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Polymer Science in Development of Sustained/Controlled Drug Delivery System

Parthiban S, Madhukumar M T*

1. Department of Pharmaceutics, Bharathi College of Pharmacy, Bharathinagara, Mandya, Karnataka, India

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ABSTRACT

This study outlines the most recent advancements in the use of synthetic, semi-synthetic, and natural polymers for drug administration. Drug delivery systems are frequently created using inorganic materials or synthetic, semisynthetic, or natural polymers. When it comes to attributes like biocompatibility, biodegradability, solvent-free manufacturing, and renewable resource availability, natural and semi-synthetic polymers frequently hold a benefit over synthetic polymers. Certain polymers are employed to provide uniform medication administration, lower the frequency of dosing, and boost the drug's potency by localizing it at the site of action. By changing the pharmacokinetic and pharmacodynamics characteristics of specific medications, the development of controlled/sustained release technologies facilitated the design of new dosage forms while improving efficacy and safety. Matrix, reservoir, and implant forms have been created using a variety of natural or synthetic polymers. This study examines current advancements in the use of synthetic, natural, and semi-synthetic polymers as drug carriers for controlled or sustained release.

Keywords: synthetic polymers, semi synthetic polymers, natural polymers, controlled / sustained drug delivery system.

Introduction

The term polymer comes from the Greek word "poly" and "mer," which imply "many parts." A polymer is "a large molecule that is composed of repeated chemical units." The smallest repeating unit is known as a "mer," and the total number of repeating units in a chain is known as polymerization. Polymer chains can be chemically or physically linked to each other. These connections, known as cross-links, allow the connected chain to function as a single entity. The polymer chains can also be chemically or physically linked to the desired medicinal ingredient. After being joined, polymers are known to hold medicinal substances within their molecules. These polymers not only transport the encapsulated therapeutic ingredient to its target site but also keep it stable for a longer period of time. [1]

The majority of pharmaceutical products intended for oral administration are traditional drug delivery systems with instant release types, which release the medication immediately to facilitate quick absorption. The following are some of the limitations of these instant release dose forms: Short half-lives need frequent dosage delivery, which raises the possibility of drug dose misses and consequently low patient compliance. The resulting peak-valley plasma concentration time profile is normal and presents a challenge in achieving steady state conditions. As the CSS therapeutic range varies, it is possible for under medication or overmedication to result from the inevitable changes in drug concentration. Values change outside the range of treatment. When overmedication happens, the varying drug levels might hasten the onset of negative effects, particularly when the medicine has a limited therapeutic index. [2]

Drug delivery with controlled or sustained release has ushered in a new era of innovative pharmaceutical technology. These dosage forms are a kind of reservoir meant to release medication continuously and steadily over an appropriate length of time in order to keep the concentration of the drug in the plasma at a therapeutic level. [3]

By reducing the frequency of drug administration, decreasing steady-state fluctuations in drug levels, increasing the safety margin of low therapeutic index drugs, maximizing drug utilization, and reducing healthcare costs through more effective therapy and shorter treatment durations, sustained/controlled release drug delivery improves patient compliance. [4]

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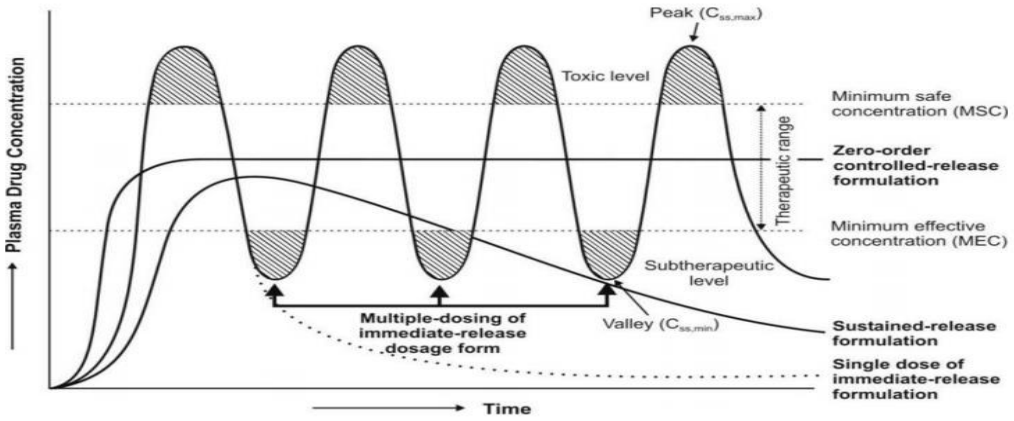

Fig.1 Plasma drug concentration v/s time profile of conventional dosing and once daily sustained and controlled release formulation.

Advantages of Sustained /controlled release dosage forms: [5]

• Reduced local and systemic side effects. - Decreased stomach discomfort.
• Improved medication utilization: - A reduction in the total amount of drugs utilized. - Low drug accumulation on chronic dosing.
• Increased treatment efficiency.
• Optimized therapy.
• Reduced drug level fluctuations, leading to more consistent pharmacological responses.

Disadvantages of Sustained /controlled release dosage forms: [2]

- Poor formulation strategies may lead to dosage dumping.
- Increased potential for first-pass metabolism.
- Dosage form's GI residence time becomes more important.
- Some dose adjustments may be less accurate.
- Cost per unit dose is higher than standard doses.
- Not all medications can be formulated into ER dose form.
- Poor correlation between in vitro and in vivo measurements.
- Limits the ability to change drug doses for different strengths.

Principle of Sustained/ controlled Release Drug Delivery Systems [6]

The traditional dose forms release the active substances into the absorption pool. The term "absorption pool" refers to the medication solution at the absorption site. The first order rate constants for drug absorption, drug release, and drug elimination are Ke, Kr, and Ka. Drug release is instantaneous in typical dosages, demonstrating that Kr>>>>>Ka. However, Kr <<\\ Ka for dosage forms with non-immediate release, meaning that the drug dose release is the rate-limiting step. It is evident that zero order kinetics exists, as the equation illustrates.

$$Kr° = \text{Rate In} = \text{Rate Out} = KeCd\ Vd$$

Where, K: Zero-order rate constant for drug release- r° Amount/time, K: First-order rate constant for overall e drug elimination-time, C: Desired drug level in the d body – Amount/volume, and V: Volume space in d 4 which the drug is distributed in liter.

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Classification of controlled/sustained drug delivery system [6] [2]

1. Dissolution type systems: A product that, for medications with high water solubility, naturally holds the drug at a slow dissolving rate and slows it down by adding enough salt or forming a derivative. These tools are typically employed in the enteric coating dosage form production process. A coating that dissolves in natural or alkaline water is used to protect the stomach from the effects of medications like aspirin. It holds off on releasing the medication from the dosage until the intestines reach a lower pH.

2. Diffusion type system: Drug molecules are transported from areas of higher concentration to areas of lower concentration. J = - D dc/dx gives the drug flux. Change in concentration 'c' with distance 'x' is equal to D = diffusion coefficient in area/time dc/dx.

3. Ion exchange: Using ion exchange resin is an appealing strategy for continuous drug delivery because the characteristic of drug release depends largely on the ionic environment of drug-containing resins and is less sensitive to environmental conditions such as enzyme content and pH at the absorption site.

4. PH-independent formulation: The majority of pharmaceuticals are weak acids or weak bases, and the release from a sustained release formulation is pH dependent. However, buffers such as citric acid salt, amino acid, and tartaric acid can be added to the formulation to help maintain a consistent pH by slowing pH-independent drug release. A buffer sustained release formulation is created by combining a basic or acidic medication with one or more buffering agents, granulating with appropriate excipients, and coating with a gastrointestinal fluid-permeable film-forming polymer. When gastrointestinal fluid passes across the membrane, the buffering agent adjusts the fluid within to an appropriate constant pH, resulting in a consistent rate of drug release.

5. Delayed release systems

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

The drugs those are

- Destroyed in stomach or by intestinal enzymes.
- Known to cause gastric irritation
- Absorbed from specific site in intestine, or exert local effect at specific GI site are formulated in such systems.

The two types of delayed release systems are

- Intestinal release systems
- Colonic release systems.

6. Osmotic pressure-controlled systems

1. A semi-permeable membrane is placed around the tablet, particle, or drug solution, allowing water to enter the tablet and eventually pump the drug solution out via the small delivery aperture in the tablet core. There are two types of osmotic pressure control systems:

I.Type 1 contains an osmotic core with drug

2. Type 2 contains the drug in flexible bag with osmotic core surrounding by optimizing formulation and processing factor, it is possible to develop osmotic system to deliver the drug of diverse nature at pre-programmed rate.

3. Altered density: Because not all of the drug contents are released in the GIT, its usage is limited; to counter this, numerous strategies for increasing the resident time in the GIT have been devised.

a) High density Approach: Pellets should have a density of 1-4 gm/cm3, which is higher than the contents of the stomach. Zinc oxide and other heavy, inert ingredients are used to coat the medication.

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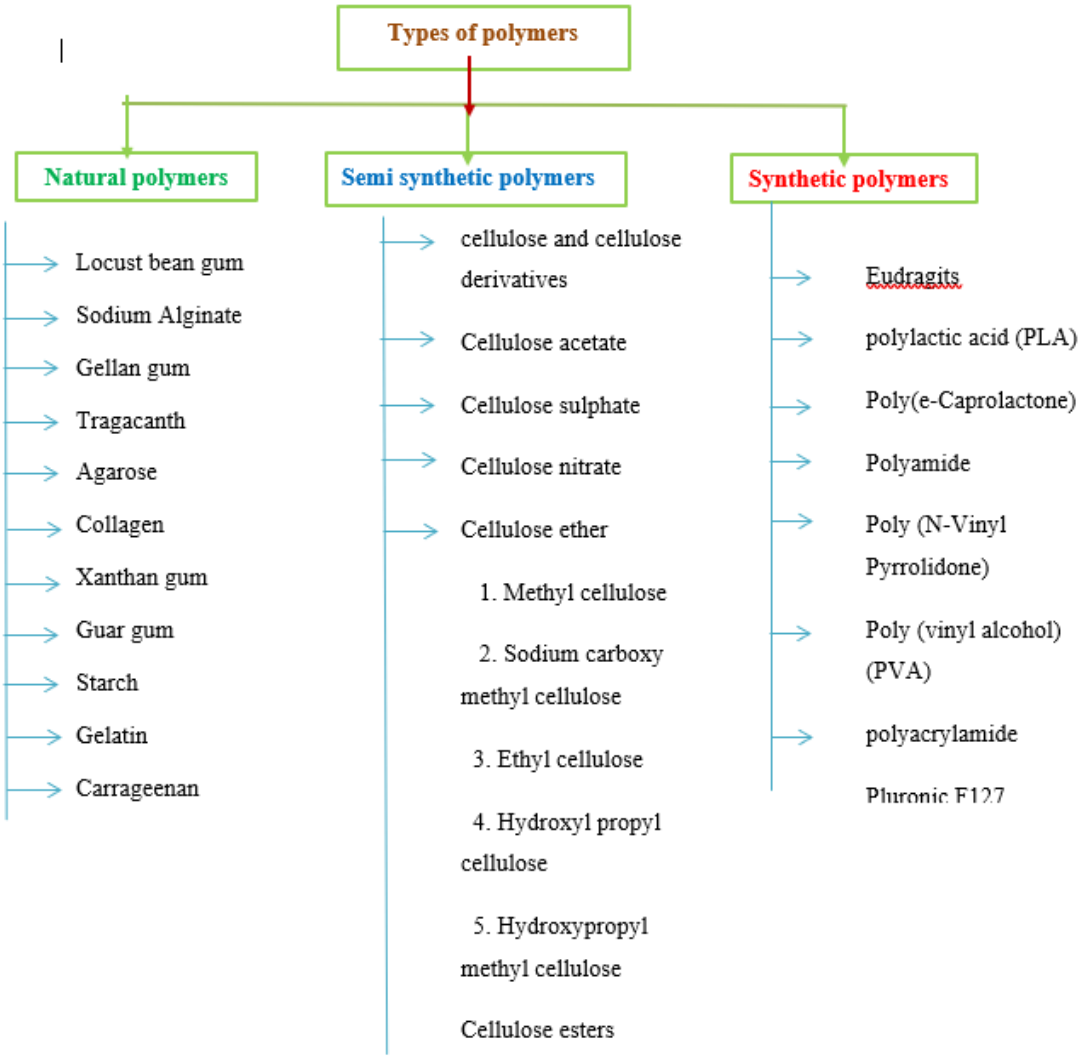
b) Low density approach: Polystyrene, pop rice, and popcorn are examples of lobular shells with a thickness less than that of gastric fluid that are used as a product carrier for sustained release. Sugar or polymeric materials such as methacryl polymer and cellulose acetate phthalate are used to undercoat the surface of these empty shells. The undercoated shell is then coated with a product mixture containing polymers such as ethyl cellulose and hydroxypropyl cellulose. As a result, the final product lingers in the gastric fluid for an extended period of time before being gradually released.



