SMART AND NATURAL POLYMERS USED FOR CONTROLLED DRUG DELIVERY

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1. INTRODUCTION

Smart polymers are composed of polymers that respond to very slight changes in the environment. They are also called ‘stimuli-responsive polymers’ or ‘environmental-sensitive polymers.[1] Smart polymers are a class of dynamically developing macromolecules with potential use in the life science and pharmaceutical fields. They respond to environmental conditions mimicking the behavior of structures and functions of living organisms to adapt to variations in nature.[2] Smart polymers have also been developed with a combination of temperature and pH responsiveness using acrylic acid and N-isopropyl acrylamide for the use of oral matrix systems. The main advantage of such a system is that a small change in pH results in sharp volume changes at a constant temperature. Examples of these polymers include polyesters, polyanhydrides, and polylactic acid.[3] Stimuli-responsive polymers offer

a drug delivery to deliver drug and that can be utilized to control rate in a stable and biologically active form.[4] Natural polymers are materials of large molecular weights from the natural origin such as plants, micro-organisms, and animals. Natural polymers possess ample scope in the drug, food, and cosmetic industries. Natural polymers are biogenic and their biological properties such as cell recognition and interactions, enzymatic degradability, semblance to the extracellular matrix, and their chemical flexibility make them materials of choice for drug delivery.[5] Substances of plant origin pose several potential challenges such as being synthesized in small quantities and is structurally complex mixtures, which may differ according to the plants' location and other variables such as the season. The application of plant-derived polymers in pharmaceutical formulations includes use in the manufacture of implants, beads, solid monolithic matrix systems, nanoparticles, and viscous liquid formulation [6]

Controlled drug delivery technology represents one of the frontier areas of science, which involves a multidisciplinary scientific approach, contributing to human health care. The development of appropriate carriers for drug delivery is a challenge for biomedical scientists. Peptides, Proteins, oligonucleotides, and genes are unstable compounds that need to be protected from degradation in the biological environment. Several studies have been reported so far in the development of these carriers, among which the design of biodegradable nanoparticles has drawn considerable interest.[7]

1.1 Merits and Demerits Of Controlled Drug Delivery System

Merits:

Controlled release systems have many advantages in comparison to routine systems. They keep the drug levels within the desired range, reduce side effects and toxicity, and improve efficacy, patient compliance, and comfort by reducing the frequency of

administration.[5] DDSs that reduce the side effects of anticancer drugs have attracted the attention of many researchers working in the cancer therapy field.

Demerits:

The negative points in using these systems include possible toxicity of the materials used, possible dose dumping, increased potential for hepatic first-pass metabolism, the necessity of surgical procedures to insert or remove the system, possible delay in onset of action, possible poor system availability, and high manufacturing costs.[8]

