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Review Article

AN REVIEW ON NATURAL POLYMERS APPROACHES TO FLOATING DRUG DELIVERY SYSTEM

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ABSTRACT

The purpose of writing this review on floating drug delivery systems (FDDS) was to compile the recent literature with special focus on the natural polymers used in mechanism of floatation to achieve gastric retention. Controlled and sustained released formulations are widely used in modern era for the delivery of various ingredients. D rugs with narrow absorption window in the gastrointestinal tract have poor absorption therefore gastro retentive drug delivery systems (GRDDs) have been developed which prolong the gastric emptying time. This review summarizes the study of various natural polymers which are used in floating drug delivery system. These natural or biodegradable polymers are very useful to reduced or minimizes the side effects of the drugs than those which are having combination with synthetic and semi -synthetic polymers. This review having lots of natural polymers like Guar gum, Tragacanth, Karaya gum, Copal gum, Dammar gum, Pectin, Na Alginate, Gelatin etc.

Keywords: *Floating Drug Delivery Approaches to improve gastric retention, Natural Polymers.*

INTRODUCTION

Oral route is the most popular and convenient route for various drugs. Oral route generally consider an ideal drug delivery system that will possess two main properties:

- It should be in a single dose for prolonging action.
- It should be deliver the active drug directly to the target site.

These considerations have led to the development of a controlled or sustained delivery system. Sustained delivery describes a drug delivery system with delayed and/or prolonged release of drug. The main purpose for developing these systems is to enhance the safety of a product to extend its duration of action. There are many disadvantages of these systems such as longer time to achieve therapeutic blood levels, more variation in bioavailability, enhanced first pass effect, and dose dumping. These systems are usually more expensive than the conventional systems. Since these products are made for the population at large, and not for an individual, they may result in higher or lower steady state drug level in different individuals. If the therapeutic range of drug is broad enough, it may not cause any problem. In spite of their disadvantages, research is continued in this area, as there is much scope to further improve currently available systems.

Oral Controlled release drug delivery systems (OCRDDS) that can be retained in the stomach for

a long time have many advantages over sustained release formulations. Controlled drug delivery

system release the drug in a controlled and prolonged manner, so that the drug could be supplied continuously to its absorption site in the upper gastrointestinal tract. [1]

The oral route is increasingly being used for the delivery of therapeutic agents because the

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low cost of the therapy and ease of administration lead to high levels of patient compliance. More than 50% of the drug delivery systems available in the market are oral drug delivery systems1. Controlled-release drug delivery systems (CRDDS) provide drug release at a predetermined, predictable, and controlled rate. Controlled-release drug delivery system is capable of achieving the benefits like maintenance of optimum therapeutic drug concentration in blood with predictable and reproducible release rates for extended time period; enhancement of activity of duration for short half-life drugs; elimination of side effects; reducing frequency of dosing and wastage of drugs; optimized therapy and better patient compliances. [2]

OCRDDS: Advantages

- Reduced dosing frequency
- Better patient convenience and compliance
- Reduced gastro intestinal (GI) side effects
- Less fluctuating plasma drug levels
- Improved efficacy/safety ratio
- More uniform drug effect
- Lesser total dose [1]

The successful development of oral controlled drug delivery systems requires an understanding of the three aspects of the system, namely.

1. The physiochemical characteristics of the drug
2. Anatomy and physiology of GIT and
3. Characteristics of Dosage forms

