INTERNATIONAL RESEARCH JOURNAL OF PHARMACY ISSN 2230 – 8407
Available online www.irjponline.com Review Article

ROLE OF NATURAL POLYMERS IN SUSTAINED RELEASE DRUG DELIVERY SYSTEM: APPLICATIONS AND RECENT APPROACHES

Prakash Pawan*, Porwal Mayur, Saxena Ashwin
Dept. of Pharmaceutics, Vivek College of Technical Education, Bijnor, U.P., India

Article Received on: 14/07/11 Revised on: 17/08/11 Approved for publication: 11/09/11

*Email: cpps10@rediffmail.com

ABSTRACT
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 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. They can also be modified in different ways to obtain tailor-made materials for drug delivery systems and thus can compete with the available synthetic excipients. Various polymers have been investigated as drug retarding agents, each presenting a different approach to the matrix system. Based on the features of the retarding polymer, hydrophilic polymers are the most suitable for retarding drug release and there is growing interest in using these polymers in sustained drug delivery. This review discusses some of the most important plant-derived polymeric compounds that are used or investigated as release retardant in sustained or controlled release drug delivery systems.
KEYWORDS Natural polymer, gums, mucilage, sustained release, controlled release.

INTRODUCTION

Protein, enzymes, muscle fibers, polysaccharides and gummy exudates are the natural polymers being used effectively in formulating the variety of pharmaceutical products. The well-known natural polymers used in pharmacy and other fields are chitosan[1], carrageenan[2], is paghula, acacia, agar, gelatin, shellac, guar gum and gum karaya[3].These natural polymers are widely used in pharmaceutical industry as emulsifying agent, adjuvant and adhesive in packaging; and also well suited for pharmaceutical and cosmetic product development.

The plant based polymers have been studied for their application in different pharmaceutical dosage forms like matrix controlled system, film coating agents, buccal films, microspheres, nanoparticles, viscous liquid formulations like ophthalmic solutions, suspensions, implants and their applicability and efficacy has been proven These have also been utilized as viscosity enhancers, stabilizers, disintegrants, solubilisers, emulsifiers, suspending agents, gelling agents and bioadhesives, binders in the above mentioned dosage form.

Sustained drug delivery systems significantly improve therapeutic efficacy of drugs. Drug-release-retarding polymers are the key performers in sustained release drug delivery system for which various natural, semi-synthetic and synthetic polymeric materials have been investigated Besides this several polymers are often utilized in the design of novel drug delivery systems such as those that target delivery of the drug to a specific region in the gastrointestinal tract or in response to external stimuli to release the drug.

Among various dosage forms, matrix tablets are widely accepted for oral sustained release as they are simple and easy to formulate. Matrix system is the specific type of release system, which prolongs and controls the release of drug that is dissolved or dispersed. Making drug-embedded matrix tablets through the direct compression of a blend of drug, retardant material and additives is one of the simplest formulation approaches. The inclusion of polymeric materials in a matrix system is a common method of modulating drug release. Various natural gums and mucilages have been examined as polymer for sustained release formulations.

Natural polymer approach in sustained release drug delivery system

The use of natural polymers and their semi-synthetic derivative in drug delivery continues to be an area of active research. Drug-release retarding polymers are the key performer in matrix systems. Various polymers have been investigated as drug retarding agents, each presenting a different approach to the matrix system. Based on the features of the retarding polymer, matrix systems are usually classified into three main groups: hydrophilic, hydrophobic and plastic. Hydrophilic polymers are the most suitable for retarding drug release and there is growing interest in using these polymers in sustained drug delivery[4].

There are various numbers of natural polymers which have been investigated as sustained release agent

Hibiscus mucilage

The mucilage is extracted from the fresh leaves of *Hibiscus rosa-sinensis. Hibiscus rosa-sinensis,* Malvaceae family commonly known as China rose is a popular landscape shrub, creates a bold effect with its medium-textured, glossy dark green leaves and with 4-6 inch wide and up to 8 inch long, showy flowers, produced throughout the year and grows up to 7-12 feet[5].

In an investigation the matrix tablets of Diclofenac sodium using *Hibiscus rosa-sinensis* leaves mucilage was design and study its release retardant activity in prepared sustained release formulations. *Hibiscus rosa-sinensis* leaves were evaluated for physicochemical properties. Different matrix tablets of Diclofenac sodium *Hibiscus rosa-sinensis* leaves mucilage were formulated. The matrix tablets found to have better uniformity of weight, hardness, friability and drug content with low deviated values. The swelling behavior, release rate characteristics and the in- vitro dissolution study proved that the dried *Hibiscus rosa-sinensis* leaves mucilage can be used as a matrix forming material for preparing sustained release matrix tablets. The kinetics of selected formulation followed zero order. It was concluded that *Hibiscus rosa-sinensis* leaves mucilage can be used as an effective matrix forming polymer, to sustain the release of Diclofenac sodium from the formulation[6].