Natural polymers on drug delivery system

Natural polymers Natural polymers have recently emerged as the preferred material for developing drug delivery systems due to their high compatibility and biodegradability when compared to manufactured polymers. These polymers can be derived from a variety of natural resources, including animals and plants, as well as from marine and microbial sources. Some common examples of natural polymers for medication delivery are shown below.

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LOCUST BEAN GUM

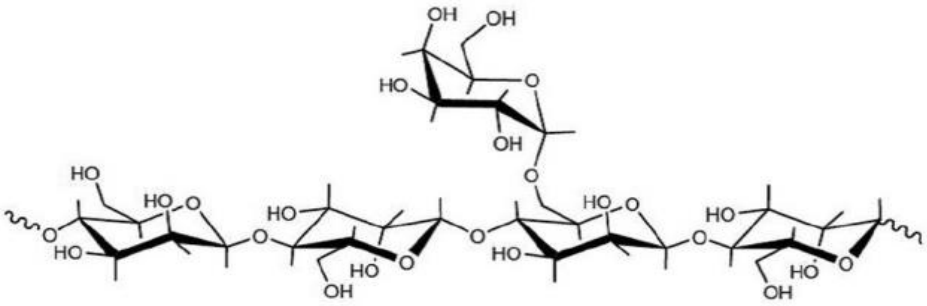

Fig. 2 Structure of locust bean gum

Locust bean gum (LBG) is a linear chain of β-d-mannopyranosyl units with unevenly spaced side branches.[5] LBG is a non-starch polysaccharide derived from Ceratonia siliqua seeds (Fabaceae), which contain galactose and mannose in a 1:4 ratio. LBG is a prominent natural polymer that is widely used in the pharmaceutical and food industries. Because of its thickening and gelling properties, this natural polymer is commonly utilized as an excipient in the manufacture of many medicinal formulations. Celecoxib loaded biodegradable microparticles made from locust bean gum and xanthan gum. In vitro investigations on medication release profile studies showed that increasing the concentration of locust bean gum and xanthan gum increase drug release retardation (Sharma et al., 2015). [7] Microspheres loaded mesalamine made from the locust bean gum by ionic gelation process can target the colon to treat ulcerative colitis. Microspheres with 0.625% locust bean gum exhibit greater sustained drug release action (Sirisha et al. 2018). [8]

Sodium Alginate

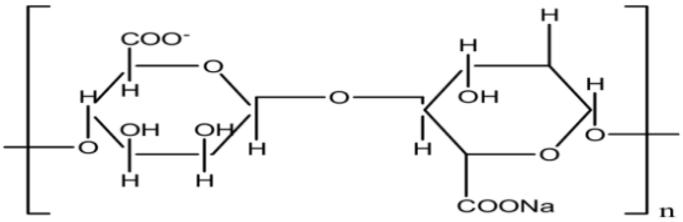

Fig. 3 Structure of sodium alginate

Sodium alginate is a linear glycuronan polymer consisting of a mixture of β-(1-4)-D-mannosyluronic acid and α-(1-4) -L-gulosyluronic acid residues, of general formula (C6H8O)n. The molecular weight is typically 20 000–240 000 kDa. It is obtained mainly from algae belonging to the family Phaeophyceae. Sodium alginate is a tasteless, practically odorless, and white to yellowish-white, fibrous powder. Sodium alginate is used in a variety of oral and topical pharmaceutical formulations. In tablet and capsule formulations used as both a binder and disintegrating agent at concentrations of 1–5% w/w. sodium alginate is widely used as a thickening and suspending agent in a variety of pastes, creams, and gels; and as a stabilizing agent for oil-in-water emulsions. [9] chitosan (CS) nanoparticles loaded with rosuvastatin were created by combining sodium alginate (SA) and polyvinyl alcohol (PVA) via the ionic gelation process to create an ideal hydrogel. Within a day, the drug-loaded CS nanoparticles in the SA/PVA hydrogel that was created showed controlled release of Rosuvastatin (Afshar, et al., 2020). [10] Cationically modified gelatin with sodium alginate (Alg) yields self-assembled hybrid polyelectrolyte complex (PEC) nanoparticles contains Curcumin. Which display continuous curcumin release (James et al., 2016). [11]

Gellan gum

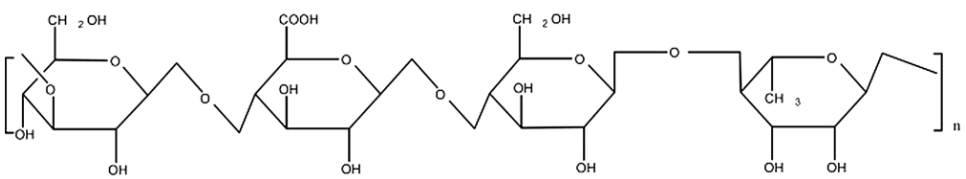

Fig. 4 Structure of Gellan gum

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Gellan gum (GG) is a linear, negatively charged exopolysaccharide. It is also called as S-60. Four repeating carbohydrates are present in the main chain of GG, which includes two d-glucose carbohydrates, one l-rhamnose, and one d-glucuronic acid. The average molecular weight of GG is around 500 kDa. Gellan gum is commercially produced through microbial fermentation using the bacteria Sphingomonas elodea or Pseudomonas elodea. It is thermo-responsive, biocompatible, biodegradable, ductile, and non-toxic. GG exhibits mucoadhesive properties. The gelling properties of gellan gum (GG) have gelling characteristics. It can create rigid, translucent gels that are stable at low pH. [12] Methotrexate (MTX)-loaded gellan gum microparticles (MTX-GG MPs) were generated utilizing simple water-in-oil (W/O) emulsion solvent diffusion process. Methotrexate-loaded gellan gum microparticles revealed 84% drug release within 24 hours (Srivastava et al., 2017). [13] Diclofenac-loaded solid hydrogel film compositions with gellan gum These polymers operate as a diffusion barrier, limiting the drug release from the formulation for a set extended time. [14]

Chitosan

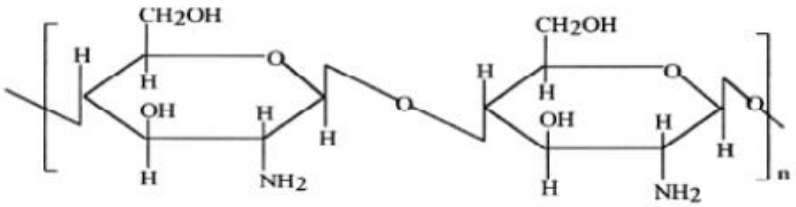

Fig. 5 Structure of Chitosan

Partial deacetylation of chitin results in the production of chitosan, which is a polysaccharide comprising copolymers of glucosamine and N-acetylglucosamine. It is primarily found in molluscs, annelids, and arthropods. Many fungi's mycelia and spores contain it as well. [15] Chitosan is commercially available in several types and grades that vary in molecular weight by 10 000–1 000 000 kDa, and vary in degree of deacetylation and viscosity. Chitosan occurs as odorless, white or creamy-white powder or flakes. Fiber formation is quite common during precipitation and the chitosan may look 'cotton like. The suitability and performance of chitosan as a component of pharmaceutical formulations for drug delivery applications has been investigated in numerous studies. These include controlled drug delivery applications, muco adhesive dosage forms, rapid release dosage forms, improved peptide delivery, colonic drug delivery systems, and use for gene delivery. [9] CS-loaded hydrogels can be used to deliver thymol, which is delivered orally via the buccal mucosa. Tymol loaded hydrogel released drug in controlled manner at less than 24 hours by diffusion (Montembault et al., 2020). [16] Chitosan-modified PLGA nanoparticles contains drug (paclitaxel). CS-PLGA nanoparticles with varying CS to PLGA ratios were synthesized utilizing a high-gravity rotating packed bed (RPB). PLGA NPs have the advantages of prolonged drug release of anticancer drug carriers (Yuan Le et al., 2019). [17]

Tragacanth

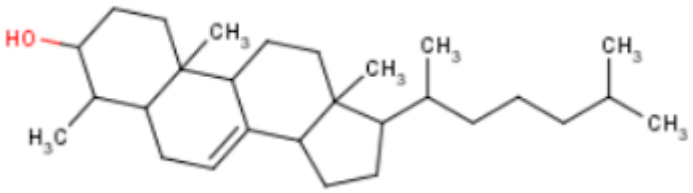

Fig. 6 Structure of Tragacanth

This gum is derived from the branches of Astragalus gummifer (Leguminosae). Tragacanth includes 20-30% of tragacanthin, a water-soluble fraction consisting of tragacanthic acid and arabinogalactan. It also contains between 60% and 70% of a water-insoluble component known as bassorin. Tragacanthic acid is made up of D-galacturonic acid, D-xylose, L-fructose, D-galactose, and other sugars. Tragacanthin is made up of uronic acid and arabinose, which dissolve in water to produce a viscous colloidal solution (sol), whereas bassorin swells to form a thick gel. [18] Tragacanth gum is used as an emulsifying and suspending agent in a variety of pharmaceutical formulations. It is used in creams, gels, and emulsions at various concentrations according to the application of the formulation and the grade of gum used. Tragacanth gum is also used similarly in cosmetics and food products, and has been used as a diluent in tablet formulations. [9] Tragacanth nanofibers laden with peppermint oil are injected by a sonochemical/microemulsion technique. The optimum formulation has a good controlled release property (92.38%) for the loaded Peppermint oil nanofibers after 18 hours (Montazer et al., 2018). [19] Tragacanth and sodium alginate composite aerogels were