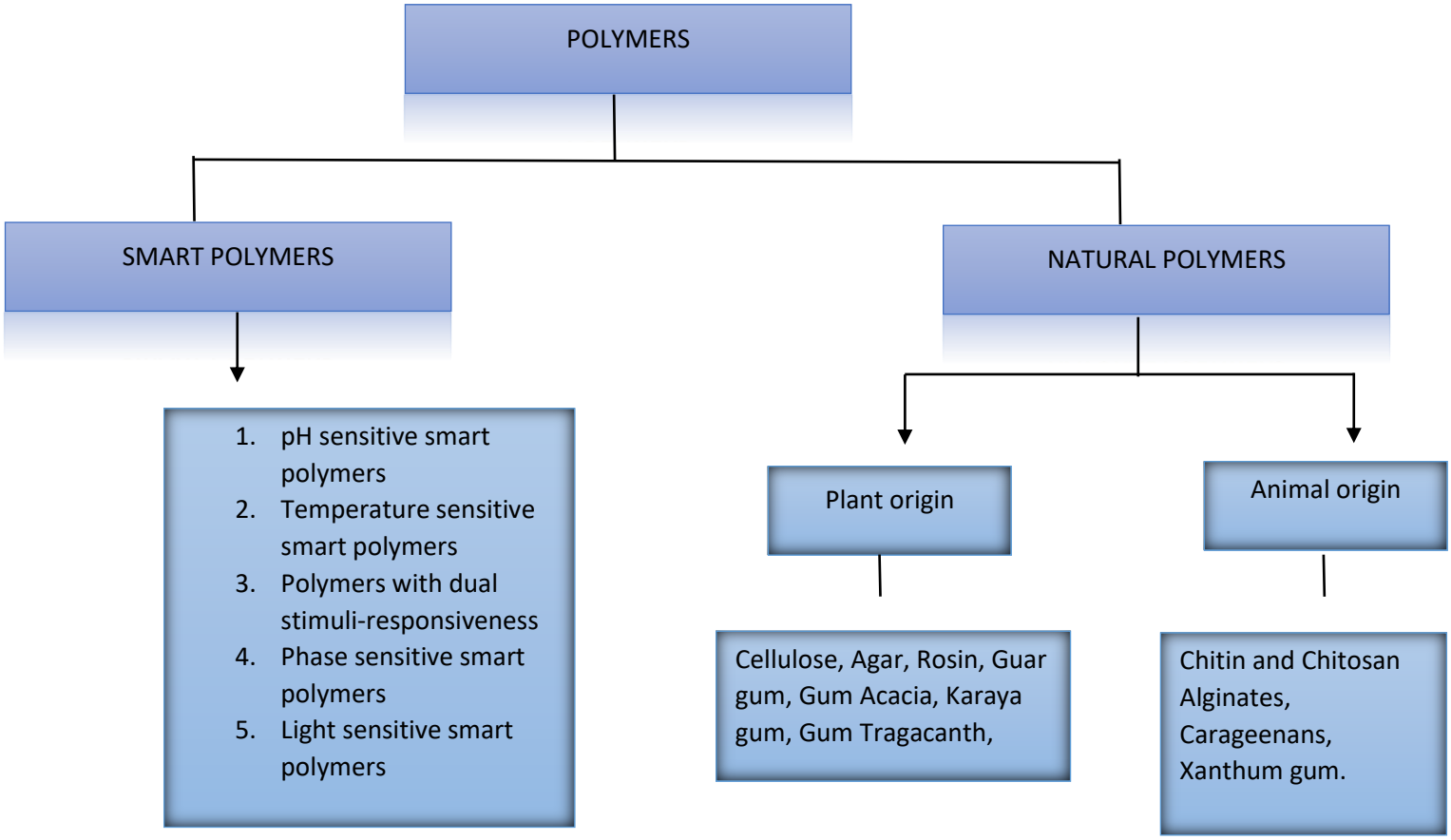
1.2 Role of Polymers for Controlled Drug Delivery System

The use of polymers is an inseparable part of the sustained dosage form. The first polymeric device developed for controlled drug release systems was done in 1960. The polymer-based controlled drug delivery systems are generally classified as Reservoir Membrane Devices and Matrix Monolithic Devices. The drug release is controlled by the polymeric membrane that surrounds the drug moiety in both of these. These polymeric membranes can be subcategorized into nonporous, microporous, hydrophobic, hydrophilic substances like hydrogels and water-swollen polymers. In transdermal drug therapy, polyacrylate, vinyl polymers, polyurethane, and cellulose derivatives are used commonly. Both acrylic and cellulosic polymers are used as film-forming agents that allow tough protective coatings.[9]

The availability of chitosan as a film-forming agent permits its wide use in the formulation of the film dosage form. Before casting into films chitosan can be dissolved in organic acids such as lactic acid and acetic acid. For the direct compression, tableting process Starch acetate (SA) polymer has been discovered as a novel and multifunctional excipient. Materials such as fibrinogen, fibrin, and collagen have been investigated as suitable carriers for novel drug delivery systems. In the terms of non-toxicity and biocompatibility to most

tissues, collagen has efficient structural, physical, chemical, and immunological properties that can be easily altered. The drug release rate is influenced by diffusion across the membrane and tablet coating so that polymer doesn't undergo two factors during its lifetime, i.e., dissolution and degradation.[9] The most commonly used water-insoluble polymers for extended-release applications are the ammonium methacrylate copolymers (Eudragit RS and RL), cellulose derivatives ethyl cellulose, and cellulose acetate, and polyvinyl derivative, polyvinyl acetate.[10]

2. CLASSIFICATION OF POLYMERS



2.1 Smart Polymers

2.1.1 pH-sensitive smart polymers

A polymer's pH responsiveness is generally obtained through the protonation and deprotonation cycle of a weak polybase and/or weak polyacid in the block copolymers at different pH or by pH-induced conformation changes copolymers.[8] pH-sensitive smart polymers are polyelectrolytes there are weak basic or acidic groups in their structure that either release or accept protons in response to change in the pH environment. In the pH-sensitive polymers, as the external pH increases swelling of the polymer also increases in the case of weakly acidic (anionic) groups called polyacids, but decreases if polymer contains weakly basic (cationic) groups known as polybases. Most of the anionic pH-sensitive smart polymers are based on polyacrylic acid (PAA) (Carbopol) or its derivatives, poly (ethyleneimine), polymethacrylic acid (PMAA), and poly (N, N-dimethylaminoethyl methacrylamide), poly (L-lysine).[1]

Ionizable polymers with a pKa value between 3 - 10 are suitable for the use of pH-responsive systems. Bases and weak acids such as phosphoric acid, carboxylic acids, and amines exit in a change in the ionization state upon change of the pH, its result in a conformational change in the swelling of hydrogels and the soluble polymers when these ionizable groups are connected to the polymer structure.[8] When polyelectrolyte chains are ionized in hydrophobic form, a poor solvent will collapse into globules and precipitate from the solution. The interplay between electrostatic repulsion and hydrophobic surface energy charges dictates the behavior of the polyelectrolytes. By generating the charge along the polymer backbone, the electrostatic repulsion increases the hydrodynamic volume of the polymer.