Aloe mucilage

The inner part of the leaves of Aloe vera (L.) Burm.f. (Aloe barbadensis Miller) many compounds with diverse structures have been isolated from both the central parenchyma tissue of *Aloe vera* leaves and the exudates arising from the cells adjacent to the vascular bundles. The bitter yellow exudates contains 1,8 dihydroxyanthraquinone derivatives and their glycosides[7]. The aloe parenchyma tissue or pulp has been shown to contain proteins, lipids, amino acids, vitamins, enzymes, inorganic compounds and small organic compounds in addition to the different carbohydrates. Many investigators have identified partially acetylated mannan (or acemannan) as the primary polysaccharide of the gel, while others found pectic substance as the primary polysaccharide. Other

polysaccharides such as arabinan, arabinorhamnogalactan, galactan, galactogalacturan, glucogalacto-mannan, galactoglucoarabinomannan and glucuronic acid containing polysaccharides have been64 isolated from the Aloe vera inner leaf gel part[8].

Dried A. vera leaf gel (acetone precipitated component of the pulp) was directly compressed in different ratios with a model drug to form matrix type tablets, including ratios of 1:0.5, 1:1, 1:1.5 and 1:2. These matrix systems showed good swelling properties that increased with an increase of aloe gel concentration in the formulation. The directly compressed matrix type tablets also showed modified release behavior with 35.45% and 30.70% of the dose released during the first hour and the remaining of the dose was released over a 6 hour period for those formulations containing the lower ratios of gel to drug, namely 1:0.5 and 1:1. The formulation that contained the highest ratio of gel to drug, namely 1:2 exhibited only a 23.25% drug release during the first hour with the remaining of the dose being released over an 8 hour period. The dried A. vera gel polysaccharide component therefore showed excellent potential to be used as an excipient in the formulation of direct compressible sustained- release matrix type tablets[9].

In another investigation matrix tablets of Glimepiride with *Aloe barbadensis miller* leaves mucilage and Povidone was formulated and studied its functionality as a matrix forming agent for sustained release tablet formulations. Physicochemical properties of dried powdered mucilage of *Aloe barbadensis miller* mucilage and Povidone tablet blend were studied. Various formulations of Glimepiride *Aloe barbadensis miller* mucilage and Povidone were prepared. They found to have better satisfactory physicochemical properties with low SD values. The swelling behavior and release rate characteristics were studied. The dissolution study proved that the dried *Aloe barbadensis miller* mucilage and Povidone combination can be used as a matrix forming material for making Sustained release matrix[10].

Fenugreek mucilage

Trigonella Foenum-graceum, commonly known as Fenugreek, is an herbaceous plant of the leguminous family. Fenugreek seeds contain a high percentage of mucilage (a natural gummy substance present in the coatings of many seeds). Although it does not dissolve in water, mucilage forms a viscous tacky mass when exposed to fluids. Like other mucilage- containing substances, fenugreek seeds swell up and become slick when they are exposed to fluids[11]. The husk from the seeds is isolated by first reducing the size, and then separated by suspending the size reduced seeds in chloroform for some time and then decanting. Successive extraction with chloroform removes the oily portion which is then air dried[12]. A different extraction procedure is also reported to isolate the mucilage from the husk. The powdered seeds are extracted with hexane then boiled in ethanol. The treated powder is then soaked in water and mechanically stirred and filtered. Filtrate is then centrifuged, concentrated in vacuum and mixed with 96% ethanol. This is then stored in refrigerator for 4 hrs to precipitate the mucilage[13].

In a study the mucilage derived from the seeds of fenugreek, was investigated for use in matrix formulations containing propranolol hydrochloride. Methocel® K4M was used as a standard controlled release polymer for comparison purposes. A reduction in the release rate of propranolol hydrochloride was observed with increase in concentration of the mucilage in comparison to that observed with hypomellose matrices. The rate of release of propranolol hydrochloride from fenugreek mucilage matrices was mainly controlled by the drug: mucilage ratio. Fenugreek mucilage at a concentration of about 66% w/w was found to be a better release retardant compared to hypomellose at equivalent content[13].

Guar gum

Guar gum comes from the endosperm of the seed of the legume plant *Cyamopsis tetragonolobus*. Guar gum is prepared by first drying the pods in sunlight, then manually separating from the seeds. The gum is commercially extracted from the seeds essentially by a mechanical process of roasting, differential attrition, sieving and polishing. The seeds are broken and the germ is separated from the endosperm. Two halves of the endosperm are obtained from each seed and are known as Guar Splits. Refined guar splits are obtained when the fine layer of fibrous material, which forms the husk, is removed and separated from the endosperm halves by polishing. The refined Guar Splits are then treated and finished into powders by a variety of routes and processing techniques depending upon the end product desired[14]. Chemically, guar gum is a polysaccharide composed of the sugars galactose and mannose. The backbone is a linear chain of 1, 4-linked mannose residues to which galactose residues are 1, 6-linked at every second mannose, forming short side- branches[15] . Guar gum is more soluble than locust bean gum and is a better emulsifier as it has more galactose branch points. It degrades at extremes of pH and temperature (e.g. pH 3 at 50°C)[16]. It remains stable in solution over pH range 5-7. Strong acids cause hydrolysis and loss of viscosity, and alkalies in strong concentration also tend to reduce viscosity. It is insoluble in most hydrocarbon solvents. Guar gum is used and investigated Guar gum is used and investigated as a thickener in cosmetics, sauces, as an agent in ice cream that prevents ice crystals from forming and as a fat substitute that adds the "mouth feel" of fat and binder or as disintegrator in tablets.

