kr>>>>Ka. Alternatively speaking the absorption of drug across a biological membrane is the rate-limiting step. For non-immediate release dosage forms,

Kr<<<Ka i.e. the release of drug from the dosage form is the rate limiting step. This causes the above Kinetic scheme to reduce to following.



Essentially, the absorptive phase of the kinetic scheme become insignificant compared to the drug release phase. Thus, the effort to develop a non-immediate release delivery system must be directed primarily at altering the release rate.

The main objective in designing the sustained release delivery system is to deliver drug at rate necessary to achieve and maintain a constant drug blood level. This rate should be analogous to that achieved by continuous intravenous infusion where a drug is provided to the patient at a constant rate. This implies that the rate of delivery must be independent of the amount of drug remaining in the dosage forms and constant over time. It means that the drug release from the dosage form should follows zero-order kinetics, as shown by the following equation:

$$K_r^o = \text{Rate In} = \text{Rate out} = K_e C_d D_d$$

Where,

K_r^o : Zero- order rate constant for drug release-Amount/time

K_e: First-order rate constant for overall drug elimination-time

C_d : Desired drug level in the body- Amount/volume

V_d : Volume space in which the drug is distributed-Litres

1.3 Advantages of sustained release formulations

1. Reduced fluctuations in circulating drug levels.
2. More uniform effect.
3. Employ less total drug that,
   a) Minimize or eliminates local side effects.
   b) Minimize or eliminates systemic side effects.
   c) Minimize drug accumulation with chronic dosing.
   d) Obtains less potentiation or reduction in drug activity on chronic use.
   4. Safety margin of potent drug is increased by technically excellent designing of formulation.
5. Improve efficiency in treatment by
   a) Cure or control of condition.

b) Improve or control of condition.
c) Make use of specific effect. E.g. SR Aspirin for morning relief of arthritis
d) Improve bioavailability of some drugs.
   6. Patient care tie is reduced.

7. Night time dosing can be avoided for patient convenience.
8. Product life time is increased in sustained release formulations. Particles of drug are coated with matrix or entire product is matrix coated for it's main function i.e. sustain action, avoid exposure of unstable drug to the environment and render it's stable.

1.4 Disadvantages of sustain release formulations:

1. If there requires immediately change during the therapy or if any significant adverse effect is noted and prompt termination of therapy is needed, Sustained release does not permit immediate termination of therapy.

2. More costly process and equipment are needed in manufacturing of SRDF's.

3. Physician has less flexibility in adjusting dosage regimen as this is fixed by design of dosage form.

4. Risk of dose dumping, usually SRDF's contain drug amount that is 3-4 times more than conventional formulations. Sometimes this large quantity of drug may get rapidly released leading to toxicity.

5. Reduced drug absorption may delay onset of action. The effect of food on drug absorption kinetics may differ markedly from one SR formulation to another.

6. Drug absorbed at specific time in GIT cannot be formulated in SRDF's.

7. Increased potential for first pass clearance.

8. For oral SRDF's effective drug release is influenced and limited by GI residence time.

9. SRDF's are designed for normal population that is on the basis of the biological half lives. Since disease state at alters drug dispositions as well as in patient variability in pharmacokinetics parameters are not accommodated.

10. Drugs which are acted upon by enzymes in intestine undergo significant enzymatic breakdown as drug remains in body for longer time.

11. In case of accidental failure of the product effective antidote may be difficult to employ.

1.5 Classification of Sustained Release Drug Delivery System

Considering the mechanism of controlling the drug release the system is classified as follows,

Chemically controlled system

1. Biodegradable system
2. Drug polymer conjugates

Diffusion controlled system

1. Matrix diffusion
2. Polymer erosion
3. Polymer swelling
4. Geometry

These systems release the drug continuously for prolonged period of time along the entire length of GIT with normal transit time.