Table 1: Applications of pH-responsive polymeric drug delivery systems.

Drug	Polymer	Application	Outcome	Ref.
Ketoprofen	Poly(acrylamide)-g-carrageenan and sodium alginate	For colon targeted delivery	Ketoprofen release was significantly increased when the pH of the medium was increased from acidic to alkaline	[1]
Fibroblast growth factor	Poly (n-isopropyl acrylamide co propyl acrylic acid-co-butyl acrylate)	To improve angiogenesis infracted myocardium	It provides the advantage of acidic Microenvironment of ischemic Myocardium	[12]
Paclitaxel and doxorubicin	Poly (ethylene glycol)-block-poly (propylene glycol)-poly (ethylene glycol)	Prolongation of survival Time in comparison with single-drug therapy	The release rate can be accelerated by Decreasing the environmental pH from acidic to alkaline	[13]

2.1.2 Temperature-sensitive smart polymers

One of the most widely used stimuli for stimuli-sensitive polymers is temperature since it is easily controlled and has practical in vitro and in vivo advantages.[8]

Temperature-sensitive smart polymers exhibiting one phase above a specific temperature and phase separation below it appears an upper critical solution temperature (USCT). On the other hand, polymer solutions that show a monophasic below a certain temperature and biphasic above it, generally exhibit the lower critical solution temperature (LCST).[1] The fact that body or body-site temperature may change upon fever, local infections, or diseases, and a drug may be released as a result of such trigger if the LCST of the material is close to body temperature is the major rationale for its use. The therapeutic agents may be introduced in such systems by various methods. The simplest is to swell the dry material up to equilibrium in a solution containing the drug. Another method is to

synthesize the gel by using a mixture of the monomer (including the initiator and the cross-linker) or the polymer (with the cross-linker) along with the drug.[1]

Table 2: Applications of temperature-responsive polymeric drug delivery systems.

Drug	Polymer	Application	Outcome	Ref.
Exenatide	PLGA–PEG–PLGA	Treatment of type II Diabetes	To produce a long-acting injectable Formulation	[14]
Docetaxel	Conjugated linoleic acid coupled with Pluronic F-127	Peritoneal dissemination of gastric cancer	Hydrogel produced controlled release and excellent antitumor activity	[15]
Ethosuximide	Chitosan with glycerophosphate disodium salt and glycerol	Injectable gels for depot therapy	To produce a sustained-release injectable Formulation	[16]
Leuprolide	Poly-benzo fulvene	For treatment of Tumors	To protect the oligopeptide drug and regulate the release rate by external temperature	[17]

2.1.3 Polymers with dual stimuli-responsiveness

Recently, stimuli-responsive polymers have been utilized in dual and multi-responsive delivery systems. This was undertaken to develop more effective, reproducible stimuli-modulated delivery. PH-responsive polymers have been more extensively used (Table 3). Notably, Wanget al. developed a novel pH and redox dual-sensitive hepatoma-targeted MPEG-b-PMAGP-SS-DOX multifunctional polymeric micelle system. This amphiphilic block conjugate displayed appreciable antitumor activity in vitro in addition to sustained and controlled drug-release kinetics.[18]

Table 3: Overview of dual-responsive carriers for stimuli-modulated drug delivery

Stimuli	Carrier	Drugs	Ref.
pH/redox	- CS-SH and DS based LbL nanocapsules - PDS-g-PEG/cRGD nanoparticles - Poly (b-amino ester) s-PEG micelles - PEG-PAsp(MEA)-PAsp(DIP) micelles	Bovine Serum -Albumin Doxorubicin	[19]

	- PEG-SS-PTMBPEC micelles - DOX-conjugated PEO-b-PMAA micelles - Polythioether ketal nanoparticles	Adriamycin Ovalbumin	
pH/magnetic	- Fe3O4 nanocarriers coated with peptide mimic Polymers - DOX-tethered Fe3O4 conjugates nanoparticles - Fe3O4 @SiO2 nanoparticles coated with PEGpoly(imidazole l-aspartame) - MCM-TAA- Fe3O4-capped MSNs mPEG-b-PMAA-b-PGMA-Fe3O4 nanoparticles	Doxorubicin HCl Doxorubicin Adriamycin	[19]
Temperature / redox	PEO-PPA-PNIPAAm polymersomes	Proteins	[19]
Temperature / magnetic	Pluronic with Fe3O4 nanoparticles	Doxorubicin	[19]
Temperature / enzyme	DNA-capped MSNs	Camptothecin, floxuridine	[19]