In an approach Sustained release tablets of furosemide were fabricated using pectin, guar gum and xanthan gum. The tablets were evaluated for physical characteristic like hardness, weight variation, fraibilty, and drug content. In-vitro release of drug was performed in PBS pH 7.2 for fifteen hours. All the physical characters of the fabricated tablet were within acceptable limits. The tablet with guar gum exhibited greater swelling index than those with pectin and xanthan gum. A better controlled drug release (80.74%) was obtained with the matrix tablet (G4) made-up of the guar gum than with the pectin and xanthan gum. It is cleared through the dissolution profile of furosemide from matrix tablets prepared using different natural polymers were retarded approx 15 hrs[17].

Besides being used as a matrix former for sustained release tablets guar gum has been investigated as a carrier for indomethacin for colon-specific drug delivery using in vitro methods Studies in pH 6.8 phosphate buffered saline (PBS) containing rat caecal contents have demonstrated the susceptibility of guar gum to the colonic bacterial enzyme action with consequent drug release. The pre-treatment of rats orally with 1 ml of 2% w/v aqueous dispersion of guar gum for 3 days induced enzymes specifically acting on guar gum thereby increasing drug release. A further increase in drug release was observed with rat caecal contents obtained after 7 days of pre-treatment. The presence of 4% w/v of caecal contents obtained after 3 days and 7 days of enzyme induction showed biphasic drug release curves. The results illustrate the usefulness of guar gum as a potential carrier for colon-specific drug delivery [18, 19].

In an investigation an attempt was made to formulate the oral controlled release zidovudine matrix tablets by using Guar gum as rate controlling polymer and to evaluate drug release parameters as per various release kinetic models. The tablets were prepared by wet granulation method. Granules were prepared and evaluated for loose bulk density, tapped density, compressibility index and angle of repose, shows satisfactory results. All the granules were lubricated and compressed using 12.6 mm flat faced punches. Compressed tablets were evaluated for uniformity of weight, content of active ingredient, friability, hardness, in vitro release studies and swelling

index. All the formulations showed compliance with Pharmacopoeial standards. The in vitro dissolution study was carried out for 12 hours using paddle (USP type II) method in phosphate buffer (pH 6.8) as dissolution media. Formulation F-1 failed to sustain release beyond 10 hours. Among all the formulation, F-2 shows 95.97% of drug release at the end of 12 hours. Selected formulation (F-2) was subjected to stability studies for 3 months, which showed stability with respect to release pattern. Fitting the in vitro drug release data to Korsmeyer equation indicated that diffusion along with erosion could be the mechanism of drug release[20].

In another approach sustained release matrix tablets of phenytoin sodium was developed. Advantages of sustained release tablets are that they can often be taken less frequently than instant release formulations of the same drug, and that they keep steady levels of the drug in the blood stream. The tablets were fabricated by the wet granulation method using water as granulating agent along with matrix materials like guar gum, sodium alginate, tragacanth and xanthan gum with varying percentage. The granules were evaluated for angle of repose, bulk density, compressibility index, total porosity, and drug content. The tablets were subjected to weight variation test, drug content, hardness, friability, and in vitro release studies. The swelling behavior of matrix was also investigated. The granules showed satisfactory flow properties, compressibility, and drug content. The I.R spectral analysis studies confirmed no interaction between phenytoin with used natural gums. All the tablet formulations showed acceptable pharmacotechnical properties and complied with in-house specifications for tested parameters. In the further formulation development process, F8 (55% guar gum with 10% acacia), the most successful formulation of the study, exhibited satisfactory drug release and could extend the release up to 12 hours. The mechanism of drug release from all the formulations was diffusion coupled with erosion[21].

Karaya gum

It is the dried gummy exudates obtained from the tree Sterculia urens Roxb. (Family Sterculiaceae). It is also known as Sterculia, Karaya, Indian Tragacanth or Bassora Tragacanth gum. It is produced in India, Pakistan and to a small extent in Africa. Karaya also differs from tragacanth in that it contains no starch and stains pink with solution of ruthenium red. It has low water solubility but swells to many times its original volume.

Karaya gum consist of an acetylated, branched heteropolysaccharide with a high component of D-galacturonic acid and D-glucuronic acid residues. The granular granular grades are used as a bulk laxative, being only next to psyllium seed in use for this purpose. The powdered gum is used in lozenges, pastes and dental fixative powders and it has proved particularly useful as an adhesive for stoma appliances. It also acts as stimulant. It is available, with frangula, as granules. The cross linked Tragacanth (Epichlorhydrin) exhibits superior wicking and swelling action and hence can be used as a potential disintegrant[22, 23].