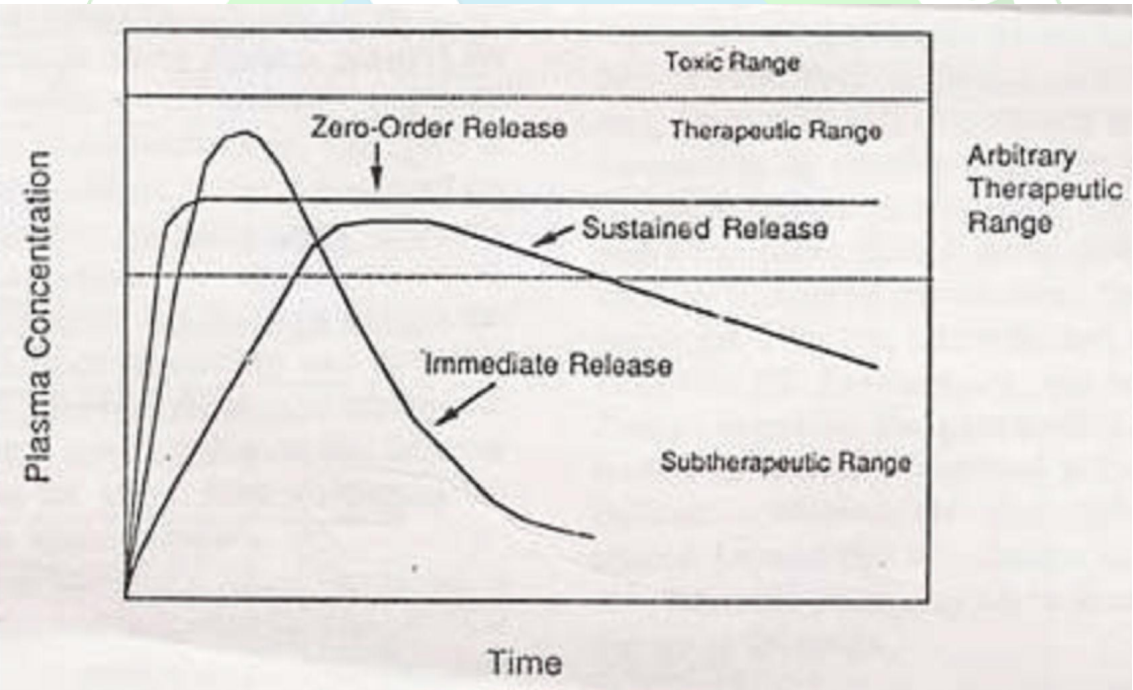

Fig. - Drug level verses time profile showing differences between zero order, controlled releases, slow first order sustained release and release from conventional tablet [2]

Good fundamental understanding of the anatomic and physiological characteristics of the human GIT is required to modulate the gastrointestinal transit time of a drug through FDDS for maximal gastrointestinal absorption of drugs and site-specific delivery. [2]

Table: comparison of conventional drug delivery system and GRDDS [3]

Conventional Drug Delivery System	*Gastro retentive Drug Delivery System*
High risk of toxicity.	Very low risk of toxicity.
Less patient compliance	Improves patient compliance
Not suitable for delivery of drugs with narrow absorption window in small intestine region.	Suitable for delivery of drugs with narrow absorption window in small intestine region.
Not much advantageous for- - Drugs having rapid absorption through GIT. - Drugs acting locally in the stomach. - Drugs which degrade in the colon.	Very much advantageous for- - Drugs having rapid absorption through GIT. - Drugs acting locally in the stomach. - Drugs which degrade in the colon.
No risk for dose dumping.	Possibility of dose dumping.

APPROACHES TO IMPROVE THE GASTRORETENTATIVE DRUG DELIVEY SYSTEM: [3,4]

Various approaches have been developed to increase the gastric retention and to achieve the control release of the drug. These have, attracted the interest of many formulators due to their advantages over the conventional drug delivery systems recently the study highlights the advantageous as well as provides an over view of the recent advances that have taken place in this arena.

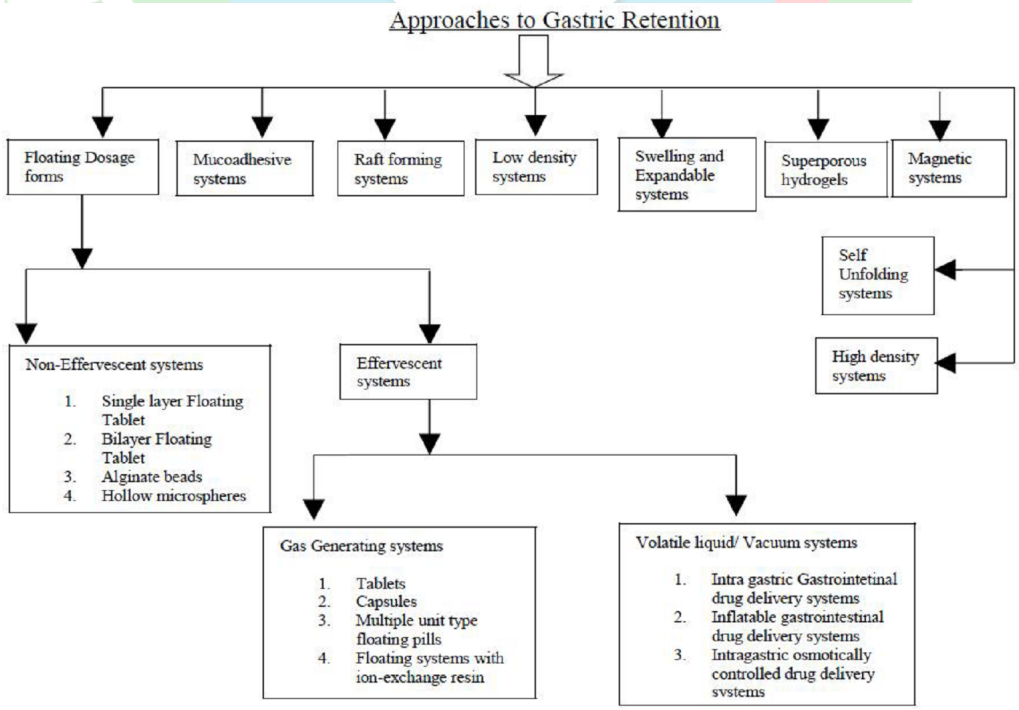

Fig-Approaches to Gastric Retention.