2.1.4 Phase-sensitive smart polymers

Phase-sensitive smart polymers are used to develop biocompatible formulations to control proteins in a stable and biologically active form. The advantages over other systems are ease of manufacture, less stressful manufacturing conditions for sensitive drug molecules, and high loading capacity.[1]

This approach employs a water-insoluble biodegradable polymer, such as poly (D, L-lactide- e-caprolactone), poly (D, L-lactide-co-glycolide), and poly (D, L-lactide), dissolved in a pharmaceutically suitable solvent to which a drug is added to form a solution or suspension. After the formulation is injected into the body, the water-miscible organic solvent dissipates and water penetrates the organic phase. This causes phase separation and precipitation of the polymer forming a depot at the site of injection. Organic solvents used in hydrophobic solvents, such as N-methyl-2-pyrrolidone (NMP), triacetin, hydrophilic solvents, tetraglycol, and benzyl benzoate.[20]

Table 4: Phase-sensitive smart polymers in drug delivery

Smart polymer system	Solvent	Drug	Ref.
PLGA	N-methyl-2-pyrrolidone (NMP), Glycofurol, Triacetin, Dimethyl sulfoxide	Leuprolide acetate, Bovine serum albumin (BSA), Leuprolide acetate, BSA	[21]
PLA	Benzyl benzoate (BB)	Levonorgestrel, Lysozyme, Testosterone	[22]
PLC	Dimethyl sulfoxide	Cisplatin	[20]

2.1.5 Light sensitive smart polymers

Owing to the possibility of producing materials that are sensitive to innocuous electromagnetic radiation (mainly in the UV, visible, and near-infrared range), light responsiveness is receiving increasing attention. Such materials could be applied at well-delimited sites of the body on demand. Several light-responsive DDSs are of single-use (the light triggers an irreversible change that provokes the release of the entire dose), while some others are capable of undergoing reversible structural changes whenever cycles of light/dark are applied and behave as multi-switchable carriers releasing the drug in a pulsatile way.[8] The macromers include one water-soluble region which is biodegradable and two free-radically polymerizable regions. Macromers are polymerized by free radical initiators under visible light excitation and ultraviolet light. The core water-soluble region can consist of PEG, PEO-PPO, poly (vinyl alcohol), proteins such as albumin, or polysaccharides such as hyaluronic acid. The biodegradable regions are made up of polylactones, polylactic acid, poly (amino acids). The most preferable polymerizable regions include acrylates, diacrylates, methacrylates. Initiators that can be used for the generation of free radicals include ethyl eosin, camphorquinone, or acetophenone derivatives.[23]

Table 5: Types of response for light-sensitive smart polymers

Chains of physical form	Types of response	Examples	Ref.
Uncross-linked-free linear chains (conjugates)	Solubilization/ precipitation	Use of polymers active compound conjugates	[24]
Amphiphilic (uncross-linked) block and surface-grafted copolymers	Micellization	Pluronics or poloxamers (PEO-PPO-PEO)	[25]
Cross-linked hydrogels	Swelling -deswelling response	Pulsed drug delivery	[26]
Modified surfaces	Responsive interfaces	New substrates for cell culture	[27]

2.2 Natural Polymers

2.2.1 Plant Origin

Cellulose

Cellulose was discovered by the French chemist Anselme Payen in 1838, which is isolated from plant matter and determined its chemical formula. Cellulose is an organic polysaccharide with the formula (C6H10O5) n, consisting of a linear chain of several hundred to over ten thousand β (1→4) linked D-glucose units.[6]

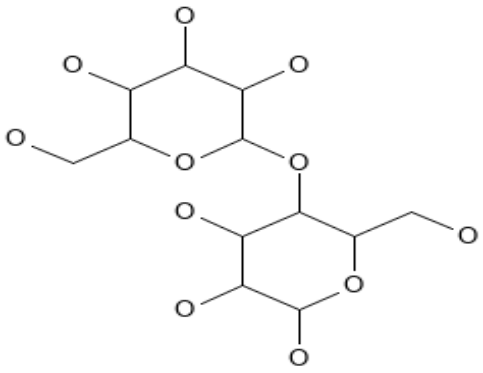


Figure 1: Structure of cellulose

Source

It can be derived from several sources using many techniques that are considered synthetic and some that might be considered non-synthetic (natural). It is available in many forms for different functions Petitioned uses in food products include as a processing aid for filtration of juices, as an anti-caking agent ingredient for shredded cheese, and as a processing aid in the form of peelable hot dog casings.[28]