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created using the sol-gel process and then supercritically dried. Tragacanth aerogels had a faster release rate, but the addition of alginate extended the model drug's release time (Al-barudi et al., 2024). [20]

Agarose

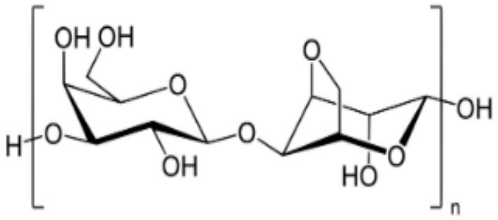

Fig. 7 Structure of Agarose

Agarose, a linear polysaccharide derived from red seaweed, contains repeated agarobiose units. It is commonly employed in agarose gel electrophoresis, but in recent decades it has piqued the interest of formulation scientists due to its solubility, as well as its biocompatibility and biodegradability, with essentially no hazardous activity. Its gelling ability at various temperatures makes it more valuable to formulation experts. It used in various oral and topical pharmaceutical application of various dosage forms like tablet, capsule, gels creams etc., [21] Controlled-release hydrogels loaded with gentamicin (GS) were formulated with use of agrose. Tannic acid (TA) and calcium chloride (CaCl2) were added as crosslinkers. When TA was added to the hydrogel formulations, the release time increased in GS-agarose hydrogels (Soylu et al., 2021). [22]

Xanthan gum

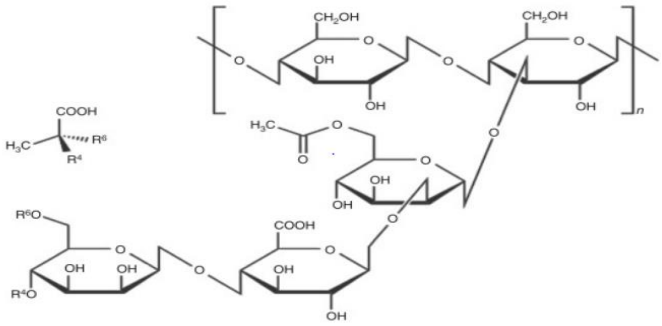

Fig. 8 Structure of Xanthan gum

The US FDA approved xanthan gum (XG) as a safe food additive in 1969, and since then, it has garnered a lot of attention. The high molecular weight (2 106 to 20 106 Da) fermentation product Xanthomonas campestris is produced by the Gram-negative bacterium. Chemically, it is made up of terminal mannose residues, glucuronic acid (b-1,2), mannose (b-1,4), and a pendant trisaccharide side chain. [23] Xanthan gum is widely used in oral and topical pharmaceutical formulations, cosmetics, and foods as a suspending and stabilizing agent. It is also used as a thickening and emulsifying agent. Xanthan gum has been incorporated in an ophthalmic liquid dosage form, Xanthan gum can be used to increase the bioadhesive strength.[9] PH-responsive hydrogels based on XG/Eudragit-S100 loaded Metformin HCl. Formulation based on a combination of XG/Eudragit-S100 polymers produced steady-state drug release at duodenal pH while releasing very little at stomach pH (Masood et al., 2022). [24] Sustained release matrix tablets of isosorbide-5-mononitrate were created, with Xanthan gum. The formulation containing 33.3% xanthan gum demonstrated a more sustained release pattern of medication over a 12-hour period (Rajat et al., 2010). [25]

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Guar gum

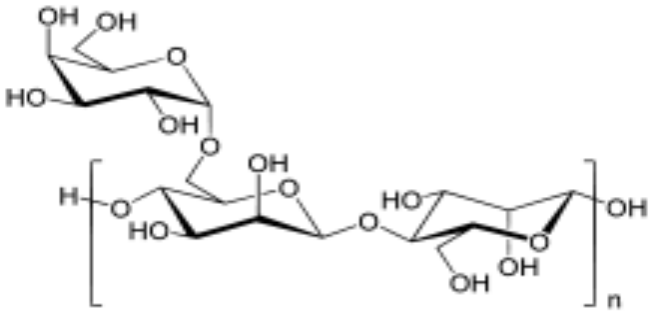

Fig. 9 Structure of Guar gum

Guar gum is obtained from the seeds of the drought-tolerant plant Cyamopsis tetragonoloba, which belongs to the Leguminosae family. The scientific literature commonly refers to the bean, guar gum flour, and galactomannan fraction as Indian cluster bean, guar, and guaran, respectively. Guar gum is made up of high molecular weight polysaccharides of galactomannans, which are linear chains of (1→4)-linked β-D-mannopyranosyl units with (1→6)-linked α-D-galactopyranosyl residues as side chains. [26] In pharmaceuticals, guar gum is used in solid-dosage forms as a binder and disintegrant. In oral and topical products as a suspending, thickening, and stabilizing agent; and also, as a controlled-release carrier. Guar gum has also been examined for use in colonic drug delivery. Guar-gum-based three-layer matrix tablets have been used experimentally in oral controlled-release formulations. [10] Guar gum-based biodegradable hydrogels have been successfully created with antihypertensive medication. The optimized formulation release 94% of drug up to 12 hours at pH 7.4 (Daud et al., 2021). [27] Create oral controlled release Zidovudine matrix tablets employing Guar using the wet granulation process. All of the formulations demonstrated sustained drug release after 12 hours (Ashok et al., 2010). [28]

Carrageenan gum

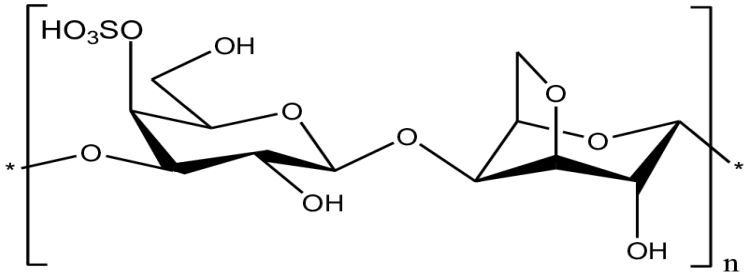

Fig. 10 Structure of Carrageenan gum

Carrageenan gum (CG) is a category of high molecular weight sulphated polysaccharides extracted from red seaweeds. It consists of alternate units of D-galactose and 3, 6-anhydro-galactose (3, 6-AG) connected by α-1, 3 and β-1, 4-glycosidic linkages. CG is a sulfated polygalactan that contains 15-40% ester-sulfate, making it an anionic polysaccharide. In the food business, CG is used as a gelling, stabilizing, and thickening ingredient, as well as fat alternatives, particularly in milk products. Carrageenan is derived from red seaweed in the Rhodophycea family, namely from the genera eucheuma, solieria, cripus, agardhiella, chondrus, hypnea, sarconema, and iridaea. [29] Rosuvastatin sustained release pills are manufactured with carrageenan in doses of 30, 40, and 50 mg. All concentration formulations exhibit sustained drug release for approximately 20 hours in an in vitro drug release testing. Higher polymer concentrations result in better regulated medication release (Srinivasa et al., 2018). [30] Chitosan and carrageenan gum are examples of natural polymers that are used to create nanoparticles. The in vitro release experiment of polymer base nanoparticles showed that the protein was released gradually and under control over duration of three weeks by the chitosan/carrageenan nanoparticles (Grenha et al., 2010). [31]

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Starch

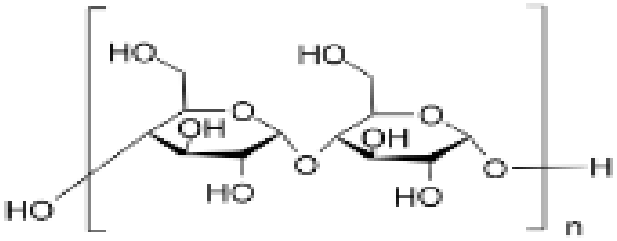

Fig. 11 Structure of Starch

Starch is the most abundant storage carbohydrate on Earth, manufactured primarily by plants and some cyanobacteria. Starch is stored as water-insoluble particles called starch granules, whereas most other species create water-soluble glycogen as a storage carbohydrate. Both polymers have comparable biological activity and chemical composition, consisting of glucose units connected by α-1,4 and α-1,6 glycosidic linkages. Starch is a versatile biomaterial that is of particular relevance in the food and non-food industries due to its abundance, low cost, non-toxic qualities, and biodegradable nature. Starch is composed of two glucan polymers, amylose and amylopectin. The latter has a significantly larger molecular weight than amylose. The typical size distribution peaks at roughly 108 Da, whereas amylose's size distribution is about two orders of magnitude smaller (106 Da). Amylopectin is by far the most abundant polysaccharide, and it essentially controls the properties of the starch granule. However, the ratio of amylopectin and amylose might vary significantly. [32] Starch-based tableted microspheres are encapsulated with Ampicillin (AMP), which is crosslinked with epichlorohydrin (EPI) using a modified water-in-oil (w/o) emulsification method. These are made with varying polymer to medication ratios. All tableted microspheres exhibit initial brust release, followed by regulated release for up to 24 hours (Mundargi et al., 2008). [33] Various starches were utilized to make controlled release tablets filled with diprophylline via direct compression. Blending multiple types of polymeric matrix formers can be an effective way to get the correct drug release kinetics. Diprophylline release from solely dextrin-based tablets is expected to be rapid because to their water solubility. Diprophylline, on the other hand, is slowly released from tablets containing chemically unmodified potato starch (Muschert er al., 2021). [34]

Gelatin

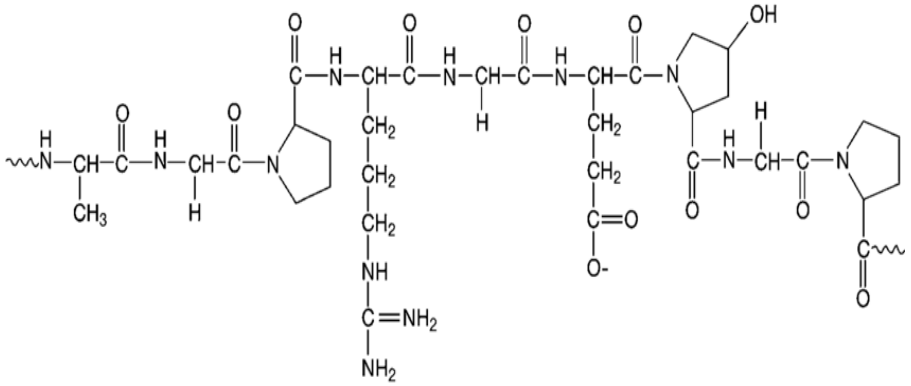

Fig. 12 Structure of Gelatin

Gelatin is a natural polymer derived from the hydrolytic degradation of protein from collagen, and its unique amino acid composition provides numerous medical benefits. Gelatin is typically available in the form of pills, granules, or powders, but it can also be dissolved in water prior to usage. Researchers have extensively studied gelatin as a matrix for three-dimensional cell growth and as a component of tissue-engineering scaffolds. Gelatin is high in protein and can be used to replace fat and carbohydrates in nutritionally balanced diets. Chemically, gelatin is made up of 18 kinds of complicated amino acids, of which glycine, proline, and hydroxyproline are the primary components. The remaining ca. 43% are different. distinguished families of amino acids, including aspartic acid, glutamic acid, arginine, and 6.8% hydrogen; gelatin is composed of 25.2% oxygen, 6.8% hydrogen, 50.5% carbon, and 17% nitrogen; gelatin has a mixture of single and double unfolded chains with hydrophilic character; additionally, the chemical structure of gelatin is made up of various polypeptide chains, with molar masses of approximately 90 103, 180 103, and 300 103 g/mol, respectively; during processing, the heat increments for gelatin will dissolve the structure into colloids, but only at temperatures below 35 to 40 °C. Gelatin should be stored below 4°C in order to increase its viscosity, which rises with concentration. Mammalian gelatin melts reversibly into a solution at 37 °C because the triple helix shape returns to the coiled state at that

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temperature. [35] Semi-interpenetrating (s-IPN) hydrogels derived from carboxymethyl guar gum (CMGG) and gelatin with improved gel characteristics for drug delivery applications. The model drug ciprofloxacin was put into the hydrogels, and the drug was released via a combination of diffusion and hydrogel degradation. New generation sIPN biopolymer hydrogels including carboxymethyl guar gum and gelatin show promise for use as a sustained drug delivery method (Ghosh et al., 2018). [36] A casting/solvent evaporation procedure was used to create films of alginate and gelatin that were cross-linked with Ca2+ and contained ciprofloxacin hydrochloride as a model drug at varying doses. Controlled release studies revealed that as the fraction of gelatin in the film increased, the amount of ciprofloxacin hydrochloride released dropped (Dong Z et al., 2006). [37]

Semi synthetic polymers

Semisynthetic polymers are generated from naturally recovered fibers and are often expanded with the addition of manufactured synthetic components. Synthetic polymers are manufactured by chemically combining polymers that do not occur naturally in a laboratory without affecting their fiber properties.