Different system under this class is:

1.6 Continuous release system

1. Dissolution controlled release system

2. Diffusion controlled release system

3. Dissolution and diffusion controlled release system

4. Ion exchange resin drug complex

5. Slow dissolving salts and complexes

6. pHdependent formulation

7. Osmotic pressure controlled system

8. Hydrodynamic pressure controlled system

1.7 Delayed transit and continuous release system

These systems are designed to prolong release of drug with increased residence time in GIT. Such dosage forms are designed to remain in the stomach. Therefore, the drug presented in such system should be stable at gastricpH.

This class includes following systems:

1. Altered density system
2. Mucoadesive system
3. Size based system.

1.8 Delayed release system

These systems are fabricated to release the drug only art specific site in the GIT.

a) The drugs are destroyed in stomach or by intestinal enzymes.
b) The drugs known to cause gastric irritation.
c) The drugs absorbed from specific site in intestine, or exert local effect at specific GI sites are formulated in such systems.

The two types of delayed release system are:

1. Intestinal release system
2. Colonic release system
   Selection of drug candidates for the sustained release drug delivery system

TABLE: Physicochemical and pharmacokinetic parameters for drug selection.

Parameter	Preferred value
Molecular weight/size	<1000
Solubility	>0.1 mg/ml forpH 1 topH 7.8
Dose	Not suitable for large dose as 0.5-1 gm.
Apparent partition coefficient	High
Absorption mechanism	Diffusion
General absorbability	From all GI segments
Release	Should not be influenced by pH and enzymes

Pharmacokinetic parameters	
Elimination half life	Preferably short
Total clearance	Should not be dose dependent
Elimination rate constant	Required for design
Apparent volume of distribution V_d	The large V_d and MEC
Absolute bioavailability	Should be 75% or more
Intrinsic absorption rate	Must be greater than release rate
Toxic concentration	Apart the values of MTC and MEC, safer the Dosage form. Also suitable for drugs with very short half-life.

1.9 Matrix Tablet

Matrix technologies have often proven popular among the oral controlled drug delivery technologies because of their simplicity, ease in manufacturing , high level of reproducibility, stability of raw materials and dosage form, and ease of scale-up and process validation. Technological advancement in the area of matrix formulation have made controlled release product development much easier than before, and improved upon the feasibility of delivering a wide variety of drugs with different physicochemical and biopharmaceutical properties.

1. Preparation of drug-embedded matrix tablet that involves the direct compression of a blend of drug, retardant material and additives is one of the least complicated approaches for delivering drug in a temporal pattern into the systemic circulation. The matrix system is commonly used for manufacturing sustained release dosage forms.
2. A wide array of polymers has been employed as drug retarding agents each of which presents a different approach to the matrix concept. Polymers forming insoluble or skeleton matrices constitute the first category of retarding materials, also classed as plastic matrix systems. The second class represents hydrophobic and water-insoluble materials, which are potentially erodible, while the third group includes polymers those form hydrophilic matrices. Plastic matrix systems, due to their chemical inertness and drug embedding ability, have been widely used for sustaining the release of drug. Liquid penetration into the matrix is the rate-limiting step in such systems unless channeling agents are used. The hydrophobic and waxy materials, on the other hand, are potentially erodible and control the release of drug through pore diffusion and erosion.
3. Polymers belonging to hydrophilic matrix systems, when exposed to an aqueous medium, does not disintegrate, but immediately after hydration develops a highly viscous gelatinous surface barrier which controls the drug release from and the liquid penetration into the centre of the matrix system.

Recently the natural gums, mucilage, latex, polysaccharide used for matrix tablet formulation. As its economic, obtained from edible source, nontoxic, biodegradable, biocompatible, easily available hence much popular than synthetic polymers.

TABLE: List of retardant material used in matrix tablet.