FLOATING DRUG DELIVERY SYSTEM

Floating systems or Hydro dynamically controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films and hollow microspheres. [5]

ADVANTAGES OF FDDS

- Floating dosage forms such as tablets or capsules will remains in the solution for prolonged time even at the alkaline pH of the intestine.
- FDDS are advantageous for drugs meant for local action in the stomach eg: Antacids.
- FDDS dosage forms are advantageous in case of vigorous intestinal movement and in diarrhoea to keep the drug in floating condition in stomach to get a relatively better response.
- Acidic substance like aspirin causes irritation on the stomach wall when come in contact with it, hence HBS/FDDS formulations may be useful for the administration of aspirin and other similar drugs.
- The FDDS are advantageous for drugs absorbed through the stomach eg: Ferrous salts, Antacids.

DISADVANTAGES OF FDDS

Main disadvantage of floating systems is that they require sufficiently high levels of fluid in the stomach for the DDS to float therein and work efficiently. However, this can be overcome by administrating the dosage form with a glass full of water (200-250 ml) with frequent meals or by coating the dosage form with bioadhesive polymers,thereby enabling them to adhere to the mucous lining of the stomach wall. The following consideration may help selecting the drug candidate for FDDS:

- Drugs that are unstable and destroyed in the gastric environment are poor candidates for FDDS.
- Drugs that are irritant to the gastric mucosa or induce gastric lesions are not good candidates for FDDS.
- Drugs that are absorbed throughout the GI tract should be discarded for FDDS as prolonging the GRT of such drugs appears to offer no advantage in terms of BA .
- Poorly acid soluble drugs may show dissolution problem in gastric fluid and, consequently may not be released to a sufficient extent. It might, therefore, be advisable not to exploit FDDS with these drugs. [5]

NATURAL POLYMERS INTRODUCTION

Polymers are large chain macromolecules containing a variety of functional groups. Blended with other low- and high-molecular-weight materials, they can be tailored for variety of applications. Polymers are widely used in pharmaceutical dosage forms and food products, which include both synthetic as well as natural polymeric materials. Depending upon the nature of polymers being used in formulations, they play an integral role in different drug delivery technologies. For example, they may be used as agents for controlled drug delivery, sustained drug delivery, targeted drug delivery and various other types of novel drug delivery systems. They may be used in taste masking, stabilization and protection in oral drug delivery systems. Also, they can bind to the particles of solid dosage formulations and change the flow characteristics of liquid dosage formulations.

The natural polymers are more superior to the synthetic polymers in respect of their highly organized macroscopic and molecular structure. This adds to their strength and biocompatibility. Moreover, their low toxicity and excellent biodegradability have also attracted researchers to pay attention towards the widespread application of natural polymers. The release rate of the drug from natural polymers depends upon several factors such as the physicochemical properties of drugs and the polymers, biodegradation rate of polymers, morphology and size of the particles, thermodynamic compatibility that exist between the polymers and the drugs, and the shape of the delivery devices. [6]

The natural polymers widely used in the form of polyelectrolyte complexes in controlled drug delivery systems include three basic types:

Neutral polymers: Hydroxypropylmethylcellulose (HPMC).

Cationic polymers: Chitosan.

Anionic polymers: κ-carrageenan, sodium alginate.

Examples of these polyelectrolyte complexes that control drug release from formulations include sodium alginate-chitosan, polyacrylic acid-chitosan, and chitosan-carrageenan. These ionic polyelectrolyte complexes of polymers affect the release of oppositively charged ionic drugs through ion exchange mechanism in dissolution medium 6. Different polymers have different release kinetics depending upon their nature such as their hydrophilicity, hydrophobicity as well as the nature of drug. Hydrophilic polymers does not disintegrate on exposure to an aqueous medium, rather they forms a highly viscous gelatinous layer that controls the drug release from the matrix system. Natural gums such as acacia tragacanth and karaya are more preferred over synthetic materials for controlled drug delivery due to their cost effectiveness, easy availability and nontoxicity. Similarly, natural gums such as agar gum, guar gum and gellan gum have been discovered to be used as polymer for sustained drug delivery. On contact with water, these hydrophilic natural gums hydrate and swell and thus used for single unit dosage formulation. The drug release kinetics from these matrices depends on the relative magnitude of polymer hydration at the moving rubbery/glassy front within the formulation as well as the rate of polymer erosion at the swollen polymer/dissolution medium front. In other words, drug release from hydrophilic matrices is known to be a complex interaction between swelling, diffusion and erosion mechanisms. [6]