In an approach a sustained release matrix tablets of water soluble Tramadol hydrochloride was developed using different polymers viz. Hydroxy propyl methyl cellulose (HPMC) and natural gums like Karaya gum (KG) and Carrageenan (CG). Varying ratios of drug and polymer like 1:1 and 1:2 were selected for the study. After fixing the ratio of drug and polymer for control the release of drug up to desired time, the release rates were modulated by combination of two different rates controlling material and triple mixture of three different rate controlling material. After evaluation of physical properties of tablet, the in vitro release study was performed in 0.1N HCl pH 1.2 for 2 hrs and in phosphate buffer pH 6.8 up to 12 hrs. The effect of polymer concentration and polymer blend concentration were studied. Different ratios like 80:20, 60:40, 50:50, 40:60 and 20:80 were taken. Dissolution data was analyzed by Korsmeyer-Peppas power law expression and modified power law expression. It was observed that matrix tablets contained polymer blend of HPMC/CG were successfully sustained the release of drug upto 12 hrs. Among all the formulations, formulation F16 which contains 20% HPMC K15M and 80% of CG release the drug which follow Zero order kinetics via, swelling, diffusion and erosion and the release profile of formulation F16 was comparable with the marketed product. Stability studies (40±2ºC/75±5%RH) for 3 months indicated that Tramadol hydrochloride was stable in the matrix tablets. The DSC and FTIR study revealed that there was no chemical interaction between drug and excipients[24].

In another investigation sustained release matrix tablets of diltiazem hydrochloride (DTZ) was developed using karaya gum (K) alone or in combination with locust bean gum (LB) and hydroxypropyl methylcellulose (H). Matrix tablets of DTZ were prepared at different ratios of drug:gum (1:1, 1:2, and 1:4) and of the gum blends (K, K/LB, K/H and K/LB/H) by direct compression. The matrix tablets were evaluated for hardness, friability, in vitro release and drug content. The formulations were also characterised by scanning electron microscopy (SEM), Fourier transform infra-red spectroscopy (FTIR) and differential scanning calorimetry (DSC). A commercial diltiazem hydrochloride product Dilzem SR, was used as a reference for comparison. The results of the study demonstrate that karaya gum alone or in suitable combination with locust bean gum and hydroxypropyl methylcellulose is suitable for formulating sustained-release matrix tablets of diltiazem[25].

In another approach oral sustained drug delivery system for freely water-soluble drug, metoprolol succinate designed using hydrophilic gums. The gums selected were karaya gum and guar gum and their combination. To study the rheological synergism between karaya gum and guar gum in different ratio (0:10-10:0) was determined and the combination having highest viscosity (6:4) was used for matrix tablet formulation. Nine batches were prepared by using karaya gum and guar gum in 15%, 20% and 25% concentration of the total weight of tablet. Matrix tablets were prepared by wet granulation method and the prepared tablets were evaluated for weight variation, content uniformity, percentage friability, hardness, thickness, swelling index and in vitro dissolution studies. All the formulation showed compliance with pharmacopoeial standards. Formulation F1, F6 and F7 showed sustained release of drug for 12 hrs with 97.65%, 98.23% and 96.98% respectively. The optimized formulation was subjected to accelerated stability studies for one month at temperature of 40 0 C and relative humidity of 75%. and showed physical stability and stability with respect to drug release pattern. The kinetic treatment showed that the formulations follow zero order with release exponent (n) was 0.8275, 0.9633 and 0.8079 for formulation F1, F6 and F7. So the combination of karaya gum and guar gum shows better prosperity for preparation of sustained release tablets as compare to individual gums[26].

Hakea gum

Hakea gum a dried exudate from the plant *Hakea gibbosa* family Proteaceae. Gum exudates from species have been shown to consist of L-arabinose and D-galactose linked as in gums that are acidic arabinogalactans (type A). Molar proportions (%) of sugar constituents Glucuronic acid, Galactose, Arabinose, Mannose, Xylose is 12:43:32:5:8. The exuded gum is only partly soluble in water[27].

Hakea gibbosa (Hakea) was investigated as a sustained release and mucoadhesive component in buccal tablets. Tablet with drug chlorpheniramine maleate (CPM) with either sodium bicarbonate or tartaric acid in a 1:1.5 molar ratio and different amount of Hakea were formulated using adirect compression technique and were coated with hydrogenated castor oil (Cutina) on all but one face. The

resulting plasma CPM concentration versus time profiles was determined following buccal application of the tablets in rabbits. The force of detachment for the mucoadhesive buccal tablets increased as the amount of Hakea gum was increased following application to excised intestinal mucosa. Addition of sodium bicarbonate or tartaric acid, as well as higher amounts of CPM, did not affect the mucoadhesive bond strength. These results demonstrate that the novel, natural gum, *H. gibbosa*, may not only be used to sustain the release but can also act as bioadhesive polymer[28].