Cellulose-Based Polymers:

- Ethylcellulose Insoluble but dispersible in water, aqueous coating system for sustained release applications.
- Carboxymethyl cellulose Super disintegrant, emulsion stabilizer.
- Hydroxyethyl and hydroxypropyl celluloses.
- Soluble in water and alcohol, tablet coating
- Hydroxypropyl methylcellulose Binder for tablet matrix and tablet coating, gelatin alternative as capsule material.
- Cellulose acetate phthalate enteric coating

Application

Its applications for cellulose derivatives include the formulation of membrane-controlled drug release systems or monolithic matrix systems. Film coating techniques for the manufacture of membrane-controlled release systems include enteric-coated dosage forms and the use of semipermeable membranes in osmotic pump delivery systems.

Microcrystalline cellulose is used in the pharmaceutical industry as a binder and diluent in tablets for both the direct compression and granulation processes. Carboxylated methylcellulose is used in drug formulations, as a binder for drugs, film-coating agent for drugs, ointment base, etc. Cellulose acetate fibers are used in Wound dressings.

Agar

Agar consists of a mixture of agaropectin and agarose. The predominant component, agarose, is a linear polymer, made up of the repeating monomeric unit of agarobiose. Agarobiose is a disaccharide made up of D-galactose and 3,6- anhydro-L-galactopyranose. Agaropectin is a heterogeneous mixture of smaller acidic molecules that gel poorly.[5]

Agar provides gels without flavor and does not need the additions of cations with strong flavors (potassium or calcium) it can be used without problems to gel food products with soft flavors.[6]

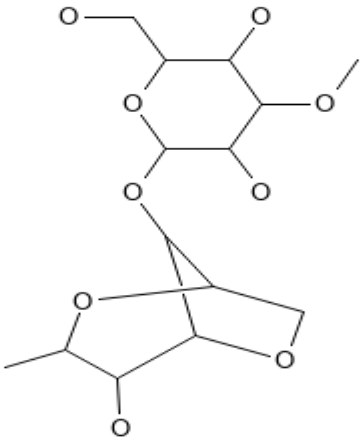


Figure 2: Structure of Agar

Source

Agar or agar-agar is the dried gelatinous substance it is obtained from Gelidium amansii (Gelidaceae) and many other species of red algae-like grailaria (Gracilariaceae) and Pterocladia (Gelidaceae).[5]

Applications

Agar is used as emulsifying agent, suspending agent, surgical lubricant, gelling agent in suppositories, tablet disintegrants, laxative, medium for bacterial culture.

Rosin

Rosin contains approximately 90% rosin acids. The rosin acids are monocarboxylic and have a typical molecular formula C20H30O2. The prominent ones include abietic acid with conjugated double bonds and pimaric acid with non-conjugated double bonds. The rosin acid molecules possess two chemically reactive centres, the double bonds, and the carboxyl group. However, rosin remains an attractive renewable source of chemicals useful for polymer synthesis or in the pharmaceutical industry.[29]

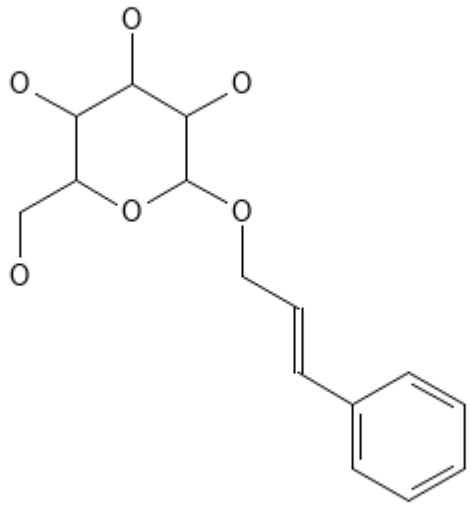


Figure 3: Structure of Rosin

Source

Rosin (also known as colophony) is a solid resinous material obtained from the oleoresin (tree sap) of live pine trees (called gum rosin), the stump wood of dead pine trees by solvent

extraction (called wood rosin), and in the pulp paper recovery process (called tall oil rosin).[30]

Application

The most important traditional applications of rosin and its derivatives include, as paper sizing agents, adhesives, printing inks, and chewing gum has declined due to escalating production labour costs. (rosin). The modified resins give more specific characteristics to the rosin to improve or change their stability, aging, color, tackiness.[31]