Matrix	**Material**
Insoluble, Inert	Polyethylene, Polyvinyl chloride, Methyl Acrylate-methacrylate co-polymer, Ethyl Cellulose
Insoluble, erodible	Carnauba wax, Stearyl alcohol , Stearic Acid, Polyethylene glycol, Castor wax Polyethylene glycol monostearate Trigrycerides
Hydrophilic	Methyl cellulose (400 cps, 400 cps) Hydroxy ethyl cellulose, Hydroxy Propylmethyl cellulose (60HG,90HG, 25CPS, 40000 CPS, 15000 CPS), Sodium carboxy methyl cellulose, Carboxy poly methylene, Sodium alginate

1.9.1. Advantages of Matrix Tablet

1. Easy to manufacture. Versatile, effective and low cost
2. Can be made to release high molecular weight compounds.
3. The sustained release formulations may maintain therapeutic concentrations over prolonged periods.
4. The use of sustain release formulations avoids the high concentration.
5. Sustain release formulations have the potential to improve the patient compliance by usage of less total drug as well as decreasing dosing frequency.
6. Reduce the toxicity by slowing drug absorption.
7. Increase the stability by protecting the drug from hydrolysis or other derivative changes in gastrointestinal tract.
8. Minimize the local and systematic side effects. Minimize drug accumulation with chronic dosing.
9. Improvement the bioavailability of some drugs.

1.9.2. Disadvantages of Matrix Tablet

1. The remaining matrix must be removed after the drug has been released.
2. High cost of preparation.
3. The release rates are affected by various factors such as, food and the rate transit through the gut.
4. The drug release rates vary with the square root of time. Release rate continuously diminishes due to an increase in diffusion resistance and/ or a decrease in effective area at the diffusion front. However, a substantial sustained effect can be produced through the use of very slow release rates, which in many applications are indistinguishable from zero-order.
5. Complete drug release may not achieve.
6. Poor In-vitro In-vivo correlation.
7. Retrieval of drug is difficult in case of toxicity, poisoning, and hypersensitivity reaction.

1.9.3. Classification **of Matrix Tablets**

- On the Basis of Retardant Material Used:
  1. Hydrophobic Matrices (Plastic matrices).
  2. Lipid Matrices.
  3. Hydrophilic Matrices.
  4. Biodegradable Matrices.
  5. Mineral Matrices.
- On the Basis of Porosity of Matrix
  1. Macro Porous Systems.
  2. Micro Porous Systems.
  3. Non-porous Systems.

1.9.3.1 On the Basis of Retardant Material Used:

1. Hydrophobic Matrices:

The concept of using hydrophobic or inert materials as matrix materials was first introduced in 1959. In this method for sustained release from an oral dosage form, the drug is mixed with an inert or hydrophobic polymer and then compressed in to a tablet. Sustained release is produced due to the fact that the dissolving drug has diffused through a network of channels that exist between compacted polymer particles. Examples

of materials that have been used as inert or hydrophobic matrices include polyethylene, polyvinyl chloride, ethyl cellulose and acrylate polymers and their copolymers. The rate-controlling step in these formulations is liquid penetration into the matrix. The possible mechanism of release of drug in such type of tablets is diffusion. Such matrix tablets become inert in the presence of water and gastrointestinal fluid.

2. Lipid Matrices:

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

3. Hydrophilic Matrices:

Hydrophilic polymer matrix systems are widely used in oral controlled drug delivery because of their flexibility to obtain a desirable drug release profile, cost effectiveness, and broad regulatory acceptance. The formulation of the drugs in gelatinous capsules or more frequently, in tablets using hydrophilic polymers with high gelling capacities as base excipient is of particular interest in the field of controlled release. Infect a matrix is defined as well as mixed composite of one or more drugs with a gelling agent (hydrophilic polymer). These systems are called swellable controlled release systems.

Table 1.3: The polymers used in hydrophilic matrices

Polymer	Example
Cellulose derivatives:	Methylcellulose 400 and 4000 cPs, Hydroxyethylcellulose; hydroxypropyl Methylcellulose (HPMC)25,100,4000, and 15000 cPs; Sodium carboxy methylcellulose
Noncellulose natural or Semisynthetic polymers:	Agar-agar, carob gum; Alginates; molasses; Chitosan, modified starches, Polysaccharides of Mannose and galactose;
Polymers of acrylic acid:	Carbopol 934, the most used variety

4. Biodegradable Matrices:

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

metabolized or excreted. Examples are natural polymers such as proteins and polysaccharides; modified natural polymers; synthetic polymers such as aliphatic poly (esters) and polyanhydrides.