Table 3: Drugs Generally Used in FDDS [1]

S. NO.	*DOSAGE FORM*	*DRUGS*
1.	Microspheres	Aspirin, Grisiofulvin, pnitroanilline, Ibuprofen, Terfinadine, Tranilast.
2.	Granules	Diclofenac sodium, Indomethacin, Prednisolone
3.	Films	Cinnarizine
4.	Powders	Several basic drugs
5.	Capsules	Chlordiazepoxide HCl, Diazepam, Furosemide, 1-Dopa, benserazide, Misoprostol, Propranolol HCl, Ursodeoxycholic acid
6.	Tablets/pills	Acetaminophen, Acetylsalicylic acid, Amoxicillin trihydrate, Ampicillin, Atenolol, Chlorpheniramine, Cinnarizine, Diltiazem, Fluorouracil, Isosorbide mononitrate, Isosorbide dinitrate, p-aminobenzoic acid, Piretanide, Prednisolone, Quinidine gluconate, Riboflavin-5'-phosphate, Sotalol, Theophylline, Verapamil HCl

ADVANTAGE OF NATURAL POLYMER:

The various advantages of natural plant based materials include:

- **Biodegradable:**
  Biodegradable is the naturally available; they are produced by all living organisms.

- **Biocompatible and non-toxic:**
  Basically, all of these plant materials are repeating sugar polysaccharides.

- **Low cost:**
  Cheaper to use as natural sources. The production cost is less compared with the synthetic material. In India and many other developing countries are dependent on agriculture and they are large amount of money investment on agricultures.

- **Environmental-friendly processing:**
  There are many types of natural compounds obtained from different plant sources which are widely used in pharmaceutical industry and collected in large quantities due to the simple production processes involved.

- **Local availability (especially in developing countries):**
  In India and similar developing countries, there is promotion for the production of plants as pharmaceutical excipients being done by government and it also provide the facilities for bulk production, like gum and mucilage because of their wide applications in industries.

- **They have better patient tolerance as well as public acceptance:** There is less chance of side and adverse effects with natural materials compared with synthetic one. For Example, Povidone. [7]

DISADVANTAGES OF NATURAL GUMS AND MUCILAGES

Microbial contamination—

The equilibrium moisture content present in the gums and mucilages is normally 10% or more and, structurally, they are carbohydrates and, during production, they are exposed to the external environment and, so there is a chance of microbial contamination. However, this can be prevented by proper handling and the use of preservatives.

Batch to batch variation—

Synthetic manufacturing is a controlled procedure with fixed quantities of ingredients, while the production of gums and mucilages is dependent on environmental and seasonal factors.

Uncontrolled rate of hydration—

Due to differences in the collection of natural materials at different times, as well as differences in region, species, and climate conditions the percentage of chemical constituents present in a given material may vary. There is a need to develop suitable monographs on available gums and mucilages.

Reduced viscosity on storage—

Normally, when gums and mucilages come into contact with water there is an increase in the viscosity of the formulations. Due to the complex nature of gums and mucilages (monosaccharides to polysaccharides and their derivatives), it has been found that after storage there is reduced in viscosity. [8]

POLYMERS USED IN GASTRO RETENTIVE DRUG DELIVERY SYSTEM [9]

Natural	***Synthetic***
Na Alginate	HPMC K4M
Pectin	HPMC K15M
Tragacanth	HPMC K100M
Gelatin	CARBOPOL 934P
Carrageenan	Ethyl cellulose
Tamaring gum	Methyl cellulose
Hibiscus rosasinesis	Sod. Carboxy methyl cellulose
Okra gum	Poly vinyl alcohol
Guar gum	Polyamides
Locust gum	Polycarbonates
Isapgulla (psyllium)	Polyalkylene glycols
Tara gum	Polyvinyl ethers
Moi gum	Esters and halides
Gum dammer	Polymethacrylic acid
Poly methyl methacrylic acid	Gum copal
Karaya gum	Microcrystalline cellulose
HPC	Sesbenia GUM
HEC	Chitosan

