

APPLICATIONS OF NATURAL POLYMERS IN NOVEL DRUG DELIVERY SYSTEMS

Abstract

Natural polymers have considerable attention as budding carriers being the delivery of drugs and other medicinal compounds. Natural macromolecules are versatile in medicine administration because of their inherent advantages in exceptional bioabsorbable, limited enzyme deterioration, specific inter connection with various biological molecules, and ease of moderation. The two required components of any medicament formulation are the active constituents and filling material. Filling material assist the production of prescription and increases their biophysical properties. As excipients, macromolecules are essential in all dosage forms. Through the release of two different drug types, hydrophilic and hydrophobic, macromolecules play a significant part in the evolution of drug distribution innovation. Due to some of the negative complication and harmful effect of synthetic drugs, products from natural sources have become an essential component of the human health care system. In solid oral medication, polymers have been widely utilized as binders, diluents, breakdown, and matrix agents. Nanoscience has just begun to produce considerable strides in biomedical applications, including more modern medication delivery methods. Because, since that natural polymers are abundant in living world, generally bioabsorbable, recyclable, defended, and insusceptible, there has been extensive investigation into producing bioabsorbable, recyclable, micrometers devices as drug delivery. The most extensively researched and used natural materials for implementation in new drug delivery include polysaccharides, resins, along with tannins.

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I. INTRODUCTION

The evolution of drug distribution has received a considerable interest recently. For various delivery methods, a number of drug delivery procedures have been hypothesized because they need occasional drug consumption, produce added effective therapeutic effects, and cause less side effects. [1]

Typically, a polymer is made up of (at least) five repeating atom arrangement, that are strung with each other. Polymers typically include more than five monomers, and some polymers in each chain. Polymers are classified depending on the molecular weight of each chain [2] therapeutic compounds, polymers have a significant function in new drug delivery methods. The primary function of the polymer is to regulate the dosage form's medication release pattern. Investigation of diffusion-controlled and solvent-activated production in drug transmission has resulted in tremendous advancement. Numerous polymers have a natural origin, such as minerals, chitin from animals, or cellulose from plants. Many of these have been around for ages. Because of their acclaimed biodegradability along with biocompatibility, compostable polymers have been employed greatly in bioscience implementation in the biomedical field, polymers are employed in long-term therapies to increase their efficacy, lessen their negative effects, and improve patient compliance.

Polymers have a variety of roles in the pharmaceutical industry, including binders in tablet formulations and viscosity and flow control agents in liquid formulations. Manage the extended, pulsatile, and targeted drug delivery systems, drug release rates. The polymer can be applied as a film coating to hide the drug's disagreeable flavor. In a controlled release drug delivery system, the initial drug concentration and polymer chain relaxation determines the rate of drug transmission from the model. The natural polymers chitosan, alginate, gelatin, collagen, and starch are frequently operated in the administration of pharmaceuticals. To deliver medications to certain locations within the body, these macromolecules can be prepared into a variety of forms, including nanocrystal, microvesicle, hydrocolloid, and films. The effectiveness, bioavailability, and toxicity of natural polymer-based drug transmission systems are strongly influenced by their surface qualities. Natural polymers, however, have limits in their usage for drug administration since it can be challenging to manage their surface properties. As a result, altering the surface of natural polymers has become a crucial field of drug delivery research.[3]

Polymeric nanoparticles are defined as submicron, spherical, polymeric particle composed of natural or artificial polymer. The size ranges between 10 and 500nm colloidal carriers. Because of their smaller size it possesses very different biological properties [2]