Guar gum

Guar gum is a galactomannan that shows an absence of uronic acid making it different from most plant gums and has one of the highest molecular weights among naturally occurring water-soluble polysaccharides. The viscosity of guar gum solution can be more appropriately termed as apparent viscosity and like most of the hydrocolloids is strongly dependent on shear rate. As guar gum is anionic, it remains stable and gives consistent viscosity over a wide pH range. The maximum viscosity is obtained in the pH range of 6–9 while the lowest is at pH 3.5.[31]

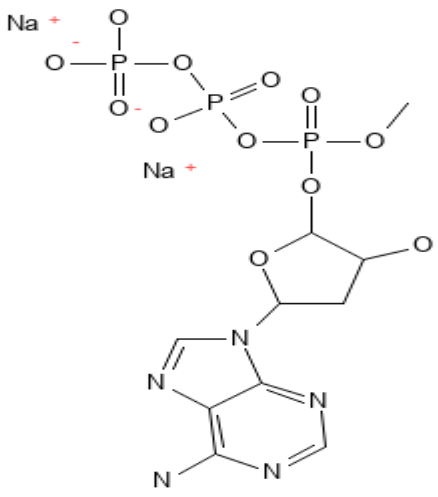


Figure 4: Structure of Guar gum

Source

Guar gum is the powder of the endosperm of the seeds of Cyamopsis tetragonolobus Linn. (Leguminosae). Guar gum is also known as guaran, Calcutta lucern, cluster bean, Cyamopsis gum, Gum Cyamopsis, Glucotard, Guarina, and Guyarem.[6]

Applications

Carboxymethyl guar film is used for the formulation of a transdermal therapeutic system. Guar gum is mainly useful for colon delivery because it can be degraded by specific enzymes in this region of the gastrointestinal tract. The gum protects the drug while in the stomach and small intestine environment and delivers the drug to the colon where it undergoes assimilation by specific microorganisms or degraded by the enzymes excreted by these microorganisms.[5] It is also used in food, paper, cosmetics, textiles, explosives, and mining industries.

Karaya Gum

Gum karaya is one of the least soluble of the exudate's gums. Due to its high viscosity, acid stability, and suspension properties, gum karaya is well good for stabilizing low pH emulsions, such as sauces and dressings. When it is dispersed in water, the gum particles are not dissolved but it absorbs water and swells extensively to more than 60 times the original volume, producing a viscous colloidal sol. The swelling behavior of gum karaya is caused by the presence of acetyl groups in its structure.[1]

Source

Karaya gum is obtained from Sterculia urens (Sterculiaceae) and is a partially acetylated polymer of rhamnose, galactose, and glucuronic acid. Swellable hydrophilic natural gums like karaya gum and xanthan gum were used as release-controlling agents in producing directly compressed matrices.[6]

Applications

Gum Karaya is used extensively in many unrelated industries because of its properties such as gel water-absorbing / moisture absorbing, and film-forming, adhesiveness abilities. It is highly resistant to hydrolysis by mild acids and most microorganisms' degradation. The major use of Gum Karaya is as a bulk laxative because of its ability to form a mucilaginous gel in contact with water. Gum Karaya is also used for diverticular disease and as a laxative. It is also widely used in the cosmetics and food industry. It is also used to design dosage forms for controllerelease systems.[6]

Gum Tragacanth

Source

This gum is obtained from the branches of Astragalus gummifer (Leguminosae). Tragacanth contains from 20% to 30% of a water-soluble fraction called tragacanthin (composed of tragacanthic acid and arabinogalactan). It also contains from 60% to 70% of a water-insoluble fraction called bass Orin. Tragacanthic acid is composed of D-xylose, D-galacturonic acid, D-galactose, L-fructose, and other sugars. Tragacanthin is composed of arabinose and uronic acid and dissolves in water to form a viscous colloidal solution, while bass Orin swells to form a thick gel.[6]

Applications

GT has been found a useful plant-derived molecule in a wide range of healthcare-related applications, such as lotions applied for external applications (hair and hand creams). Due to its remarkable stability in wide ranges of pH and temperatures, GT is commonly used as an emulsifier in food, drugs, and related industries with an exceptionally long shelf life. For instance, GT is being applied as an emulsifying/suspending agent in pharmacological

industries. Moreover, GT has been historically used as an analgesic and a conventional therapy in curing cough and lip fissures.[32]

2.2.2 Animal origin:

Chitin and chitosan

Chitin is the polysaccharide derivative containing amino and acetyl groups and is the most abundant organic constituent in the skeletal material of the invertebrates. It is found in annelids, molluscs, arthropods, and also as a constituent of the mycelia and spores of many fungi.[6]

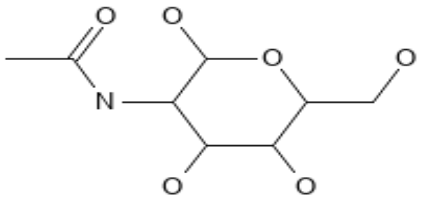


Figure 5: Structure of Chitin

The new polyelectrolyte complex gel beads based on Phosphorylated Chitosan (PCS) were developed for the controlled release of ibuprofen in oral administration.