Tamarind gum

Tamarind xyloglucan is obtained from the endosperm of the seed of the tamarind tree, *Tamarindus indica*, a member of the evergreen family[29]. Tamarind Gum, also known as Tamarind Kernel Powder (TKP) is extracted from the seeds. The seeds are processed in to gum by seed selection, seed coat removal, separation, hammer milling, grinding and sieving. Tamarindgum is a polysaccharide composed of glucosyl : xylosyl : galactosyl in the ratio of 3:2:1 . Xyloglucan is a major structural polysaccharide in the primary cell walls of higher plants. Tamarind xyloglucan has a (1 4)-!-D-glucan backbone that is partially substituted at the O-6 position of its glucopyranosyl residues with "-D-xylopyranose[30]. Some of the xylose residues are !-D-galactosylated at O-2 .It is insoluble in organic solvents and dispersible in hot water to form a highly viscous gel such as a mucilaginous solution with a broad pH tolerance and adhesivety[31, 32] . Tamarind gum is non Newtonian and yield higher viscosities than most starches at equivalent concentrations. This has led to its application as stabilizer, thickener, gelling agent and binder in food and pharmaceutical industries. In addition to these, other important properties of tamarind seed polysaccharide (TSP) have been identified recently[33, 34]. They include noncarcinogenicity, mucoadhesivity, biocompatibility, high drug holding capacity and high thermal stability[35]. This has led to its application as excipient in hydrophilic drug delivery system[33-35]. Magnetic microspheres of tamarind gum and chitosan were studied. The magnetic microspheres were prepared by suspension cross-linking technique. Microspheres formed were in the size range of 230 - 460 µm.The magnetic material used in the preparation of the microspheres was prepared by precipitation from FeCl and FeSO solution basic medium**.**

In a study the tamarind seed polysaccharide (TSP) was isolated from tamarind kernel powder and this polysaccharide was utilized in the formulation of matrix tablets containing Diclofenac Sodium by wet granulation technique and evaluated for its drug release characteristics. Hardness of the tablets was found to be in the range of 4.0-6.0 kg/cm2. The swelling index increased with the increase in concentration of TSP. Increase in polymer content resulted in a decrease in drug release from the tablets. The tablets showed 96.5-99.1% of the labeled amount of drug, indicating uniformity in drug content. The drug release was extended over a period of 12h. The release of the formulations matched with the marketed sustained release tablets with a similarity factor of 83.52. The in-vitro release data of the formulations followed zero order kinetics[36].

In a recent investigation the solution of xyloglucan the polysaccharide from tamarind kernel powder was carried out by aqueous extraction-non aqueous precipitation method. Various batches of tablets were formulated using NSAID drug ketoprofen using drug: polymer in different ratios with non-aqueous wet granulation technique. The hardness of the tablets was found to be between 4.5-5.5 kg/cm2 with friability values less than 0.3%. The weight variation and the drug content were within the standard limits. The in-vitro dissolution studies of the ketoprofen tablets showed a slow and sustained release over a period of 12 h. The increase in polymer content decreased the drug release from the tablets which may be attributed by the formation of gel layer surrounding the core drug. The IR spectral studies confirmed the good compatibility between the drug and the polymer in the dosage form. Thus isolation of tamarind seed polysaccharide has proven to be an effective drug retardant[37].

Okra gum

Okra gum, obtained from the fruits of *Hibiscus esculentus,* is a polysaccharide consisting of D-galactose, L-rhamnose and L-galacturonic acid[38]. Okra gum is used as a binder. In study okra gum has been evaluated as a binder in paracetamol tablet formulations[39]. These formulations containing okra gum as a binder showed a faster onset and higher amount of plastic deformation than those containing gelatin. The crushing strength and disintegration times of the tablets increased with increased binder concentration while their friability decreased. Although gelatin produced tablets with higher crushing strength, okra gum produced tablets with longer disintegration times than those containing gelatin.

In a study this was finally concluded from the results that okra gum maybe a useful hydrophilic matrixing agent in sustained drug delivery devices. In another study Okra gum was evaluated as a controlled release agent in modified release matrices, in comparison with sodium carboxymethyl cellulose (NaCMC) and hydroxypropylmethyl cellulose (HPMC), using paracetamol as a model drug. Okra gum matrices provided controlled release of paracetamol for more than 6 h and the release rates followed time-independent kinetics. The release rates were dependent on the concentration of the drug present in the matrix. Okra gum compared favourably with NaCMC, and a combination of Okra gum and NaCMC, or on further addition of HPMC resulted in near zero order release of paracetamol from the matrix tablet. The results indicate that Okra gum matrices could be useful in the formulation of sustained release tablets for up to 6 h[40].

The main aim of this study was to optimize and evaluate the floating tablets of atenolol that prolongs the gastric residence time. Semi-synthetic polymer, HPMC K100M and natural polymer i.e. okra gum were used as release retarding agents by its swelling nature. Sodium bicarbonate was used as a gas-generating agent, Atenolol were prepared by direct compression method. The prepared tablets were evaluated for physicochemical parameters and found to be within range viz. hardness, swelling index, floating capacity, thickness, and weight variation. Further, tablets were evaluated for in vitro release characteristics for 8 hrs. The concentration of okra gum with a gas-generating agent was optimized to get the sustained release of atenolol for 8hrs, drug release from all the formulations followed first order kinetics and higuchi's mechanism. The optimized (F6) formulation has better release rate. Based on the diffusion exponent (n) value, the drug release was found to be diffusion controlled[41].