GELATIN

Gelatin is a translucent, colorless, brittle (when dry), flavorless solid substance, derived from the collagen inside animals skin and bones. It is commonly used as a gelling agent in food and pharmaceuticals. Gelatin is produced by partial hydrolysis of collagen extracted from the boiled bones, connective tissues, organs and some intestines of animals such as domesticated cattle, and pigs. The approximate amino acid composition of gelatin is glycine 21%, proline 12%, hydroxyproline 12%, glutamic acid 10%, alanine 9%, arginine 8%, aspartic acid 6%, lysine 4%, serine 4%, leucine 3%, valine 2%, phenylalanine 2%, threonine 2%, isoleucine 1%, hydroxylysine 1%, methionine and histidine<1%and tyrosine<0.5%. Some modifications of gelatin for drug delivery are PEGylatedgelatin nanoparticles , fluoride anion-modified gelatin nanogel system for ultrasound-triggered drug release, antibody modified gelatin nanoparticles as drug carrier system for uptake in lymphocytes, agar

modified gelatin A and gelatin B, thiolmodified gelatin nanoparticles for intracellular DNA delivery , hydrophobic hexanoyl anhydrides grafting to the amino groups of primitive gelatin ,cationised gelatin ,DNA-loaded gelatin nanoparticles ,modified

gelatin microspheres impregnated collagen scaffold .

of DNA. Daocheng et al (2008) Kaul et al (2002) prepared PEG-modified gelatin nanoparticles for long-circulating intracellular delivery preparedAdriamycin gelatin nanogel,modified with fluoride anion by co-precipitation method with fluoride anion and Sodium sulfate targeted and controlled drug release delivery systemfor cancer and other diseases. Balthasar et al (2005) used gelatin nanoparticles for the attachment of biotinylated anti-CD3 antibodies by avidin-biotin-complex formation. These antibody modified nanoparticles represent a promising carrier system for the specific drug targeting to Tlymphocytes. Saxena et al (2011) prepared agar-gelatin compositions& tablets made of agar, gelatin A, gelatin B and their blends agar-gelatin A, agar-gelatin B, gelatin A-gelatin B in 1:1 ratio.Salbutamol is themodel drug. [10]

XANTHAN GUM

Xanthan is an extracellular heteropolysaccharide produced by fermentation of the bacterium Xanthomonas campestris. The primary structure (fig. 7) of this naturally produced cellulose derivative contains a cellulose backbone (-D-glucose residues) and a trisaccharide side chain of -D-mannose- -Dgluronic acid – -D-mannose attached with alternate glucose residues of themain chain.

It is a hydrophilic polymer, which until recently had been limited for use in thickening, suspending, and emulsifying water-based systems It appears to be gaining appreciation for the fabrication ofmatrices with uniformdrug release characteristics.

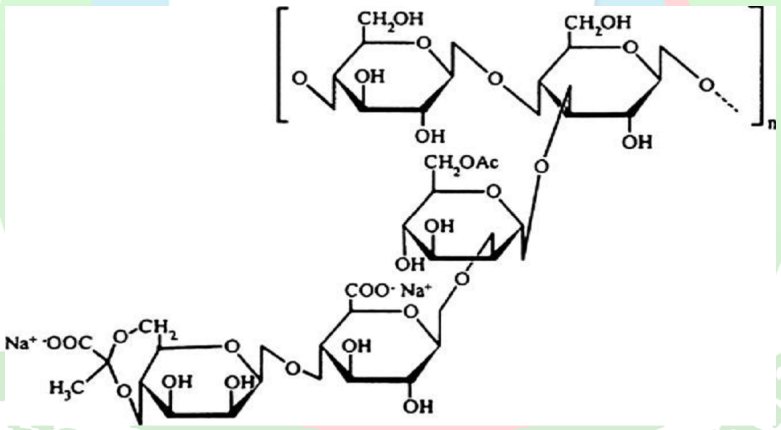

fig.- Structure of xanthan.

Some modifications of xanthan for drug delivery are gelatinized starch–xanthan gum hydrogel system, acrylamide-graftedxanthan gum, Graft copolymerization of ethylacrylate onto xanthan gum, xanthan combined with Konjac glucomannan, xanthan combined with boswellia gum (3:1), xanthan gum combined with guar gum(10:20), xanthan gumcombined with locust bean gumin 1:1 ratio. Combined xanthan gum with Konjac glucomannan to producematrix tablets of Cimetidine. Prepared rapidly disintegrating core tablets coated with a mixture of xanthan gum and guar gum. It was found that the xanthan gum:guar gum mixture (10:20) coated tablets were able to deliver the drug to the colon. 5-FU was used as model drug. Prepared 5-FU Compressed coated tablets with a mixture of xanthum gum and boswellia gum (3:1) and studies also showed that XG play a major role in retardation of drug release. Investigate the utilization of xanthan-grafted copolymer of acrylamide as a controlled release matrix for antihypertensive drugs such as atenolol and carvedilol. Prepared sustained release floating tablets of diltiazem HCl using xanthan gum for