Cellulose and cellulose derivatives

Cellulose is widely dispersed among natural bioresources on the planet, with an annual production of around 50 billion tons. Cellulose, made up of thousands of repeating D-glucose units linked by β-1,4 glycosidic linkages, is hydrophilic and may be chemically modified. Because of its unique structure and specific features, such as biocompatibility, renewability, non-toxicity, and environmental friendliness, cellulose has become widely used in a variety of industries in recent years, including food, paper, biomaterials, and pharmaceuticals. The use of acid hydrolysis and mechanical treatments on natural cellulose sources can produce cellulose of various sizes and forms.

Natural cellulose can be changed by the attachment of functional groups, allowing the production of water-soluble cellulose derivatives. For example, methylcellulose (MC), carboxymethyl cellulose (CMC), and hydroxypropyl methyl cellulose (HPMC) can be made by replacing the surface hydroxyl groups with methyl, carboxymethyl, and hydroxypropyl methyl groups, respectively, via etherification reactions. [38]

Cellulose acetate

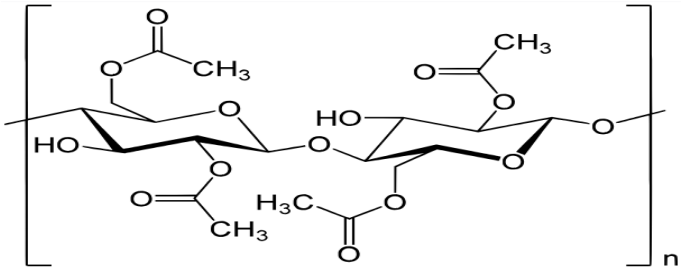

Fig. 13 Structure of Cellulose acetate

Paul Schützenberger initially manufactured cellulose acetate (CA) in 1865 from wood pulp treated with acetic anhydride. Another method for generating cellulose acetate involves reacting cotton with acetic acid and utilizing sulfuric acid as a catalyst. Cellulose is first treated with acetic acid to ensure uniform acetylation, then dehydrated and reacted with acetic anhydride using an appropriate catalyst-solvent system such as sulfuric acid-anhydrous acetic acid. The resultant product is cellulose triacetate, which can be acid-hydrolyzed to a lesser degree of substitution to generate cellulose diacetate, then cellulose acetate. The degree of substitution (DS) is a significant feature of this cellulose ester since it affects solubility and biodegradability. Nowadays, different CA preparation strategies have been established, including ring-opening esterification, trans-esterification, and esterification with iminium chloride or N, N-carbonyldiimidazole. Cellulose acetate has strong mechanical qualities, is insoluble in water, and is hydrolytically stable. Biodegradability, biocompatibility, non-toxicity, and low cost are characteristics associated with its natural origin. [39]

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Cellulose sulfate

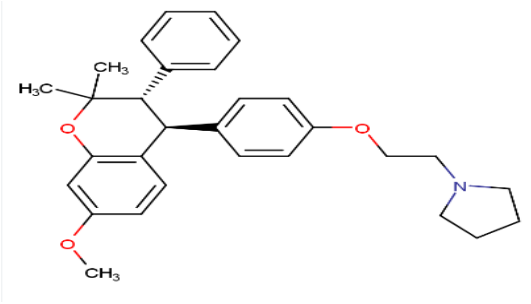

Fig. 14 Structure of Cellulose sulfate

Cellulose sulfate (CS) is a cellulose ester formed through heterogeneous, homogeneous, or quasi-homogeneous sulfation. CS has various advantages over virgin cellulose, such as increased water solubility and antibacterial characteristics at high concentrations. For heterogeneous sulfation, pure cellulose is reacted with a sulfating agent (e.g., sulfuric acid) in an appropriate reaction media, such as isopropyl alcohol. Following this reaction, the surface's hydroxyl groups are replaced with sulfate ones. R.G. Schweiger initially demonstrated homogeneous sulfation in 1979, resulting in CS with a high substitution degree and an intermediate reaction product, cellulose nitrite, by dissolving cellulose in a SO3-pyridine complex and using N, N-dimethylformamide as a co-solvent. The quasi-homogeneous method is based on acetosulfation and has been described as a progressive dissolving of cellulose in N,N-dimethylformamide mixed with a mixture of sulfating and acetylating agent (e.g., chlorosulfuric acid/acetic anhydride), followed by cleaving of acetyl groups during precipitation, resulting in the conversion of cellulose acetate-sulfate into CS. The molecular weight and degree of substitution have a significant impact on the biological properties of CS. For example, greater molecular weight CS had a stronger microbicidal effect against human papillomavirus (HPV), yet a higher substitution degree was found to boost 3T3 fibroblast cell growth in vivo. [39]

Cellulose nitrate

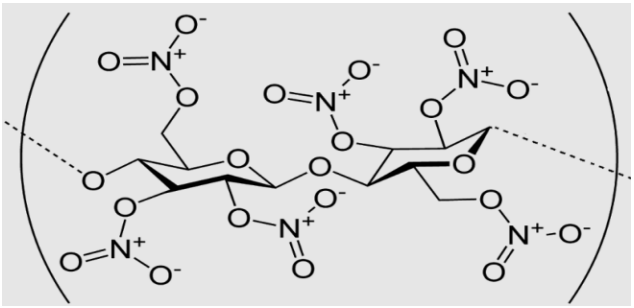

Fig. 15 Structure of Cellulose nitrate

Nitrocellulose (CN), often known as gun cotton, is the primary ingredient in smokeless gunpowder because it decomposes explosively. CN is made by nitrating cellulose derived from wood pulp or cotton linters using a powerful nitrating agent (such as nitric acid). Studies have shown that sulfuric acid is a good addition for stabilizing the nitration mixture and preventing unintentional detonations. The electrophilic assault of NO2 + ions on the OH moieties causes the hydroxyl groups on the surface of cellulose to be replaced with nitrate esters during the nitrification process. [39]

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Cellulose ether

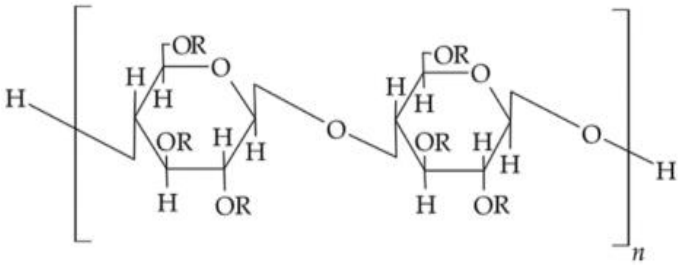

Fig. 16 Structure of Cellulose ether

Cellulose ethers are commonly utilized as excipients in matrix tablet formulations. When the cellulose ethers come into touch with water, they swell, and a hydrogel coating form surrounding the tablet's dry core. The hydrogel acts as a diffusion barrier for water molecules that penetrate the polymer matrix and release drug molecules. [40]

1. Sodium carboxymethyl cellulose

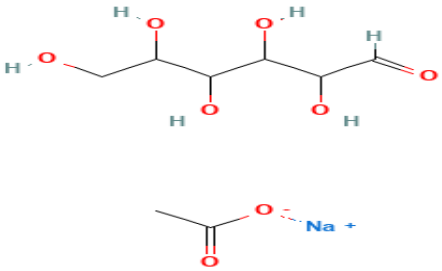

Fig. 17 Structure of Sodium carboxymethyl cellulose

It is a low-cost soluble and polyanionic polysaccharide derivative of cellulose used in medicine, pharmacology, and cosmetics. This polymer's several useful properties make it a popular thickener, suspending aid, stabilizer, binder, and film-former in a wide range of applications. [40] Levosulpiride sustained-release formulations were created by compressing various cellulose derivatives such as CMC sodium, HPC, and HPMC in various polymer-to-drug weight ratios to act as release modifiers. A formulation containing 75% CMC sodium exhibits sustained drug release for 8 hours of investigation (Samie et al., 2018). [41] Polymeric beads containing diclofenac sodium were created using hydrophilic polymers, sodium carboxymethyl cellulose (Na CMC), and sodium alginate. The inotropic gelation process was used to create particle beads of Na CMC and Na alginate, with calcium chloride acting as a crosslinking agent. At the end of the 10-hour dissolution study, all formulations demonstrated sustained drug release (Dhanaraju et al., 2009). [42]

2. Methylcellulose

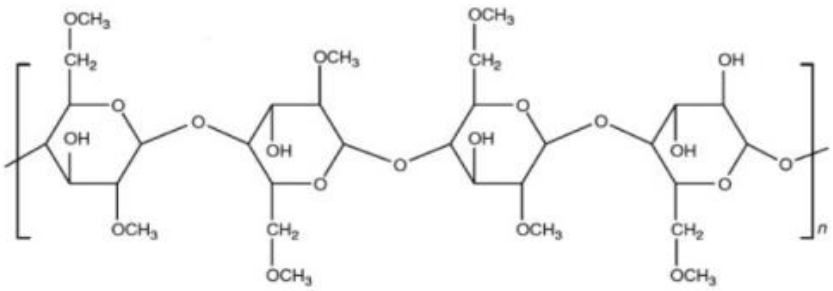

Fig. 18 Structure of Methylcellulose

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MC resembles cotton in appearance and is neutral, odorless, tasteless, and inactive. It swells in water and generates a transparent to opalescent, viscous, colloidal solution; it is insoluble in the majority of popular organic solvents. However, aqueous MC solutions can be diluted with ethanol. MC solutions remain stable throughout a wide pH range (2 to 12), with no apparent change in viscosity. They can be used as bulk laxatives to treat constipation, as well as in nose drops, ophthalmic preparations, burn ointments, and other similar preparations. [40] Non-toxic nanocomposites-based bio-films derived from methylcellulose (MC) can help to mitigate the environmental issues associated with synthetic polymers. A new simple method for isolating cellulose nanocrystals (CNC) from jute waste is effectively used here. In vitro permeation studies using the Franz diffusion cell revealed diffusion-mediated sustained drug release from the devices as a result of interaction between MC and CNC via H-bonding, electrostatic interaction between the hydrophilic polymer/CNC chains and the drug, and the formation of a tortuous path (Orasugh et al., 2018). [43] Create methyl cellulose (MC)-based in situ gelling formulations of ketorolac tromethamine (KT) to improve its ocular bioavailability. At 37 °C, MC showed the highest viscosity and slowest drug release. HPMC: 2:1 solution with 7% w/v NaCl (Bhowmik et al., 2010). [44]