5. Mineral Matrices:

These consist 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 (Phaephyceae) by the use of dilute alkali.

1.9.3.2 On the Basis of Porosity of Matrix:

Matrix system can also be classified according to their porosity and consequently,

Macro porous; Micro porous and Non-porous systems as follows:

1. **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 large than diffusing molecule size.
2. **Micro porous Systems:** Diffusion in this type of system occurs essentially through pores. For micro porous systems, pore size between 50-200A^0, which is slightly larger than diffusing molecules size.
3. **Non-porous Systems:** 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.

1.9.4 Polymers used in matrix tablet:

Table1.4: Polymers used in Matrix Tablets

Polymers	Example
Natural gums	Xanthan gum, Guar gum, Karaya gum
Hydrogels	Polyhydroxyethyle methylacrylate (PHEMA), Cross-linked polyvinyl alcohol (PVA), Cross-Linked polyvinyl pyrrolidone (PVP), Polyethylene oxide (PEO)
Soluble polymers	Polyethylene glycol (PEG), Polyvinyl alcohol (PVA), Poluvinyl pyrrolidone (PVP), Hydroxypropyl methyl cellulose (HPMC)

Biodegradable polymers	Polylactic acid (PLA), Polyglycolic acid(PGA) Polycaprolactone (PCL), Polyanhydrides
Non biodegradable polymers	Polyethylene vinyl acetate (PVA), Polydimethyl siloxane (PDS), Polyether urethane (PEU), Polyvinyl chloride(PVC)
Mucoadhesive polymers	Polycarbophil, Sodium carboxymethyl cellulose, Polyacrylic acid,Tragacanth

1.9.5 Mechanism of Drug Release

1. Dissolution controlled systems

A drug with slow dissolution rate will demonstrate sustaining properties, since the release of the drug will be limited by the rate of dissolution. In principle, it would seem possible to prepare extended release products by decreasing the dissolution rate of drugs that are highly water-soluble. The rate limiting step of dissolution is diffusion across the boundary layer. This can be done by;

- Preparing an appropriate salt or derivative
- Coating the drug with a slowly dissolving materials- encapsulation dissolution control.
- Incorporation the drug into a tablet with a slowly dissolving carrier- matrix dissolution control (a major disadvantage is that the drug release rate continuously decreases with time). The dissolution process can be considered diffusion-layer-controlled, where the rate of diffusion from the solid surface to the bulk solution through an unstirred liquid film is the rate-determining step. The dissolution process at steady-state is described by the Noyes- Whitney equation:

$$\frac{dC}{dt} = \frac{DA(Co - C)}{h}$$

Where,
dC/dt: dissolution rate
D: dissolution rate constant (equivalent to the diffusion coefficient divided by the thickness of the diffusion layer D/h)
Co: saturation solubility of the solid
C: concentration of solute in the bulk solution
A: Surface area
h: Diffusion layer thickness.

Noyes-Whitney equation predicts that rate of release can be constant if the following parameters are held constant:

- Surface area
- Diffusion coefficient
- Diffusion layer thickness

- Concentration difference.

These parameters, however, are not easily maintained constant, surface area, and this is the case for combination diffusion and dissolution systems.

2. Diffusion controlled systems

Diffusion systems are characterized by the release rate of a drug being dependent on its diffusion through an inert membrane barrier. Usually, this barrier is an insoluble polymer. In general, two types or subclasses of diffusion systems are recognized: reservoir devices and matrix devices. It is very common for the diffusion-controlled devices to exhibit a non-zero order release rate due to an increase in diffusion resistance and a decrease in effective diffusion area as the release proceeds.

Rate of drug release from matrix diffusion controlled drug delivery systems is time dependent as defined by

$$dQ/dt = A[C_R D_{P/2t}]^{1/2}$$

Where, A: the loading dose of drug initially dispersed in polymer matrix.

CR: drug solubility in polymer.

D_P: diffusivity of drug molecules in the polymer matrix.