In an approach the Colon targeted tablet formulation was developed using okra polysaccharide (*Abelmuschus esculentus*) as a microbially triggered material and also as the carrier. Okra polysaccharide was isolated from *Abelmuschus esculentus* and used for tablet formulation with Ibuprofen as model drug. The matrix tablets with four different proportions of the okra (20%, 30%, 40% & 50%) with 1% ethyl cellulose in all the four formulations and the formulations were coded as WO1, WO2, WO3, & WO4. In all the formulations constant 100 mg Ibuprofen were incorporated. The formulations were evaluated for their hardness, weight variation, friability, and drug content and were characterized by FTIR. Matrix tablets were subjected to *in vitro* drug release studies. The release studies were carried out for 2 hours in pH 1.2, 3 hours in pH 7.4 phosphate buffer and for 10 hours in pH 6.8 PBS. The % Release of these formulations i.e. WO1, WO2, WO3 & WO4 were found to be 20.75, 18.48, 13.37 & 11.99 respectively at 5th hour. The fifth

matrix tablet (WO5) with 10% ethyl cellulose, 40% okra polysaccharide and 100 mg ibuprofen was formulated. The % cumulative release of this formulation (WO5) was found to be 4.59 at 5th hour. Among the above, WO3 was chosen as the optimized formulation for further studies. The *in vitro* dissolution studies were carried out with pH 1.2, pH 7.4 and the study continued in pH 6.8 PBS with rat cecal matter at 6th hour in simulated colonic fluid in order to mimic conditions from mouth to colon. The post five hour studies were carried out without rat cecal also as a control. The observation made was that the maximum release was 98.09% at 10th hour with rat cecal matter and a mere 32.70 % and 46.98% without rat cecal matter at 8th and 10th hour respectively. These findings were confirmed by in vivo investigation using X-ray images of rabbits ingested with okra matrix tablets (WO5) containing barium sulphate as contrast medium instead of Ibuprofen. The tablet began to disintegrate at 8th hour of tablet ingestion. These observations drive us to conclude that the okra polysaccharide under investigation has the potential to carry the drug almost intact to the intended site i.e. Colon where it undergoes degradation due to the presence of anaerobic microbes there. Thereby both the aims contemplated are achieved[42].

In an another approach preparation and evaluation of aceclofenac sustained release matrix tablets was carried out using various proportions of natural polymer *Abelmoschus esculentus* mucilage powder (i.e., Drug : Polymer ratio – 1:0.2, 1:0.4, 1:0.6, 1:0.8, 1:1) as release controlling factor by wet granulation method. To study the influence of different proportions of polymer on In vitro drug release characteristics of dosage form was evaluated in 6.8 PH phosphate buffer for 12 hours. Also friability, weight variation, hardness, disintegration drug time, content uniformity was studied according to Indian Pharmacopeia. All the formulations showed good fit in zero order kinetics along with diffusion mechanisms. In vitro release showed that formulation F3 containing D: P ratio – 1:0.6 gave prolonged release for 12 hours. Analysis of drug release rate from matrix system indicated drug was release by supercase-II transport mechanism[43].

Mimosa pudica mucilage

Mimosa pudica (family Mimosaceae), commonly known as sensitive plant, is a diffuse undershrub found widely in the tropical and subtropical parts of India. Seeds of M. pudica yield mucilage, which is composed of d-xylose and d-glucuronic acid. Mimosa seed mucilage hydrates and swells rapidly on coming in contact with water. During earlier study in our laboratory, the disintegrating and binding properties of Mimosa seed mucilage were evaluated. In the present work, we have isolated and characterized Mimosa seed mucilage and evaluated its sustained-release properties employing diclofenac sodium (DS) as a model drug. The matrix tablet of DS was formulated using wet granulation method and evaluated for appearance, weight variation, hardness, friability, in vitro drug release, swelling, and erosion behavior[44].

In a study the sustained-release properties of Mimosa pudica seed mucilage was investigated. Matrix tablets of diclofenac sodium containing different proportions of mucilage and dibasic calcium phosphate as diluent were formulated by wet granulation method. The tablets had uniform physical appearance, average weight, drug content, and adequate hardness. The results of in vitro release conducted using USP type II dissolution rate apparatus, in a dissolution media comprising of 900 mL of 0.1 N HCl for 2 h followed by phosphate buffer (pH 6.8) for 24 h at 37°C and 50 rpm, revealed that as the proportion of mucilage in the matrix was increased there was a corresponding decrease in the release of drug. Further, the matrix tablets were found to release the drug following Higuchi square root release kinetics, with the mechanism of release being diffusion for tablets containing higher proportion of mucilage and a combination of matrix erosion and diffusion for tablets containing smaller proportion of mucilage. The swelling and erosion studies revealed that, as the proportion of mucilage in tablets was increased, there was a corresponding increase in percent swelling and a decrease in percent erosion of tablets. The SEM photomicrographs showed gelling structures in tablets containing higher percentage of mucilage, while both pores and gelling structures were present on the surface of tablets containing smaller proportion of mucilage and commercial formulation. On comparative evaluation, the dissolution profile from formulation containing mucilage to drug in the proportion of 1:40 was found to be similar to the commercial sustained-release formulation of diclofenac[45].

CONCLUSION

The use of natural gums for pharmaceutical applications is attractive because they are economical, readily available, non-toxic, and capable of chemical modifications, potentially biodegradable and with few exceptions, also biocompatible. Majority of investigations on natural polymers in sustained release drug delivery systems centered around polysaccharides. Natural gums can also be modified to have tailor-made products for drug delivery systems and thus can compete with the synthetic controlled release excipients available in the market.