3. Ethyl cellulose

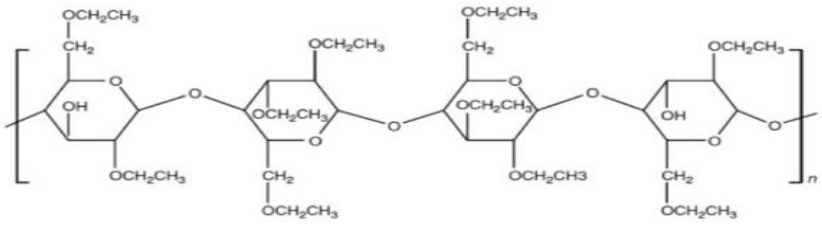

Fig. 19 Structure of Ethyl cellulose

It is the non-ionic, pH-insensitive cellulose ether, which is insoluble in water but soluble in many polar organic solvents. It is employed as a non-swellable and insoluble component in matrix or coating systems.
- When water-soluble binders are not suitable for dose processing due to the active ingredient's water sensitivity, EC is frequently used.
- It can be used to coat one or more active compounds in a tablet to keep them from reacting with other materials or each other.
- It prevents discoloration of oxidizable chemicals like ascorbic acid and allows for easy compression of tablets and other dosage forms. - It can also be employed alone or in combination with water-soluble polymers to create sustained release film coatings, which are commonly utilized for coating micro particles, pellets, and tablets.

In addition to EC, HEC is a non-ionic water-soluble cellulose ether that may be easily dispersed in cold or hot water to produce solutions with various viscosities and desired characteristics, but it is insoluble in organic solvents. When a non-ionic material is required for oral or topical treatments, it is employed as a modified release tablet matrix, film maker, thickening, stabilizer, and suspending agent. [40] The poorly water-soluble immunosuppressive drug tacrolimus was created with ethyl cellulose (EC) polymer as a release retardant. Drug (5 mg) was stacked atop sugar spheres (518.3 mg) containing Hypromellose (5 mg) to convert the drug from crystalline to amorphous. The drug-layered pellets were then recoated with EC polymer (0.5-1.5 mg) via a fluid bed granulator. These pellets release the medication in a steady manner for 24 hours (Shin et al., 2018). [45] Diclofenac sodium extended-release hydrophobic matrix tablets are made from ethyl cellulose polymer in two different grades: Ethocel Standard Premium and Ethocel Standard FP Premium. The matrix tablets were made using a wet granulation process. Ethyl cellulose grades with finer particle sizes demonstrated superior control over medication release rates (Goswami et al., 2014). [46]

4. Hydroxypropyl cellulose

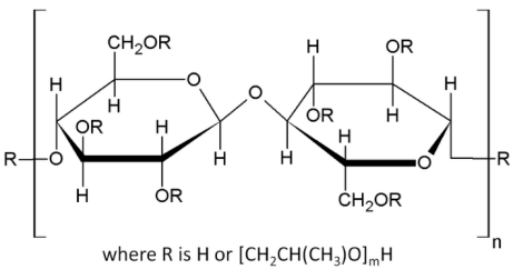

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Fig. 20 Structure of Hydroxypropyl cellulose

It is non-ionic water-soluble, pH-insensitive cellulose ether. It has multiple applications, including thickening, tablet binding, modified release, and film coating. Solid dispersions comprising a polymer blend, such as HPC and EC, allow for precise control over the rate of release of a very water-soluble medication, such as oxprenolol hydrochloride. In this situation, the water-soluble HPC swells in water and becomes caught in the water-insoluble EC, slowing the release of the medication. These investigations demonstrated a linear relationship between the rate of release of the water-insoluble medication and its interaction with the polymer. [40] Ofloxacin floating tablets were developed using NaHCO3 as a gas-forming agent, Na alginate as a retarding agent, and HPC as a matrix material. The pills could float on the surface of artificial stomach fluid for 12 hours, allowing them to manage drug delivery (Qi X et al., 2015). [47] A temperature-responsive chitosan (CS)/hydroxyl propyl cellulose (HPC) blend Nano spheres demonstrated a well-controlled and sustained FLU release pattern throughout a 24-hour period. Nano spheres loaded with Flurbiprofen were generated using various CS/HPC blend ratios and production circumstances. CS/HPC blend nano spheres demonstrated a well-controlled and sustained FLU release pattern throughout a 24-hour timeframe (Işıklan et al., 2020). [48]

5. Hydroxypropyl methyl cellulose

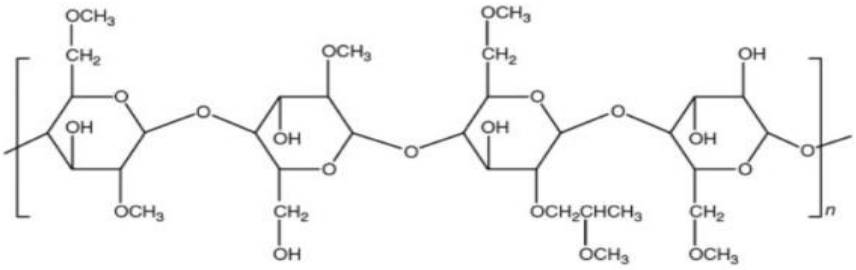

Fig. 21 Structure of Hydroxypropyl methyl cellulose

HPMC is water-soluble cellulose ether that can be utilized as a hydrophilic polymer in the formulation of controlled release tablets. Water penetrates the matrix, hydrating the polymer chains, which gradually separate from the matrix. Because it is widely recognized that drug release from HPMC matrices occurs via two mechanisms: drug diffusion through the swelling gel layer and matrix erosion of the swollen layer, quantifying the percentage contribution of diffusion and erosion to overall drug release is critical. [40] A thermo responsive injectable hydrogel loaded with insulin is created by combining hydrophobically modified hydroxypropyl methyl cellulose (HM-HPMC) with cyclodextrin (CD). The HM-HPMC/β-CD hydrogel composition produced long-lasting hypoglycemia effects due to insulin release from the gel matrix (Okubo et al., 2020). [49] Create hydroxypropyl methyl cellulose-based controlled release matrix tablets for theophylline with different drug: polymer ratios (1:1 and 1:2). The results showed that a higher drug: polymer ratio (1:2) resulted in more regulated drug release than a lower drug: polymer ratio (1:1) (Sekharan et al., 2011). [50]

Cellulose esters

Cellulose acetate phthalate is a partial acetate ester of cellulose that has been treated with phthalic anhydride. One carboxyl of phthalic acid is esterified with cellulose acetate. The resulting product has around 20% acetyl groups and 35% phthalyl groups. In the acid form, it is soluble in organic solvents but insoluble in water. The salt produced is highly soluble in water. This combination of qualities makes it beneficial in enteric coating of tablets because it is resistant to the acid condition of the stomach and soluble in the more alkaline environment of the intestinal system. [40]

Synthetic polymers

Synthetic polymers have received significant attention from formulators for the delivery of therapeutic proteins and peptides. These polymers have been proven to enhance the pharmacokinetics and circulation times of integrated medicinal compounds. Synthetic polymers frequently serve a passive role as medication transporters.

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Eudragits

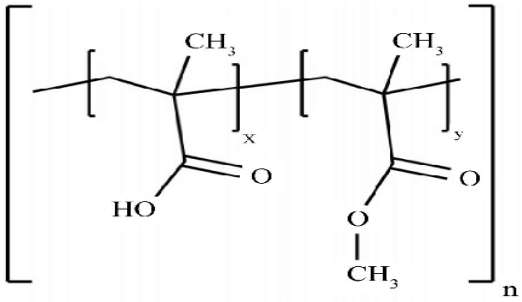

Fig. 22 Structure of Eudragits

Eudragits are synthetic polymers formed via the polymerization of acrylic acid (prop2-enoic acid; CH2=CHCOOH) and methacrylic acids, or their esters such as butyl ester or dimethyl aminoethyl ester. Eudragits, as synthetic polymers, are delivered in highly reproducible forms, as opposed to cellulosic derivatives, whose physicochemical properties can vary depending on the source of raw material. Methacrylate copolymers are created using free-radical polymerization, in which various acrylate and methacrylate derivatives are integrated into the polymer via chain growth processes. Variations in chains Length is acquired by a variety of termination and transfer processes. The chemical nature, distinguishing properties, and applications of several forms of Eudragit are available. Eudragit E (soluble below pH 5.5) is used in taste masking; anionic Eudragit L and S (soluble above pH 6 and 7, respectively) are used in colon targeting/enteric coating; neutral types Eudragit RL and RS (pH-independent solubility) and Eudragit NE and NM (swellable and permeable) are used in sustained release drug delivery. [51] Eudragit E 100 and polycaprolactone (PCL)-containing floating microspheres for improved stomach retention and medication release was successfully synthesized using the oil-in-water solvent evaporation process. Metronidazole benzoate, an anti-protozoal medication, was employed as a model medicine. In vitro drug release tests demonstrated that microspheres may release drugs in a continuous and sustained way for up to 12 hours in simulated stomach juice (Farooq et al., 2017). [52] Famotidine tablets were manufactured utilizing the direct compression technique with Eudragit RL 100 polymer. Tablets were produced with varying eudragit concentrations. All formulations exhibit regulated drug release during 24 hours of research (Rabani et al., 2022). [53]

Polylactic acid (PLA)

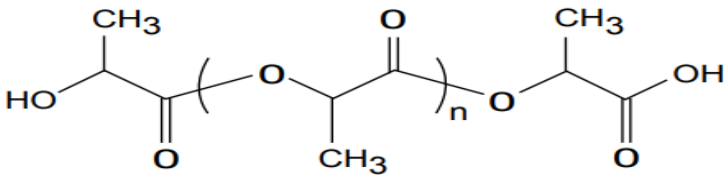

Fig. 23 Structure of Polylactic acid (PLA)

PLA is a thermoplastic biodegradable polymer synthesized by polymerizing lactic acid monomers or cyclic lactide dimers. Lactic acid is produced through the fermentation of natural carbohydrates such as maize or wheat, as well as agricultural or food waste products. PLA has a variety of biological applications, including sutures, stents, dialysis medium, and drug delivery systems. Aliphatic polyester is biodegraded through bulk erosion. Hydrolysis cleaves the lactide/glycolide chains into acids, which are then removed from the body via the Krebs cycle, primarily as carbon dioxide and urine. [54] Berberine (BBR)-loaded PLA nanoparticles (NPBs) were created utilizing coaxial electrospray (CES) to address BBR's poor bioavailability. The release of NPBs was tested at pH 7.4 and 5.8. NPBs had a slower release profile than free BBR in both pH values, and the rate of BBR release was greater and faster in acidic pH than in physiological pH. This study created a new technique to preparing NPBs utilizing the CES procedure in order to improve efficiency and control BBR release (Shyu et al., 2001). [55] The spray-drying procedure produces polylactic acid microspheres that release anticancer drugs. Increasing the inlet temperature and polymer concentration resulted in a stable particle form and a slower drug dissolving rate. The in-vitro release of anticancer medication from microspheres lasted seven days (Ghaffarzadegan et al., 2020). [56]