Reservoir consist of core (reservoir) and coating membrane i.e. diffusion barrier. Active ingredients diffuse from reservoir through the coating membrane. The drug depot is surrounded by polymeric hydrogel membrane.

Diffusion in matrix devices

In this model, drug in the outside layer 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 moving toward the interior. It follows obviously that for this systems 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. Derivation of the mathematical model to describe this system involved the following assumptions:

- A pseudo-steady state is maintained during drug release;
- The diameter of the drug particles is less than the average distance of drug diffusion through the matrix;
- The diffusion coefficient of drug in the matrix remains constant (no change occurs in the characteristics of the polymer matrix).
- The bathing solution provides sink conditions at all times;
- No interaction occurs between the drug and the matrix;
- The total amount of drug present per unit volume in the matrix is substantially greater than the saturation solubility of the drug per unit volume in the matrix (Excess solute is present).
- Only the diffusion process occurs.

In a hydrophilic matrix, there are two competing mechanism involved in the drug release: Fickian diffusion release and relaxation release. Diffusion is not only pathway by which a drug is released from the matrix; the

erosion of the matrix following polymer relaxation contributes to the overall release. The relative contribution of each component to the total release is primarily dependent on the properties of a given drug.

Advantages of hydrophilic matrix tablets

With proper control of manufacturing process, reproducible release profile are possible. They variability associated with them is slightly less than that characterizing coated release forms. Their capacity to incorporate active principles is large, which suits them to delivery of large doses.

Disadvantages of hydrophilic matrix tablet

For a hydrophilic sustained release matrix tablet, in which the release is mainly controlled by erosion of the swollen polymer gel barrier at the tablet surface, the presence of food may block the pores of the matrix and inhibit the drug release rate.

The hydrophilic polymers are grouped in three broad categories:

A) Non-cellulose natural or semi synthetic polymer

These are products of vegetable origin and are generally used as such Pectin, Agar, Alginate, Guar gum, Chitosan, Modified starches are commonly used polymers.

B) **Polymers of acrylic acid**

These are arranged in carbomer group and commercialized under the name of carbopol. The major disadvantage of this type of polymer is itspH dependent gelling characteristics.

C) **Cellulose ether**

This group of semi-synthetic cellulose derivatives is the most widely used group of polymer. Non-ionic such as hydroxyl propyl methyl cellulose (HPMC) of different viscosity grades are widely used group of polymers. Non- ionic such as HPMC of different viscosity grades is widely used.

4. Bioerodible and combination of diffusion and dissolution system:

Strictly speaking, therapeutic system will never be dependent on dissolution or diffusion only. In practice, the dominant mechanism for release will overshadow other processes enough to allow classification as either dissolution rate-limited or diffusion-control release. As a further complication these systems can combine diffusion and dissolution of both the drug and matrix material. Drugs not only can diffuse out of the dosage form, as with some previously described matrix systems, but also the matrix itself undergoes a dissolution process. The complexity of the system arises from the fact that as the polymer dissolves the diffusion path length for the drug may change. This usually results in a moving boundary diffusion system. Zero order release is possible only if surface erosion occurs and surface area does not change with time.

Swelling-controlled matrices exhibit a combination of both diffusion and dissolution mechanisms. Here the drug is dispersed in the polymer, but instead of an insoluble or non-erodible polymer, swelling of the polymer occurs. This allow for the entrance of water, which causes dissolution of the drug and diffusion out of the swollen matrix. In this system the release rate is highly dependent on the polymer-swelling rate and drug solubility. This system usually minimizes burst effects, as rapid polymer swelling occurs before drug release.

With regards to swellable matrix systems, different models have been proposed to describe the diffusion, swelling and dissolution processes involved in the drug release mechanism. However the

key element of the drug release mechanism is the forming of a gel layer around the matrix, capable of preventing matrix disintegration and further rapid water penetration.