the treatment of angina and hypertension. Prepared modified Release Tablet Formulation of Metoprolol Succinate using hydroxypropyl methylcellulose and Xanthan Gum. Ahmed et al(2010) developed a constant rate delivery formulation of diclofenac sodiumto release the drug in intestine. Matrix tablets and triple-layer matrix tablets were formulated by using locust bean gum(LG), xanthan gum(XG) and amixture LG: XG in 1:1 ratio asmatrix forming agent, and anionic SCMC were compressed on both the surfaces of the matrix core.

Prepared controlled delivery system for propranolol hydrochloride using the synergistic activity of locust bean gumand xanthan gumto avoid first pass effect. [10]

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 undehusked 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 41 product desired . 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 .

Guar gum is more soluble than locust bean gum and is a better emulsifier as it has more galactose branch points. It degrades 43 at extremes of pH and temperature (e.g. pH 3 at 50°C). 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 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. 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 44 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- 45 specific drug delivery. [11]

Tara Gum:

Tara gum is obtained from the endosperm of seed of Caesalpinia spinosa, commonly known as tara. It is small tree of the family Leguminosae or Fabaceae. Tara gum is a white, nearly odorless powder. It is produced by separating and 56 grinding the endosperm of the mature black color seeds. The major component of the gum is a galactomannan polymer similar to the main components of guar and locust bean gums, consist of a linear main chain of (1-4)-Dmannopyranose units with D-galactopyranose units attached by (1-6) linkages. The ratio of mannose to galactose in tara gum is 3:1. Produce highly viscous solutions, even at 1% concentration. Tara gum requires heating to disrupt aggregation and full dissolution, whereas guar gum is soluble in cold water.

Tara gum is used as a thickening agent and stabilizer in a wide range of food applications around the world. The use of tara gum as a controlled release carrier in the formulation of gastro retentive controlled release tablets and emulsions for drugs like metformin hydrochloride, ciprofloxacin hydrochloride nimodipine, nifedipine, carvedilol, clozapine has been claimed in patents. [11]

Khaya gum:

Khaya gum is a polysaccharide obtained from the incised trunk of the tree Khaya grandifoliola (family Meliaceae). It is known to contain highly branched polysaccharides consisting of D galactose, L-rhamnose, D-galacturonic acid and 4-O-methyl-D-glucoronic acid. Khaya gum has been shown to be useful as a binding agent in tablet formulations. Khaya gum is a hydrophilic polymer and has been shown to possess emulsifying properties comparable with acacia gum. The fact that the gum is naturally available, inexpensive and non-toxic has also fostered the interest in developing the gum for pharmaceutical use. Further work has also shown its potential as a directly compressible matrix system in the formulation of controlled release tablets. Khaya gum has been successfully evaluated as a controlled release agent in comparison with hydroxypropylmethylcellulose (HPMC) using paracetamol (water soluble) and indomethacin (water insoluble) as model drugs. Tablets were produced by direct compression and the in-vitro drug release was assessed in conditions mimicking the gastrointestinal system. Khaya gum matrices provided a controlled release of paracetamol for up to 5 h. The release of paracetamol from khaya gum matrices followed timeindependent kinetics and release rates were dependent on the concentration of the drug present in the matrix. A combination of khaya gum and HPMC gave zero-order time-independent release kinetics. In another study Khaya and albizia gums were evaluated as compression coatings for target drug delivery to the colon using indomethacin and paracetamol as model drugs. The core tablets were compression-coated with 300 and 400 mg of khaya gum & albizia gum respectively and also a mixture of khaya and albizia gum (1:1). Drug release studies indicated that khaya and albizia gums were capable of protecting the core tablet in the physiological environment of the stomach and small intestine, with albizia gum showing greater ability than khaya gum. The release from tablets coated with the mixture of khaya and albizia gums was midway between the two individual gums, indicating that there was no interaction between the gums. Studies carried out using rat caecal matter in phosphate-buffered saline at pH 6.8 (simulated colonic fluid) showed that the gums were susceptible to degradation by the colonic bacterial enzymes, leading to release of the drug. The results demonstrate that khaya gum and albizia gum have potential for drug targeting to the colon. [11]