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Poly(e-Caprolactone)

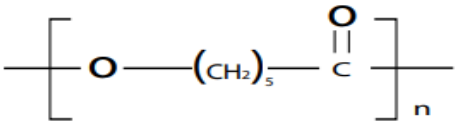

Fig. 24 Structure of Poly(e-Caprolactone)

Poly(e-caprolactone) is a polyester-based biodegradable polymer formed via ring-opening polymerization of e-caprolactone. PCL has the tendency and capability to adjust its physical, chemical, and mechanical properties by copolymerization or blending with a wide range of other polymers, making it extremely adaptable in nature. It has been discovered that copolymerization of PCL with another polymer alters the chemistry of the system, resulting in changes in critical system characteristics such as solubility, ionic behavior, crystal behavior, and so on. Whereas combining PCL with another polymer mostly impacts the system's physical properties, such as mechanical strength, which is why micelles or hydrogels arise following copolymerization. The emulsion solvent evaporation process was used to create LPV-loaded PCL nanoparticles (NPs). An in vitro drug release investigation revealed bi-phasic sustained release characteristic of LPV from nanoparticles. Optimized LPV NPs had a significantly higher oral bioavailability than free LPV solution. These nanoparticles release the medicine in a regulated manner over time (Ravi et al., 2015). [57] Etoricoxib-loaded composite injectable Chitosan gel (CICGs) as a dual-purpose (visco-supplement and intra-articular drug delivery depot) therapeutic therapy for osteoarthritis. CICGs were created by scattering MPs in a chitosan-ammonium hydrogen phosphate solution and incubating at 37 °C. In vitro drug release characteristics of CICGs were shown to be more regulated than MPs and bare chitosan gel (BCGs) (Arunkumar et al., 2016). [58]

Polyamide

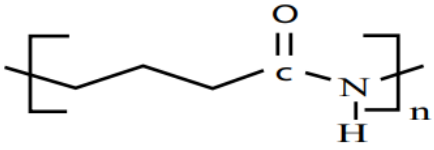

Fig. 25 Structure of Polyamide

Polyamides are the polycondensation products of a diacid chloride (succinyl chloride) with a diamine, such as 1, 2-bis (3-aminopropyl amine) ethane. These are semi crystalline thermoplastic polymers with amide groups separated by alkanes in their typical chain. The alkane segments and the number of carbon atoms between the nitrogen atoms determine the kind of polyamide. Polyamides can also include naturally occurring proteins such as collagen and silk. The most popular synthetic polyamide is nylon, which is recognized for its high tensile strength and is used to make sutures, balloons (angiography), and catheters. Kolawole described a biodegradable and biocompatible monolithic drug delivery system made of polyamide that is rate-modulated to control bioactive release. [21]

Poly (N-Vinyl Pyrrolidone)

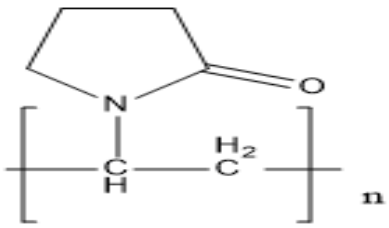

Fig. 26 Structure of Poly (N-Vinyl Pyrrolidone)

Poly (N-vinyl pyrrolidone) is water soluble and has found widespread use in practically every aspect of the pharmaceutical industry. It is generated from the condensation of N-vinyl pyrrolidone and possesses all of the properties of an ideal polymer, such as biocompatibility, nontoxicity, solubility in a number of solvents, including water, chemical stability, etc. This polymer has roughly

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equal chances of forming complexes with hydrophilic and hydrophobic medicinal molecules. Initially, the polymer was intended to be employed as a plasma volume expander, but as the pharmaceutical industry has changed and advanced, PVP has proven to be an excellent excipient in formulation development. [21] The water-in-oil (W=O) emulsion method was used to manufacture chitosan-poly (vinyl pyrrolidone) blend microspheres loaded with the anti-diabetic medication metformin hydrochloride (MH). The release rates of MH-loaded formulations were investigated as a function of blend composition and crosslinking agent concentration. The medicine was released in a regulated manner for up to eight hours (Narayana et al., 2012). [59] PVP hydrogels with various theophylline contents were produced. Polymeric hydrogels released drugs by diffusion and erosion. Hydrogel with 1:3 concentrations proved effective in supporting theophylline for longer periods of time when compared to other drug/polymer concentrations (1:2 and 1:1) (Ahmad et al., 2013). [60]

Poly (vinyl alcohol) (PVA)

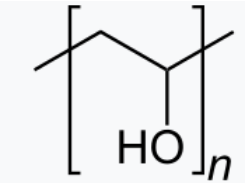

Fig. 27 Structure of Poly (vinyl alcohol) (PVA)

Poly (vinyl alcohol) (PVA) is a water-soluble synthetic polymer. It has a backbone made entirely of carbon atoms and is biodegradable under both aerobic and anaerobic conditions. It was created via the hydrolysis of polyvinyl acetate. PVA was discovered in 1924, when a solution of poly (vinyl alcohol) was created by saponifying poly (vinyl ester) with caustic soda solution. As a result, PVA is categorized into two types: fully hydrolyzed (A) and partially hydrolyzed (B), with partially hydrolyzed PVA being employed in food and pharmaceutical applications. [61] A PVA hydrogel-loaded dexamethasone (DEX) drug delivery system has been developed and cross-linked with various doses of glutaraldehyde (GA). The higher density of GA in the PVA matrix resulted in lower swelling and water absorption. The in vitro release assessment of DEX revealed a burst release after 6 hours, followed by a continuous release over 25 days (Seyfoddin et al., 2019). [62] Create a chemically cross-linked PVA-AA hydrogel for pH-responsive and regulated valsartan administration. Hydrogels were produced utilizing the free radical polymerization process. In an aqueous solution, the polymer (PVA) was chemically bonded with the monomer (acrylic acid). Ethylene glycol di-methacrylate (EGDMA) and benzoyl peroxide (BPO) were utilized as cross-linkers and initiators. These polymeric matrices have the potential to serve as a carrier for regulated valsartan delivery (Sohail et al., 2014). [63]

Polyacrylamide

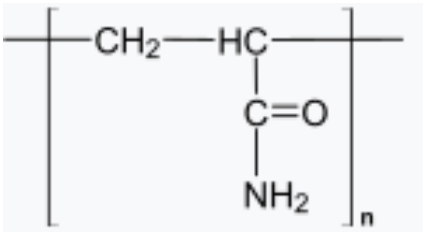

Fig. 28 Structure of Polyacrylamide

The word "polyacrylamide" loosely refers to any polymer that contains acrylamide as one of its monomers. More precisely, its IUPAC nomenclature is poly (prop-2-enamide), which describes it as a water-soluble polymer generated by the polymerization of either acrylamide monomers or N,N′-methylenebis(acrylamide). Polyacrylamide with only acrylamide monomers is nonionic; other monomers such as acrylate or 2-acrylamido-2-methylpropane sulfonate (AMPS) can be copolymerized at various percentages to form anionic PAM; 1,4 dimethyldiallylammonium, ethanaminium (N, N, N-trimethyl-2-((1-oxo-2-propenyloxy), and 1,2-dimethyl-5-vinylpyridinum are common co-monomers for cationic PAM. The molecular weight (MW) of commercial PAM ranges from 105 to over 107 Da. High MW PAM (>106 Da) has a broader range of applications due to its high viscosity, drag reduction capability, and water retention property. [64] Acrylamide-grafted-guar gum (pAAm-g-GG) was synthesized and blended with chitosan (CS) to form interpenetrating polymer network (IPN) hydrogel microspheres by the emulsion cross-linking process with glutaraldehyde (GA) as a cross-linker. Polymers mix IPN hydrogel microspheres have a prolonged drug release mechanism (Kajjari et al., 2011). [65] Semi-interpenetrating network hydrogels were created utilizing various ratios of silk fibroin/acrylamide mixes cross-linked with N, N-Methylenebisacrylamide. The manufactured hydrogel releases the medication in a sustained manner (Mandal et al., 2009). [66]

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Pluronic F127

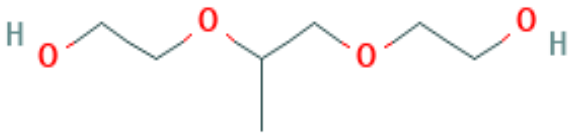

Fig. 29 Structure of Pluronic F127

PF127 is composed up of repeated PEO and PPO units, with PPO being the core region. PEO is hydrophilic in nature and surrounds the hydrophobic component of PF127, known as PPO. PF127 has been demonstrated to be non-irritant and cytocompatible with diverse cell types, and it has been approved by the FDA as a biomaterial for the delivery of therapeutic proteins and peptides.198, 199 PF127 ensures the thermo stability of added proteins. Incorporated therapeutic proteins have been shown to be totally recovered from PF127-based thermosensitive gel following dissolving in excess buffer at body temperature and/or biological fluid. Because of its thermo-reversible properties, PF127 remains liquid at room temperature but quickly transforms to a semi-solid, stiff gel at body temperature, depending on the concentration applied. Because of its sol-gel transition property, PF127 is easily delivered into the body by an invasive route. [1] A PF127-based thermo sensitive gel method loaded with interleukin-1 receptor-I (IL-1RI) was used to increase medication pharmacokinetics and therapeutic potential. When compared to IL-1Ra aq, IL-1Ra loaded in PF127 gel released more slowly and for longer time (Akash et al., 2012). [67] Pluronic F127 (PF127)-based formulations of timolol maleate (TM) are intended to improve its ocular bioavailability. The formulation's viscosity based on the use of polymers with Pluronic F127. The viscosity of formulations incorporating thickening agents ranged from PF-MC 3% to PF-HPMC 2%, PF-CMC 2.5%, and PF127 15%. 15% PF127 formulations incorporating 3% methylcellulose produced the slowest medication release rate (El-Kamel et al., 2002). [68]

Polyglycolic acid (PGA)

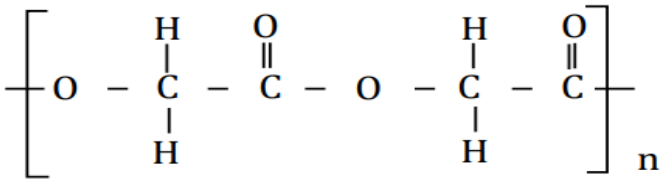

Fig. 30 Structure of Polyglycolic acid (PGA)