1.10 Natural polysaccharides (Mucilage's):

Nature has provided us a wide variety of materials to help improve and sustain the health of all living things either directly or indirectly. In recent years there have been important developments in different dosage forms for existing and newly designed drugs and natural products, and semi-synthetic as well as synthetic excipients often need to be used for a variety of purposes. Gums and mucilages (polysaccharides) are widely used natural materials for conventional and novel dosage forms. Mucilages are normal product of plant metabolism, produced inside the cell of plant. They are slimy masses with water, but not dissolved. Mucillages are esters of sulphuric acid. These natural materials have advantages over synthetic ones since they are chemically inert, nontoxic, less expensive, biodegradable and widely available. They can also be modified in different way to obtain tailor-made materials for drugs delivery systems and thus can complete with the available synthetic excipients. Polysaccharides are polymers of simple sugar building blocks; they are made by repeated units of monomers which are same or different. Polysaccharides made by same monomers called as homopolysaccharide and after hydrolysis of polysaccharides as different monomers obtained called as heteropolysaccharide.

1.10.1 Advantages of Natural mucilage

Excipient is non-toxic in nature. (Chemically these are carbohydrates composed of repeating sugar (monosaccharide) units. Hence, they are non-toxic.

1. Economic consideration and easily local available.
2. Erodible sources (Most mucilage's are obtained from edible sources).
3. These are biodegradable polymer no any adverse impact on humans or environmental health.
4. Also Biocompatible with few exceptions.
5. Environmental-friendly processing (mucilage's from different are easily collected in different seasons in large quantities due to the simple production processes involved).
6. Better patient tolerance as well as public acceptance.
7. There is less chance of side, adverse effects with natural materials compared with synthetic.
8. Capable for physical and chemical modification.

1.10.2 Disadvantages of Natural Mucilage's

1. Slow extraction, expensive isolation and purification process.
2. Microbial contamination (The equilibrium moisture present in the gums and mucilage is normally 10% or more).
3. Self degradation tendency.
4. During production they are exposed to the external environment so enhance of microbial contamination and degradation.

5. Batch to batch variation (Synthetic manufacturing is a controlled procedure with fixed quantities of ingredients, While the production of gums and mucillages is dependent on environmental and seasonal factors).
6. Uncontrolled rate of hydration (Due to differences in the collection of natural materials at different times, different region, species, and climate conditions the percentage of chemical constituents present in given material may vary).
7. Reduced viscosity on storage.
8. Some are photosensitive mucilage'

1.11Physical modification methods:

Natural gums can also be modified to have tailor-made materials for drug delivery systems. Therefore, in the years to come there is going to be continued interest in the natural gums and their modifications with the aim to have better materials for drug delivery systems. Several polysaccharides such as sodium alginate, chitosan, guar gum, xanthum gum, pectin, gellan gum have been employed either alone or in combination with their native or modified forms to control the drug release from different types of delivery system, but these just had a limited degree of success. In recent years, graft copolymers designed primarily for medical applications have entered the arena of controlled release.

Chemical and physical methods are used for cross linking of polysaccharides. In physical cross linking dissolution is prevented by physical interaction which exists between different polymer chains and a molecular interaction between polymers can be achieved by exposure to dry heat, saturated steam, microwave technology, UV .In chemical cross linking covalent bonds are present between different polymer chains.

1) Physical modification
    a) Physical Crosslinking
    b) Microwave modification
2) Chemical Modification
    a) Carboxymethylation
    b) Chemical Crosslinking
    c) Grafting
    d) Curing
    e) Blending

CONCLUSION

In the present review different works on natural polysaccharides were studied in terms of their use as excipients in various formulations. Gums and mucilages are widely used natural materials for conventional and novel dosage forms. These natural materials have advantages over synthetic ones since they are chemically inert, nontoxic, less expensive, biodegradable and widely available. Recently, much attention has been paid to the modification of natural polysaccharides in order to obtain novel hybrid materials. These modified polysaccharides could be applied in the design of various stimuli-responsive controlled release systems such as, matrix tablets. This contribution is intended to develop other natural sources as well as with modifying existing natural materials for the formulation of novel drug delivery systems, biotechnological applications and other delivery systems.

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