In studies khaya gum used as binding agent in tablets, for drug targeting and controlled release has been reported. Odeku et al. evaluated khaya gum as a controlled release agent in tablet formulations. Paracetamol tablets were formulated by employing direct compression method. From their studies, it was found that khaya gum provide controlled release of drug for 5 hr. Also combination of khaya gum and hydroxypropylmethylcellulose showed zero-order time independent release kinetics. Thus, tablets matrices composed of khaya gum could be utilized to obtain sustain release. In another study studied khaya and albizia gum coating for drug targeting to the colon. Odeku et al. evaluated khaya gum as binder in tablets. Paracetamol was used as model drug. All fabricated tablets possess friability value less than 1%. Tablet formulations containing khaya gum as binder had lower tensile strength values. [12]

Gum Copal:

Gum copal (GC) is a natural resinous material of plant Bursera bipinnata (family Burseraceae). Copal, a resinous material, is obtained from the plants of araucariaceae and caesalpinaceae, a subfamily of leguminoaceae. Copal resin (CR) contains agathic acid, a diterpenoid and related lobdane compounds along with cis-communic acid, trans-communic acid, polycommunic acid, sandaracopimaric acid, agathalic acid,

monomethyl ester of agathalic acid, agatholic acid and acetoxy agatholic acid. CR obtained from leguminoaceae family contains copalic acid, pimaric acid, isopimaric acid, dehydro-dehydroabietic acid, dehydroabietic acid and abietic acid.

Medicinally, Copal is used in the treatment of headache, fever, burns and stomach ache. In dentistry, it is used as binding media in dental products and in treatment of micro leakage in teeth. Recently, Copal gum has been evaluated as matrix-forming material for sustaining the drug delivery.

In an independent study copal resin was investigated as a film forming agent . The free films, prepared in alcohol by solvent evaporation technique, were brittle with high tacking property. Addition of 1% w/w propylene glycol improved the mechanical properties of copal resin films, whereas glyceryl monostearate, sorbitan mono-oleate and sorbitan monolaurate in 15% w/w reduced the tackiness significantly. CR films showed good swelling property in phosphate buffer (pH 7.4). It was concluded that it can be used as a coating material for sustained release and colon-targeted drug delivery. [11]

Attama et al. observed the effect of gum concentration on the release rate of glibenclamide and found that when the concentration of gum copal and gum damar (GD) was increased, the drug release rate was decreased due to the formation of a dense matrix around drug molecules that prevent them to escape and dissolve. When drug release was studied using gum copal alone, it was found to follow zero order kinetics, hence used to prepare sustained release formulations. [6]

Gum Dammar:

Gum dammar (GD) is a whitish to yellowish natural gum of plant Shorea wiesneri (family Dipterocarpaceae). It contains about 40% alpha-resin (resin that dissolves in alcohol), 22% beta resin, 23% dammarol acid and 2.5% water. It has been used for water-resistant coating and in pharmaceutical and dental industries for its strong binding properties. In India, Sal damar has been widely utilized in the indigenous system of medicine. Natural gum copal and gum damar as novel sustained release matrix forming materials in tablet formulation was evaluated.

Matrix tablets were prepared by wet granulation technique using isopropyl alcohol as a granulating agent. Diclofenac sodium was used as a model drug. Effect of gum concentration (10, 20 and 30% w/w with respect to total tablet weight) on in vitro drug release profile was examined. Matrix tablets with 30% w/w gum copal and gum damar showed sustained drug delivery beyond 10 h. Drug release from gum copal matrix tablets followed zero order kinetics while gum damar (10 and 20% w/w) was found suitable to formulate the insoluble plastic matrix that releases the drug by diffusion. It was concluded that both gums possess substantial matrix forming property that could be used for sustained drug delivery. [11]

Gum dammar in the concentration range of 10–20% forms insoluble plastic matrix and releases the drug by mechanism of diffusion. When release data was applied to different models, it was found that formulation with 10-20% w/w gum concentration best fitted to Higuchi square root kinetic but when examined with 30% w/w gum concentration, it obeys zero order release kinetics. Hence, GD could be used in sustained drug delivery formulation. [6]

Karaya gum

It is a hydrophilic naturally occurring gum obtained from Sterculia urens and composed of galactose, rhamnose and glucuronic acid. It swells in water and thus used as release rate controlling polymers in different formulations. It possessed very low hydration capacity and higher erosion. When release studies were investigated, karaya gum was found to produce zero order drug release along with erosion of matrices. Gangadharappa et al. used Karaya gum to develop gastric floating drug delivery system of verapamil hydrochloride and studied its effect on drug release. It was observed that it swells on contact with aqueous medium and at a specific concentration of