Ring-opening polymerization of glycolide, a cyclic diester of glycolic acid, is a typical method for producing PGA. PGA is a strong, rigid, crystalline polymer having a melting point of 225°C and a glass transition temperature (TG) of 36°C. PGA, unlike PLA and other closely similar polyesters, is insoluble in most polymer solvents. PGA, also known as Dexon™, was the first synthetic absorbable suture to be commercially commercialized in 1970. It possesses outstanding fiber-forming capabilities. PGA has limited solubility and a high melting point. Limits its usage in medication delivery applications. Lactide/glycolide polymers have a wide range of hydrophilicity, making them useful in constructing controlled release system materials. It is not harmful and completely biodegradable. The polymer is primarily a byproduct of carbon absorption (from glucose or starch) and is used by bacteria as an energy storage molecule that can be digested when other common energy sources are unavailable. [54] When chlorhexidine was loaded into mesoporous silica nanoparticles with grafted PGA, it released in a pH-dependent manner. The sophisticated nanocarrier system with PGA grafted over MSN demonstrates regulated release (Akram et al, 2021). [69]

Poly (lactide-co-glycolide)

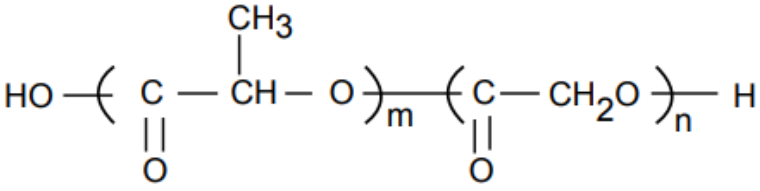

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Fig. 31 Structure of Poly (lactide-co-glycolide)

PLGA Both L- and DL-lactides have been employed in co-polymerization. The ratio of glycolide to lactide in different compositions allows for control over the degree of crystallinity of the polymers. When crystalline PGA is co-polymerized with PLA, the degree of crystallinity decreases, resulting in higher rates of hydration and hydrolysis. As a result, it is possible to conclude that the copolymer's degradation period is proportional to the monomer ratio utilized in manufacture. In general, the higher the glycolide concentration, the faster the breakdown rate. However, the 50:50 PGA:PLA ratio is an exception to this rule, as it degrades the fastest. PLGA is employed in a variety of medication delivery applications. [54] Ciprofloxacin was immobilized in PLGA NPs using the Nano precipitation technique. NPs with high drug loading efficiency were produced using PLGA 50; 50. Ciprofloxacin was released in a sustained manner from PLGA-loaded NPs. The use of ciprofloxacin in this manner increases stomach time retention and residence while also improving bioavailability (Bukhari et al, 2023). [70] The solid-in-oil-in-water (s/o/w) approach, which employs the anionic surfactant sodium dodecyl sulfate (SDS), was used to create negatively charged poly (lactic-co-glycolic acid) (PLGA) microspheres with an encapsulated hydrophilic antibiotic (amoxicillin). In-vitro drug release demonstrated a continuous release profile lasting at least 31 days, with minimal early burst release (Czernuszka et al, 2008). [71]

Poly (Ethylene Glycol)

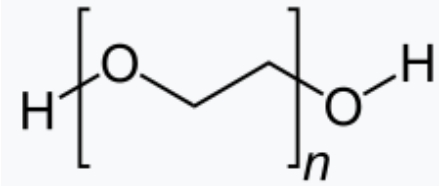

Fig. 32 Structure of Poly (Ethylene Glycol)

PEG is produced through the polymerization of ethylene glycol. PEG can have a linear or branching structure, depending on the polymer's molecular mass. It is soluble in the majority of organic solvents, but research studies demonstrate that each PEG molecule is closely connected with two or three water molecules, giving the PEG a hydrophilic character. PEG was initially developed for separating and purifying aids, as a matrixing system, lubricating medical devices, and an excipient in semisolids, suppositories, Tablets, etc. The hydrophilic nature of PEG stems from the fact that the water molecule connected to each monomer makes it a good material for creating a shield, such as an impact for the attached medicine against enzymatic degradation, quick renal clearance, and interactions with cell surface proteins. This property of the polymer has prompted scientists to employ it for PEGylation of medicines and proteins. [21]

The solvent evaporation method was used to prepare metoprolol tartrate-loaded microspheres with different amounts of an ethylcellulose and polyethylene glycol-6000 mixture. The optimal formulation has a 1:1:2.5 ratio of EC, PEG, and MT. In vitro experiments demonstrated that the drug release was extended by 10 hours when compared to ordinary metoprolol (Malipeddi et al, 2016). [72]

Incorporating subtilosin, an antimicrobial peptide, into covalently cross-linked polyethylene glycol (PEG)-based hydrogels for vaginal delivery. The PEG-based hydrogels (4% and 6% [wt/vol]) released subtilosin in two phases: an initial rapid release rate of 4.0 g/h (0 to 12 h) followed by a slow, continuous release rate of 0.26 g/h (12 to 120 h) (Rajan et al, 2014). [73]

Conclusion

Since their introduction, polymers have piqued the curiosity of formulation scientists. Various diffusion- and dissolution-controlled formulations have been produced to far, and medical science is making positive and rapid progress in this area. The debate concludes that by combining pharmaceuticals into natural, semi-synthetic, and synthetic polymers, dosage forms that release the medication over a longer period of time can be created in a number of dosage forms. Polymers have an important role in drug delivery, therefore their selection of Polymers play a vital part in medication production. However, while selecting polymers, attention must be made to consider their toxicity, medication compatibility, and degradation patterns. Based on this review, we may conclude that natural polymers are a good substitute for semi-synthetic and synthetic polymers, and that many of the adverse effects of semi-synthetic and synthetic polymers can be avoided by utilizing natural polymers.

References

1. Hamid Akash MS, Rehman K, Chen S. Natural and synthetic polymers as drug carriers for delivery of therapeutic proteins. Polym Rev. 2015;55(3):371- 406.
2. Suresh R, Chandra S, Kavibharathi S, Sheikalisha A, Sangeetha S, Raviprakash R. A review on sustained release drug delivery system. World J Pharm Res. 2021;10(3):128 -149.
3. Kaleemullah M, Jiyauddin K, Thiban E, Rasha S, Al-Dhalli S, Budiasih S, Gamal OE, Fadli A, Eddy Y. Development and evaluation of Ketoprofen sustained release matrix tablet using Hibiscus rosa-sinensis leaves mucilage. Saudi Pharm J. 2017;25(5):770-79.
4. Jadhav P, Deore P, Gangurde A. an overview of sustained release matrix system. Int J Curr Sci. 2022;12(1):649-62.
5. Pareek SP, Kumawat S, Sharma V, Sharma D, Rathore DS, Agarwal M. Review on sustained release technology. Int J Pharm Boil Sci Arch.2019;7(6):29-38.
6. Kumar AR, Aeila AS. Sustained release matrix type drug delivery system: An overview. World J. Pharm. Pharm. Sci. 2019; 24(9):470-80.
7. Navneet Sharma NS, Deshpande RD, Deepak Sharma DS, Sharma RK. Development of locust bean gum and xanthan gum based biodegradable microparticles of celecoxib using a central composite design and its evaluation. Ind Crops Prod. 2016;82(1):161-170
8. Sirisha VN, Eswariah MC, Rao AS. A novel approach of locust bean gum microspheres for colonic delivery of mesalamine. Int J Appl Pharm. 2018;10(1):86-93.
9. Rowe C, Sheskey P, Quinn M. Handbook of pharmaceutical excipients. Libros digitales-Pharmaceutical Press;2009.
10. Afshar M, Dini G, Vaezifar S, Mehdikhani M, Movahedi B. Preparation and characterization of sodium alginate/polyvinyl alcohol hydrogel containing drug-loaded chitosan nanoparticles as a drug delivery system. J Drug Deliv Sci Technol. 2020;56(1):101530-36
11. Sarika PR, James NR. Polyelectrolyte complex nanoparticles from cationised gelatin and sodium alginate for curcumin delivery. Carbohydr Polym. 2016;14(8):354-61.
12. Zia KM, Tabasum S, Khan MF, Akram N, Akhter N, Noreen A, Zuber M. Recent trends on gellan gum blends with natural and synthetic polymers: A review. Int J Biol Macromol. 2018;10(9):1068-87.
13. Dhanka M, Shetty C, Srivastava R. Methotrexate loaded gellan gum microparticles for drug delivery. Int J Biol Macromol. 2018;1(10):346-56.
14. Carmona-Moran CA, Zavgorodnya O, Penman AD, Kharlampieva E, Bridges Jr SL, Hergenrother RW, Singh JA, Wick TM. Development of gellan gum containing formulations for transdermal drug delivery: Component evaluation and controlled drug release using temperature responsive nanogels. Int J Pharm. 2016;509(1-2):465-76.
15. Kim JK, Kim HJ, Chung JY, Lee JH, Young SB, Kim YH. Natural and synthetic biomaterials for controlled drug delivery. Arch Pharm Res. 2014;3(7):60-8.
16. Peers S, Montembault A, Ladavière C. Chitosan hydrogels for sustained drug delivery. J Control Release. 2020;3(26):150-63.
17. Lu B, Lv X, Le Y. Chitosan-modified PLGA nanoparticles for control-released drug delivery. Polym. 2019;11(2):1-14.
18. Kulkarni Vishakha S, Butte Kishor D, Rathod Sudha S. Natural polymers–A comprehensive review. Int. J. Res. Pharm. Biomed. Sci. 2012;3(4):1597-613.
19. Ghayempour S, Montazer M. A novel controlled release system based on Tragacanth nanofibers loaded Peppermint oil. Carbohydr Polym. 2019;20(5):589-95.
20. Al-barudi A, Sinani G, Ulker Z. Biodegradable polysaccharide aerogels based on tragacanth and alginate as novel drug delivery systems. J Solgel Sci Technol. 2024;109(3):748-56
21. Pandey SP, Shukla T, Dhote VK, Mishra DK, Maheshwari R, Tekade RK. Use of polymers in controlled release of active agents. Basic fund drug deliv. 2019; 1(4): 113-172
22. Soylu HM, Chevallier P, Copes F, Ponti F, Candiani G, Yurt F, Mantovani D. A novel strategy to coat dopamine-functionalized titanium surfaces with agarose-based hydrogels for the controlled release of gentamicin. Front Cell Infect Microbiol. 202;11(1):1-7.
23. Odeku OA, Okunlola A, Lamprecht A. Microbead design for sustained drug release using four natural gumsInt J Biol Macromol. 2013;58 (1):113-20.
24. Masood N, Razaque G, Shahwani G, Shirazi J, Nawaz H, Masood M, Anees M, Tariq H. Formulation and In Vitro Characterization of Xanthan Gum/Eudragit Controlled Release Hydrogel Using Metformin as a Model Drug. Pak-Euro J. Med. Life Sci. 2022;5(1):81-92.
25. Kar R, Mohapatra S, Bhanja S, Das D, Barik B. Formulation and in vitro characterization of xanthan gum-based sustained release matrix tables of isosorbide-5-mononitrate. Iran J Pharm Res: 2010;9(1):13-19.
26. Mudgil D, Barak S, Khatkar BS. Guar gum: processing, properties and food applications—a review. J Food Sci Technol. 2014;51(3):409-418.
27. Daud H, Ghani A, Iqbal DN, Ahmad N, Nazir S, Muhammad MJ, Hussain EA, Nazir A, Iqbal M. Preparation and characterization of guar gum based biopolymeric hydrogels for controlled release of antihypertensive drug. Arab J Chem. 2021;14(5):1-14.
28. Yadav AS, Kumar PA, Vinod R, Rao BS, Kulkarni SV. Design and evaluation of guar gum based controlled release matrix tablets of Zidovudine. J Pharm Sci Tech. 2010;2(3):156-62.