The PCS gel beads were readily prepared from soluble phosphorylated chitosan by using tripolyphosphate (TPP), ionotropic gelation with counter polyanion, at pH 4.0. The %release of ibuprofen from PCS gel beads was found to be increased as the pH of the dissolution medium increased.[6]

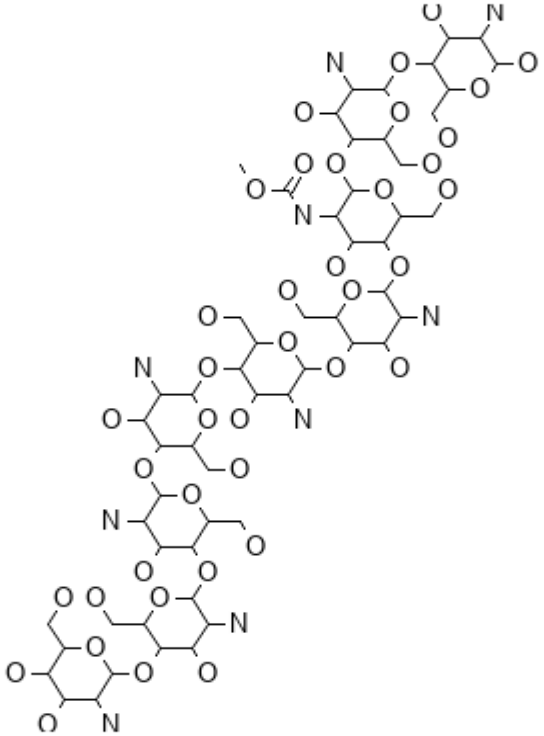


Figure 6: Structure of Chitosan

Applications

Chitosan is effective and safe absorption enhancers to improve mucosal (nasal, peroral) delivery of hydrophilic macromolecules such as peptide and protein drugs and heparins.

Alginate

Alginate, a natural biopolymer has been efficiently used for expulsion of various substantial metals and colorants from hydrated solutions because of the presence of negatively charged carboxyl group. (alginate) Alginate is comprised of biocompatibility, nontoxicity, hydrophilicity, and l-guluronic acid, and a linear copolymer of b-(1-4) of d-mannuronic sublimates obtained from the cell walls of brown algae.[33]

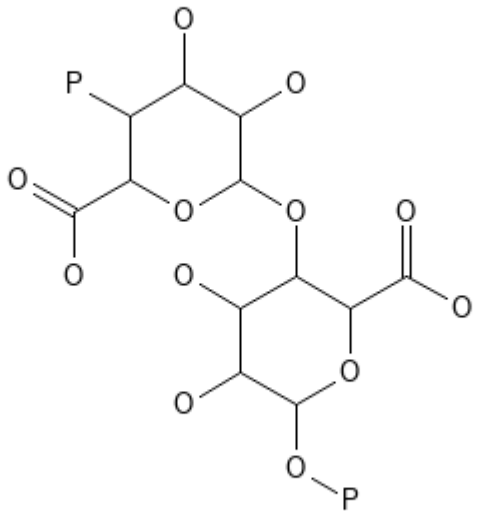


Figure 7: Structure of Alginate

Source

Alginates or alginic acids is an anionic polysaccharide that is linear, unbranched polysaccharides found in brown seaweed and marine algae such as Laminaria Hyperborea, Ascophyllum nodosum, and Macrocystis pyrifera.

Applications

Alginates beads are widely used for decontamination by eliminating various aquatic pollutants like heavy metals, various classes of coloured contaminants (dyes), several organic/inorganic pollutants through meta-biologically mediated or Physico-chemical pathways such as adsorption, precipitation, ion exchange, reverse osmosis, evaporation, floatation, oxidation, and biosorption processes. (alginate) It is also used as stabilizers in emulsions, suspending agents, tablet binders, and tablet disintegrants.[5]

Carrageenan's

Carrageenan (CG) is the general name for a group of high molecular weight sulphated polysaccharides obtained by extraction of red seaweeds formed by alternate units of D-galactose and 3, 6-anhydro-galactose (3, 6-AG) joined by α-1, 3 and β-1, 4-glycosidic linkage. CG is a sulphated polyglactin with 15-40% ester-sulphate content, which makes it an anionic polysaccharide.[34]