Several polymers from plant origin have been successfully used and others are being investigated as excipients in the design of dosage forms for effective sustained release drug delivery. Some polysaccharides obtained from plants shown excellent potential as carrier materials in matrix type controlled release dosage forms such as microparticles, beads, tablets and cross-linked hydrogels. Plant polysaccharides have been investigated for their film forming properties, while others have been chemically or physically modified. These semi-synthetic polymers are extensively used in the formulation of conventional dosage forms and are under investigation for use.

REFERENCES

1. Dutta AC. Botany. 6th edn. Oxford University Press, Calcutta 1995; 134.
2. Evans WC, Trease and Evans. Pharmacognosy.14th edn, Harcourt Brace & Co., Asia Pvt. Ltd, Singapore. 1996; 196, 208, 209, 213-215, 462, 555.
3. The Wealth of India: A Dictionary of Indian Raw Materials and Industrial Products Raw Materials Series. Publications and Information Directorate, CSIR, New Delhi. revised series, Vol 1A 1985; 43-44, 148.
4. Rishabha Malviya, Pranati Srivastava and G.T. Kulkarni. Applications of Mucilages in Drug Delivery - A Review -Advances in Biological Research 2011;5 (1).
5. Ross IA. Medicinal Plants of the World—Chemical Constituents, Traditional and Modern Medicine Uses.Totowa: Humana Press; 1999; 155-63.
6. Jani GK, Shah DP. Assessing *Hibiscus rosa-sinensis Linn* as an Excipient in Sustained Release Tablets. Drug Develop Ind Pharm 2008; 34(8):807–16.
7. Vazquez B, Avila G, Segura D, Escalante B. Anti-inflammatory activity of extracts from Aloe vera gel. J Ethnopharmacol 1996; 55:69-75.
8. Choi S, Chung MH. A review on the relationship between Aloe vera components and their Biologic effects. Semin Integr Med 2003; 1:53-62.
9. Jani GK, Shah DP, Jain VC, Patel MJ, Vithalan DA. Evaluating mucilage from *Aloe Barbadensis* Miller as a pharmaceutical excipient for sustained-release matrix tablets. Pharm Technol. 2007; 31:90-98.
10. Hindustan Abdul et al. Design and evaluation of sustained release matrix tablets of glimepiride based on combination of natural and synthetic polymers. International journal of applied biology and pharmaceutical technology. 2010;1(3): 770-777.
11. Petropoulos GA. Fenugreek: The genus Trigonella. In: Petropoulus GA, (Ed.), Botany. London: Taylor and Francis 2002; 9–17.
12. Avachat AM, Gujar KN, Kotwal VB, Patil S. Isolation and evaluation of fenugreek husk as granulating agent. Indian J Pharm Sci 2007; 69(5):667-79.
13. Ali N, Hossein N, Afagh K, Tarifeh S, Hadi V, Ford JL. An In Vitro Evaluation of Fenugreek Mucilage as a Potential Excipient for Oral Controlled-Release Matrix Tablet. Drug Dev Ind Pharm 2008; 34:323–29.
14. Guar Gum Manufacturing Process [Online]. 2009 [cited 2009June 16] From: URL: http://www.guargum.biz/guargum_manufacturing_process.htm
15. URL:http://en.wikipedia.org/wiki/Guar_gum [cited 2009june 18]
16. Martin Chaplin. Water Structure and Behavior: Guar Gum. London South Bank University. April 2006.

17. Sourabh Jain, SK Yadav and UK Patil. Preparation and Evaluation of Sustained Release Matrix Tablet of Furosemide using Natural Polymers. Research J. Pharm. and Tech. 2008; 1(4).
18. Al-Saidan SM, Krishnaiah YSR, Patro SS, Satyanaryana V. In Vitro and In Vivo Evaluation of Guar Gum Matrix Tablets for Oral Controlled Release of Water-soluble Diltiazem Hydrochloride. AAPS Pharm Sci. Tech 2005; 6 (1): E14-21.
18. Prasad YVR, Krishnaiah YSR, Satyanarayana S. In vitro; evaluation of guar gum as a carrier for colon-specific drug delivery. J. Control. Release 1998; 51: 281-87.
19. Amit.S.Yadav, Ashok Kumar P,Vinod R, Someshwara Rao B, Suresh V Kulkarni. Design and Evaluation of Guar Gum Based Controlled Release Matrix Tablets of Zidovudine. Journal of Pharmaceutical Science and Technology 2010; 156-162.
20. Md Sajid ali, Swati Singh, Awdhesh kumar, Sant singh, Md Tahir Ansari, Gurudutta pattnaik, preparation and in vitro evaluation of sustained release matrix tablets of phenytoin sodium using natural polymers, International Journal of Pharmacy and Pharmaceutical Sciences 2010
21. James EF Reynolds, Martindale. The Extra Pharmacopoeia, 30th edn. The Pharmaceutical Press, London. 1993; 652, 904, 1217-1221.
22. Kokate CK, Purohit AP and Gokhale SB. Pharmacognosy. 22nd edn. Nirali Prakashan. Pune, 2003; 136, 147-148, 150, 152-154, 157, 441.
24. Raghavendra raon G , Gandhi sagar , Patel tarun. Formulation and evaluation of sustained Release matrix tablets of tramadol hydrochloride. International Journal of pharmacy and Pharmaceutical sciences, 2009