29. Zia KM, Tabasum S, Nasif M, Sultan N, Aslam N, Noreen A, Zuber M. A review on synthesis, properties and applications of natural polymer based carrageenan blends and composites. Int J Biol Macromol. 2017;96(1):282-301.
30. Srinivasa R, Ratnam B. Formulation and optimization of sustained release tablets of rosuvastatin using HPMC K4M, HPMC K100M and carrageenan. Int J Chem Tech Res. 2018;11(05):376-86.
31. Grenha A, Gomes ME, Rodrigues M, Santo VE, Mano JF, Neves NM, Reis RL. Development of new chitosan/carrageenan nanoparticles for drug delivery applications. J Biomed Mater Res. 2010;92(4):1265-72.
32. Apriyanto A, Compart J, Fettke J. A review of starch, a unique biopolymer–Structure, metabolism and in planta modifications. Plant Sci. 2022;31(8):111-23.
33. Mundargi RC, Shelke NB, Rokhade AP, Patil SA, Aminabhavi TM. Formulation and in-vitro evaluation of novel starch-based tableted microspheres for controlled release of ampicillin. Carbohydr Polym. 2008;71(1):42-53.
34. Elgaied-Lamouchi D, Descamps N, Lefevre P, Rambur I, Pierquin JY, Siepmann F, Siepmann J, Muschert S. Starch-based controlled release matrix tablets: Impact of the type of starch. J Drug Deliv Sci Technol. 2021;6(1):102-52.
35. Alipal J, Pu'Ad NM, Lee TC, Nayan NH, Sahari N, Basri H, Idris MI, Abdullah HZ. A review of gelatin: Properties, sources, process, applications, and commercialisation. Materials Today: Proceedings. 2021;4(2):240-50.
36. Ghosh SK, Das A, Basu A, Halder A, Das S, Basu S, Abdullah MF, Mukherjee A, Kundu S. Semi-interpenetrating hydrogels from carboxymethyl guar gum and gelatin for ciprofloxacin sustained release. Int J Biol Macromol. 2018;120(1):1823-33.
37. Dong Z, Wang Q, Du Y. Alginate/gelatin blend films and their properties for drug controlled release. J Memb Sci. 2006;280(1-2):37-44.
38. He X, Lu W, Sun C, Khalesi H, Mata A, Andaleeb R, Fang Y. Cellulose and cellulose derivatives: Different colloidal states and food-related applications Carbohydr Polym. 2021;25(5):1-40.
39. Oprea M, Voicu SI. Recent advances in composites based on cellulose derivatives for biomedical applications. Carbohydr polym. 2020;24(7):1-90.
40. Kamel S, Ali N, Jahangir K, Shah SM, El-Gendy AA. Pharmaceutical significance of cellulose: A review. Express Polym Lett. 2008;2(11):758-78.
41. Samie M, Bashir S, Abbas J, Samiullah KH, Nargis AM, Habibullah JA, Muhammad N. Design, formulation and in vitro evaluation of sustained-release tablet formulations of levosulpiride. Turk J Pharm Sci. 2018;15(3):309-18.
42. Dhanaraju MD, Sundar VD, NandhaKumar S, Bhaskar K. Development and evaluation of sustained delivery of diclofenac sodium from hydrophilic polymeric beads. J Young Pharm. 2009;1(4):301-04
43. Orasugh JT, Saha NR, Sarkar G, Rana D, Mishra R, Mondal D, Ghosh SK, Chattopadhyay D. Synthesis of methylcellulose/cellulose nano-crystals nanocomposites: Material properties and study of sustained release of ketorolac tromethamine. Carbohydr Polym. 2018;18(8):168-80.
44. Bhowmik M, Das S, Sinha J, Bag S, Chattopadhyay D, Ghosh LK. Methyl cellulose based sustained release thermosensitive in situ fast gelling ocular delivery of ketorolac tromethamine. Asian J Chem. 2010;22(3):2147-54
45. Shin TH, Ho MJ, Kim SR, Im SH, Kim CH, Lee S, Kang MJ, Choi YW. Formulation and in vivo pharmacokinetic evaluation of ethyl cellulose-coated sustained release multiple-unit system of tacrolimus. Int J Biol Macromol. 2018;10(9):544-50.
46. Goswami KO, Khurana GA, Marwaha RK, Gupta MI. Development and evaluation of extended-release ethyl cellulose-based matrix tablet of diclofenac sodium. Int J Pharm Pharm Sci.2014;6(6):296-301
47. Qi X, Chen H, Rui Y, Yang F, Ma N, Wu Z. Floating tablets for controlled release of ofloxacin via compression coating of hydroxypropyl cellulose combined with effervescent agent. Int J pharm. 2015;489(1-2):210-215.
48. Işıklan N, Erol ÜH. Design and evaluation of temperature-responsive chitosan/hydroxypropyl cellulose blend nanospheres for sustainable flurbiprofen release. Int J Biol Macromol.. 2020;15(9):751-62.
49. Okubo M, Iohara D, Anraku M, Higashi T, Uekama K, Hirayama F. A thermo responsive hydrophobically modified hydroxy propyl methylcellulose/cyclodextrin injectable hydrogel for the sustained release of drugs. International Journal of Pharmaceutics. 2020;57(5):1-30.
50. Sekharan TR, Palanichamy S, Tamilvanan S, Shanmuganathan S, Thirupathi AT. Formulation and evaluation of hydroxypropyl methylcellulose-based controlled release matrix tablets for theophylline. Indian J Pharm Sci. 2011;73(4):451-56.
51. Thakral S, Thakral NK, Majumdar DK. Eudragit®: a technology evaluation. Expert Opin Drug Deliv. 2013;10(1):131-49.
52. Farooq U, Khan S, Nawaz S, Ranjha NM, Haider MS, Khan MM, Dar E, Nawaz A. Enhanced gastric retention and drug release via development of novel floating microspheres based on Eudragit E100 and polycaprolactone: synthesis and in vitro evaluation. Des Monomers Polym. 2017;20(1):419-33.
53. Rabani T, Jan SU, Razaque G, Gul R, Khan KA, Rashid F, Tufail M. Formulation and assessment of controlled release tablets of famotidine by using eudragit RL 100 polymer. Pak J Pharm Sci. 2022;1(1):1779-86
54. Gavasane AJ, Pawar HA. Synthetic biodegradable polymers used in controlled drug delivery system: an overview. Clin Pharmacol Biopharm. 2014;3(2):1-7.
55. Fu, F.-L. Mi, T.-B. Wong, S.-S. Shyu YJ. Characteristic and controlled release of anticancer drug loaded poly (D, L-lactide) microparticles prepared by spray drying technique. J Microencapsul. 2001;18(6):733-47.
56. Ghaffarzadegan R, Khoee S, Rezazadeh S. Fabrication, characterization and optimization of berberine-loaded PLA nanoparticles using coaxial electrospray for sustained drug release. DARU J. Pharm. Sci. 2020; 2(8):237-52.

57. Ravi PR, Vats R, Dalal V, Gadekar N, N A. Design, optimization and evaluation of poly-ε-caprolactone (PCL) based polymeric nanoparticles for oral delivery of lopinavir. Drug Dev Ind Pharm. 2015;41(1):131-40.
58. Arunkumar P, Indulekha S, Vijayalakshmi S, Srivastava R. Poly (caprolactone) microparticles and chitosan thermogels based injectable formulation of etoricoxib for the potential treatment of osteoarthritis. Mater Sci Eng. 2016;6(1):534-44.
59. Narayana Reddy CL, Swamy BY, Prasad CV, Madhusudhan Rao K, Prabhakar MN, Aswini C, Subha MC, Rao KC. Development and characterization of chitosan-poly (vinyl pyrrolidone) blend microspheres for controlled release of metformin hydrochloride. Int J Polym Mater. 2012;61(6):424-36.
60. Ahmad B, Abbas S, Iqbal Z, Bashir S, Ali J. Synthesis of cross linked PVP hydrogels and its use for the control release of anti-asthmatic drugs. Middle East J Sci Res. 2013;1(4):273-83.
61. Halima NB. Poly (vinyl alcohol): review of its promising applications and insights into biodegradation. RSC advances. 2016; 6(46):39823-32.
62. Long J, Nand AV, Bunt C, Seyfoddin A. Controlled release of dexamethasone from poly (vinyl alcohol) hydrogel. Pharm Dev Technol. 2019;24(7):839-48.
63. Sohail M, Ahmad M, Minhas MU, Ali L, Munir A, Khalid I. Synthesis and characterization of graft PVA composites for controlled delivery of valsartan. Lat Am J Pharm. 2014;33(8):1237-44.
64. Xiong B, Loss RD, Shields D, Pawlik T, Hochreiter R, Zydney AL, Kumar M. Polyacrylamide degradation and its implications in environmental systems. NPJ Clean Water. 2018;1(1):1-9.
65. Kajjari PB, Manjeshwar LS, Aminabhavi TM. Novel interpenetrating polymer network hydrogel microspheres of chitosan and poly (acrylamide)-grafted-guar gum for controlled release of ciprofloxacin. Ind Eng Chem Res. 2017;50(23):13280-87.
66. Mandal BB, Kapoor S, Kundu SC. Silk fibroin/polyacrylamide semi-interpenetrating network hydrogels for controlled drug release. Biomater. 2009;30(14):2826-36.
67. Akash MS, Rehman K, Li N, Gao JQ, Sun H, Chen S. Sustained delivery of IL-1Ra from pluronic F127-based thermosensitive gel prolongs its therapeutic potentials. Pharm res. 2012;2(9):3475-85.
68. El-Kamel AH. In vitro and in vivo evaluation of Pluronic F127-based ocular delivery system for timolol maleate. Int J Pharm. 2002;241(1):47-55.
69. Akram Z, Aati S, Ngo H, Fawzy A. pH-dependent delivery of chlorhexidine from PGA grafted mesoporous silica nanoparticles at resin-dentin interface. J Nano biotech. 2021;1(9):1-6.
70. Bukhari A, Fatima Z, Atta M, Nazir A, Alshawwa SZ, Alotaibi HF, Iqbal M. Poly lactic-co-glycolic acid nano-carriers for encapsulation and controlled release of hydrophobic drug to enhance the bioavailability and antimicrobial properties. DOSE-RESPONSE. 2023;21(1):1-12.
71. Xu Q, Czernuszka JT. Controlled release of amoxicillin from hydroxyapatite-coated poly (lactic-co-glycolic acid) microspheres. J Control Release. 2008 Apr; 127(2):146-53.
72. Malipeddi VR, Awasthi R, Dua K. Formulation and evaluation of controlled release ethylcellulose and polyethylene glycol microspheres containing metoprolol tartrate. Interv Med Appl Sci. 2016;8(2):60-7.
73. Sundara Rajan S, Cavera VL, Zhang X, Singh Y, Chikindas ML, Sinko PJ. Polyethylene glycol-based hydrogels for controlled release of the antimicrobial subtilosin for prophylaxis of bacterial vaginosis. Antimicrob Agents Chemother. 2014;58(5):2747-53.

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