23.3% produced sustained drug release for 8 h. Similarly, Moin et al. prepared sustained release tablets of diltiazem hydrochloride using locust bean gum (LB) and karaya gum along with hydroxypropyl methylcellulose (HPMC) in different ratios. It was found from the investigation that LB gum alone could not control the drug release while Karaya gum possessed the better drug retarding capability. [6]

Foster et al. prepared gastric retentive gel composed of sodium alginate and karaya gum. The in vivo study was carried out in rats. The time for gastric residence for gel was found 1 to 8 hr. They suggested that sodium alginate karaya gum gels can be utilized for designing gastric retentive dosage forms. Babu et al. studied solid dispersion of nimodipine prepared with modified gum karaya. Solid dispersions were formulated by cogrinding method. The dissolution rate of drug from solid dispersions was significantly higher than that of physical mixtures and pure drug. [12]

Aloe Mucilage

Many compounds with diverse structures have been isolated from both the central parenchyma tissue of Aloe mucilage is obtained from the leaves of Aloebarbadensis Miller. Aloe Vera leaves and the exudate arising from the cells adjacent to the vascular bundles. The bitter yellow exudate contains 1,8- dihydroxyanthraquinone derivatives and their glycosides . 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 (oracemannan) as the primary polysaccharide of the gel, while others found pectic substance as the primary polysaccharide. 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 1:2exhibited 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 Aloe Vera gel polysaccharide component therefore showed excellent potential to be used as an excipient in the formulation of direct compressible sustained- release matrix type tab. [13]

Almond Gum:

Almond gum is obtained from the tree Prunus communis which is a water soluble gum extrudes from the wounds on almond trees. The constitution of almond gum includes aldobionic acid, L-arabinose L-galactose, D-mannose etc. It contains different components which have emulsifier, thickener, suspending pharmaceutical, adhesive, glazing agent and stabilizer. Gum obtained from Almond as a binder in tablet formulations was studied.

Neem Gum:

Neem gum is obtained from the trees of Azadirachta indica belongs to the family Meliaceae. Each and every part of the tree (bark, leaves, root and fruit) serves a certain purpose. Neem gum contains mannose, glucosamine, arabinose, galactose, fucose, xylose and glucose. In a study Neem gum used as a binder in pharmaceutical dosage forms. A sustained release matrix tablets of Nimesulide using the fruit mucilage of Azadirachta indica was studied. [14]

Cashew Gum:

Cashew gum is the exudate from the stem bark of Anacardium occidentale Linn (family, Anarcardiaceae). Cashew gum is chemically composed of 61 % galactose, 14 % arabinose, 7 % rhamnose, 8 % glucose, 5% glucuronic acid and < 2 % other sugar residues, while

hydrolysis of the gum yields L-arabinose, L-rhamnose, D-galactose and glucuronic acid The gum has a highly branched galactan framework comprising of chains of (1 →3)-linked β–D-galactopyranosyl units interspersed with β- (1→ 6) linkages. Gelling potentials of a natural gum obtained from plant Anacardium occidentale was studied. Cashew gum mucilage used as a binder for the preparation of metronidazole tablet formulations. A controlled delivery system was developed for diclofenac sodium using Cashew nut tree gum, HPMC and Carbopol. [14]

Fenu Greek 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. Ability of the husk to form mucilage, its binding properties in solid dosage forms were studied. Mucilage derived from the seeds of fenugreek evaluated as a matrix formulation containing propranolol hydrochloride. Methocel K4M was used as a standard controlled release polymer for comparison. Gelling potentials of Fenugreek mucilage was evaluated. [14]

Mango Gum:

Mango gum is a dried gummy exudate polysaccharide obtained from the bark of Mangifera indica, belongs to the family Anacardiaceae. Physical, thermal, sorption and functional properties of a mango gum were characterized. The results obtained in this study establish the fundamental characteristics of mango gum. Gum of Mangifera indica (mango) as a tablet binder employing paracetamol as a model drug, resin of mangifera indica (mango) as a tablet retardant polymer in the formulation development of sustained release of drugs, employing diclofenac sodium as a model drug was studied. Mouth dissolving tablets of metformin hydrochloride was prepared using mango gum powder as disintegrant.

Ocimum Mucilage:

Ocimum mucilage is obtained from the seeds of Ocimum americanum commonly called as Ocimum canum belongs to the Family: Lamiaceae (Labiatae). Seeds are having Nutlets with narrowly ellipsoid, punctulate black. Polysaccharides composed of xylose, arabinose, rhamnose and galacturonic acids. Pharmacognostic and phytochemical evaluation of Ocimum americanum was studied. Mucilage from the seeds of Ocimum americanum was explored as a tablet disintegrant. [14]

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