II. ADVANTAGES AND DRAWBACKS OF NATURAL POLYMERS

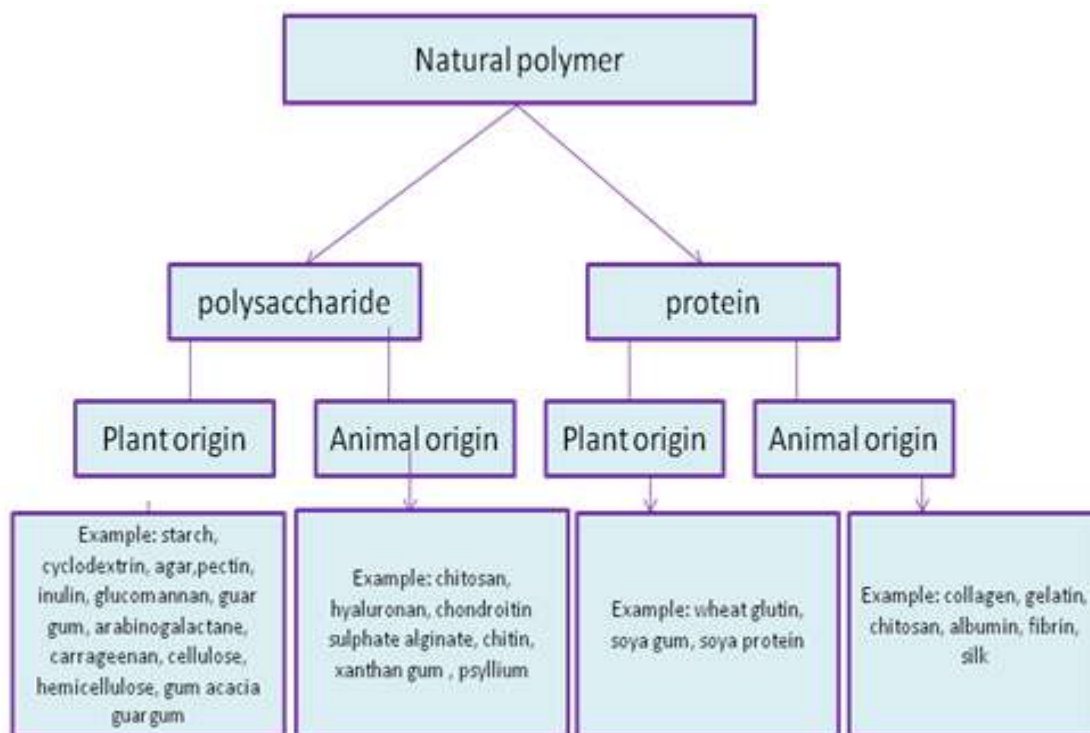
- 1. Advantages:** Natural polymer-based innovative drug delivery systems have several benefits that enhance pharmacokinetics and boost the biodistribution of medicinal drugs to target organs. [4, 5]
 - **Stabilization of the Drug:** The polymer can shield the medicine from the physiological setting, improving its in vivo stability.[4]

- **Localized Delivery of Drug:** Systemic exposure of the drug can be decreased since the drug can be execute straight at the location where biological activity is required. [4]
- **Controlled Transmission of Drug :** The medication is allow to leave from the capsule in the course of time, and transdermic drug release systems, focused, and insulin are hardly the examples of novel drug delivery systems.[6]
- **Lack of Side Effect:** they provide the imperative safety without any side effect .[7]
- **Attainability:** They are available in large quantities all over the place.[7]

2. Drawbacks [8]

- **Foreign Matter:** Throughout the time of preparation, they are uncover to the surrounding environment so there are possibility of microorganism pollutant.
- **Dissimilarities between Batches:** Natural polymer formation is reliant on the environment and numerous biotic and abiotic elements, whereas synthetic manufacturing is a regulated process with defined number of materials.
- **The Uncontrolled Rate of Hydration:** The number of chemical elements existing in a specific substance may vary due to dissimilarity in the assembling of raw materials at different times, as well as differences in geography, order, and weather pattern.
- **Delay Procedure:** Natural polymers have step by step manufacturing as the creation based on the ecological and lots of constituent.
- **Heavy Metal Pollutant:** There are possibilities of Heavy metal pollutants many times connected with herbal fillers.

III. CLASSIFICATION



IV. GENERAL MECHANISMS OF DRUG DELIVERY FROM POLYMER [9]

There are three basic process through which active constituents can be transmitted –

- 1. Diffusion:** When a medication or active constituent's flows from the polymer that makes up the prolonged release pattern, diffusion takes place. When a medicament diffuses, it leaves the polymer sheet and enters surrounding medium. Since active principal has a gradually increasing gap to be transmitted and needs a extended diffusion time to let go, using this diffusion system, the librationrate declines eventually. When a delivery system is introduced into a biological environment, the chosen composition of polymer modeland plant derived medium must permit the drug diffusion through the orifice of the polymer in the absence of any switch in the polymer itself.
- 2. Degradation:** The necessity to withdraw the drug transmission system once the active constituents has been librated is eliminated by biodegradable polymers, which break down inside the body as a result of normal biotic procedure. The majority of biodegradable polymers are made to break down into physiologically acceptable and smaller molecules through hydrolysis of the polymer chains. A libration rate that is corresponding to the exterior area of the drug delivery system is achieved by fewbiodegradable polymers, nearly all remarkable the poly anhydrides and polyorthoesters, in which the break down only takes place at the outside of the polymer.
- 3. Swelling:** Initially dry, they will take up water or other biofluids when inseminate within the anatomy and expand. The medicine can spread out from the swelled matrixinto the surrounding living world because swelling increases the formulation's aqueous solvent concentration and polymer mesh size.

V. CLASSES OF NATURAL POLYMERS

The polymers are recognized to be important in the realm of pharmaceutical medication research and technology and act as protein carriers. Natural polymers are important in drug delivery systems because they have reactive sites that can be used for cross-linking, legends conjugation, and other changes, which makes them perfect drug carriers for a variety of therapeutic property. [10]

- 1. Starch:** Starch is produced by plants and stored in their structures as a source of energy. Cellulose is most prevalent carbohydrate found in theflora world as a unprocessed material, second only to cellulose. The principle source of carbohydrates in plants, starch serves as a reserve food source during times of germination, development, and dormancy. Each starch's characteristics are closely related to its plant source. A heterogeneous polymer of α -D-glucose unit is starch. The dehydrated glucose units are mostly connected by α - (1, 4) bonds, with α -(1, 6) connections playing a smaller role. Amylose and amylopectin are two distinct structural types that make up the biopolymer. Amylopectin is a subdivide molecule consist of thousand glucose units, whereas amylose is a straight chain of a number of hundred glucose molecules.[11]