23. Afrasim Moin and HG Shivakumar. Formulation of Sustained-Release Diltiazem Matrix Tablets Using Hydrophilic Gum Blends. Tropical Journal of Pharmaceutical Research June 2010; 9 (3): 283-291.
26. V N Deshmukh, Development and evaluation of sustained release matrix tablet using hydrophilic gums as release modifier, Journal of Pharmacy Research 2009
25. Peter FK, Alistair MS, Shirley CC. Molecular Structures Of Gum Exudates From Hakea Species. Phytochemistry 1999; 34(3):709-713.
26. Alur HH, Pather SI, Mitra AK, Johnston TP. Evaluation of the Gum from *Hakea gibbosa* as Sustained-Release and Mucoadhesive Component in Buccal Tablets ,Pharm Dev Technol 1999; 4(3):347.
27. Shankaracharyan B. Tamarind-Chemistry, technology and uses: A critical appraisal. J Food Sci Technol 1998; 35(3): 193-208.
28. Khanna M, Nandi RC, Sarin JPS. Standardisation of Tamarind Seed Polyose for Pharmaceutical Use. Indian Drugs 1987; 24: 268–69.
29. Khanna M, Dwivedi AK, Singh S. Polyose from Seeds of *Tamarindus indica* of Uniqu Property and Immense Pharmaceutical Use, In: Trends in Carbohydrate Chemistry,Vol. 4, Dehra Dun: Surya International Publications 1997;79–81.
30. Kulkarni D, Dwivedi DK, Sarin JPS, Singh S. Tamarind Seed Polyose: A PotentialPolysaccharide for Sustained Release of Verapamil Hydrochloride as a Model Drug. Indian J Pharm Sci 1997; 59 (1): 1–7.
31. Rao PS, Ghosh TP, Krishna S. Extraction and purification of tamarind seed polysaccharide. J Sci Ind Research 1946; 4:705.
34. Sano M, Miyata E, Tamano S, Hagiwara A, Ito N, Shirai T. Lack of carcinogenicity of tamarind seed polysaccharide in B6C3F mice. Food and Chem Toxicol 1996; 34:463-67.
32. Burgalassi S, Panichi L, Saettone MF, Jacobsen J, Rassing MR. Development and in vitro/in vivo testing of mucoadhesive buccal patches releasing benzydamine and lidocaine. Int J Pharm 1996; 133:1-7.
33. R.Deveswaran, Sindhu Abraham, S.Bharath, B.V.Basavaraj, Sharon Furtado,V.Madhavan. Design and Characterization of Diclofenac sodium tablets containing Tamarind seed polysaccharide as Release retardant, International Journal of Pharm Tech Research CODEN. April-June 2009;1(2): 191-195.
34. Bharath Srinivasan, Anusha Ganta, Deveswaran Rajamanickam, Basavaraj Basappa Veerabhadraiah, Madhavan Varadharajan. Evaluation of tamarind seed polysaccharide as a drug release retardant International Journal of Pharmaceutical Sciences Review and Research, 2011; -31.
35. Tavakoli N, Ghasemi N, Taimouri R, Hamishehkar H. Evaluation of okra gum as a binder in tablet dosage forms. Iranian J Pharm Res 2004; 2:47.
36. Emeje MO, Isimi CY, Kunle OO. Evaluation Of Okra Gum As A Dry Binder In Paracetamol Tablet Formulations. Continental J. Pharmaceutical Sciences 2007; 1:15 – 22.
37. Kalu VD, Odeniyi MA, Jaiyeoba KT. Matrix properties of a new plant gum in controlled drug delivery. Arch Pharm Res 2007; 30(7): 884-89.
38. Edukondalu V et al. Formulation and evaluation of oral floating tablets of Atenolol using Okra gum. Scholars Research Library Der Pharmacia Lettre 2011; 3(3): 342-349
39. Llango K B, Manisha Mishra, Sridurga Devi, Rajsekaran A, Senthil kumar M, Subburaju T. In vitro and in vivo evaluation of okra polysaccharide-based colon-targeted drug delivery systems. International Journal of Pharmaceutical Sciences Review and Research
40. Dhana Lakshmi B, Sivannarayana T, Pavan G, Chandana G, Sirisha K, Yogaiah T. Formulation and evaluation of aceclofenac matrix tablets using *abelmoschus esculentus* mucilage as a polymer. Journal of Advances in Drug Research,2011:7-11
41. Alvarez-Manceñido F, Landin M, Lacik I, Martínez-Pacheco R. Konjac
42. glucomannan and konjac glucomannan/xanthan gum mixtures as excipients for controlled drug delivery systems. Diffusion of small drugs. Int J Pharm 2008; 349:11-18.
43. 45. Kuldeep Singh, Ashok Kumar, Naresh Langyan, and Munish Ahuja. Evaluation of Mimosa pudica Seed Mucilage as Sustained-Release Excipient. APS PharmSciTech. 2009 December; 10(4): 1121–1127 .