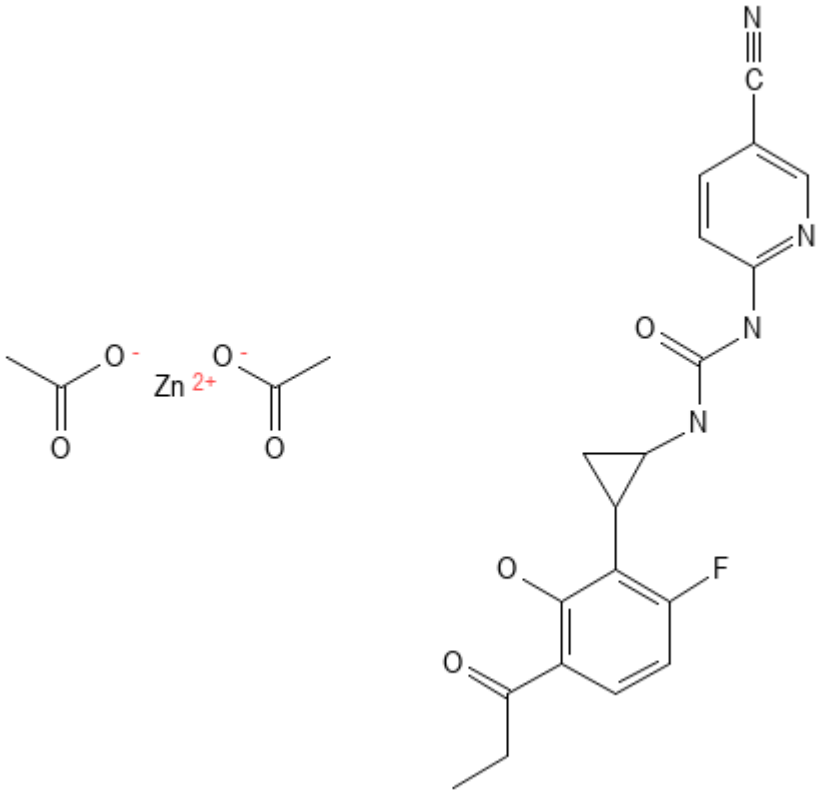


Figure 8: Structure of Carrageenan

Source

Carrageenan is extracted from red seaweed of the Rhodophyceae family, commonly from genera such as Eucheuma, solieria, cripus, agardhiella, chondrus, hypnea, sarconema, iridaea, Gigartina stellate, and agardhiella. Eucheuma and Kappaphycus seaweeds are the most commonly cultivated seaweed across Malaysia and Southeast Asia.[34]

Applications

Carrageenan's are used for the induction of experimental inflammation and inflammatory pain. Carrageenan's have many applications in non-food and food productions. In the food industry, carrageenan is generally used because of its excellent physical and functional properties such as, stabilizing ability, gelling, emulsifying, and thickening agent, and has been utilized to enhance the quality of dairy sweets, puddings, cheese. They can also be used as stabilizers and binders in the meat manufacturing industries for the production of low-calorie sandwiches.

Xanthan Gum

Xanthan gum has a high molecular weight extracellular polysaccharide it is produced by the fermentation of the gram-negative bacterium Xanthomonas campestris. The primary structure is naturally produced by cellulose derivative contains a cellulosic backbone (β-D-glucose residues) and a trisaccharide side chain of β-D-mannose-β-D-glucuronic acid-α-D-mannose attached with alternate glucose residues of the main chain. Xanthan gum shows high ability to retard drug release than synthetic hydroxypropyl methylcellulose.[6]

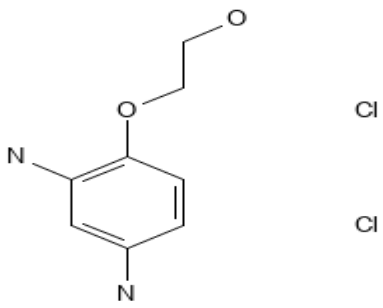


Figure 9: Structure of Xanthan gum

Applications

Xanthan gum is widely used in oral and topical formulations, cosmetics, and in the food industry as a suspending and stabilizing agent. It has also been used to prepare sustained release matrix tablets.

CONCLUSION

Smart polymers and natural polymers play an important role in drug delivery. Here we can say that smart polymers have a very wide range of applications and have an exciting future. The smart polymer also provides a link between therapeutic needs and drug delivery. While natural polymers it is very advantageous for controlled drug delivery. It shows fewer side effects comparatively than synthetic polymers. Natural polymers are also used for nanoformulation for targeting and sustained delivery with fewer side effects.

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