Due to the starch's non toxic, economical, and wide availability, thermoplastic resin films are one of the most encouraging replacements for synthetic polymers in the

wrapping industry. However, several film properties are influenced by the makeup of the starch granules, as measured by the amylose content and phosphate monoesters, as well as the starch's molecular weight. This work used the casting method to create biodegradable thermoplastic amyllum films from potato, rice starch, maize and wheat. It was assessed how each starch's grain structure affected the ultrastructure, translucency, moisture characteristics, crystalline, and mechanical feature of the films. The most translucent and opaque starch films were made of potato and corn respectively. All of the films exhibited uniform interior structures that were highly amorphous and free of pores.[12]

Starch is a frequently utilized as thin strip carrier for nasal medication delivery that has been shown to improve the soaking up of each water repellent medicines and hydrophane macromolecular pharmaceuticals. Maize starch is the most favored class for medicament applications, with drum-dehydrated waxy maize starch being considered best due to its superior bioadhesive characteristic when compared to starch treated in other ways.[13]

Advantages: Simple tablet composition, the capability for a steady release rate over time, and the capacity to combine significant concentrations of medications with various physicochemical features.[11]

- 2. Pectin:** Pectins are biopolymers with numerous uses due to their complexity and structural variety. Even though, although pectins from various sources have similar structural traits, many of these features vary depending on the species and physiological stage of the plant. Additionally, the chemical characteristics of pectin, such as the amounts of galacturonic acid, methoxyl, and acetylation, influence how it is used.[14]

The pectin backbone is a straight chain of α -(1-4)-linked D-galacturonic acid that is found in the pectin family of complex polysaccharides. Pectins can thicken, bind to water, and stabilize in addition to being employed as gelling agents. [15] Pectin is constructed in the cell envelope of developing and dividing plants. Pectin has been considered as a diluent in a variety of pill.[16] Pectin gel beads are an essential means to manage the liberation of a drug inside the digestive tract.[17] Pectic compounds are typically divided into four parts: protopectin, pectic acid, pectinic acid, and Pec. Pec is one of the many different biopolymers and is a type of dissoluble heteroglycans that is recovered chemically or enzymatically from the main cell walls of terrestrial plants. Because to their various origin and techniques of drawing out, Pec has a higher spectrum of structural variability. Due to its outstanding qualities, including non-poisonous, bioabsorbable, compostable, economical, germicidal, and anti-inflammatory capabilities, pec is known as a viable contender in the drug release system.. Pec can be obtained from a different of origin, which include apple pomace, citrus peels and sugar beet pulp. Undoubtedly, the main source of Pec comes from the by-products of tropical and subtropical fruit. However, it is crucial to note that the drawing out methods and additional factors like the drawing out duration, different type of acid, temperature, pH, and liquid-solid ratios have an impact on the Pec production.[18, 19]

- 3. Carrageenan:** Carrageenans are sulfated polysaccharides, precede with Iota (i-), Kappa (j-), and Lambda (k)-carrageenan. K-carrageenan predominates in kappaphycus alvarezzi

(red algae). There are many *Kappaphycus* spp. on reef flats and reef edges that are between anear about 1 and 17 m deep.[20]

While the Iota type is elastic and creates a gel, the Gamma type produces viscosity. It is utilized in the production of prolonged release tablets as well as hydrogel beads and tablet excipients. Alginate, potassium, and calcium can all be used to cross-link it. Additionally, it is utilized in the creation of innovative sustainable release products[21] used especially as thickeners or gelling polymers. [22]

Carrageenan is recognised as a potential biological material for producing food wrapping films because of its distinctive mechanical behaviour, water vapour barrier, surface hydrophobicity, light protection, and thermal characteristics. In light of growing environmental protection awareness, an alternative bio-based, polymer-based food packaging material has gained a lot of interest since it is freely accessible, non-toxic, and biodegrades over of a few weeks at a specific temperature and humidity level. Polysaccharides, lipids, and proteins are frequently used as film-forming substrates for biodegradable packaging materials. In this context, hydroxyl-rich carrageenan is thought to be a particularly promising material due to its remarkable gelling and film-forming abilities. To make carrageenan-based composite films, functional substances like polyphenols and enzymes are frequently added to carrageenan substrates.[23]

- 4. Hyaluronic acid:** The straight polysaccharide hyaluronic acid, also known as hyaluronan and hyaluronate, is biodegradable, biocompatible, and viscoelastic. It is a naturally occurring biopolymer, and higher animals' tissues may contain naturally occurring hyaluronic acid. The concentrations are highest in the synovial fluid of articular joints and the vitreous humour of the eye. The straight, unbranching polyanionic disaccharide units that make up hyaluronic acid are made of glucuronic acid (GlcUA) and N-acetyl glucosamine (GlcNAc), which are alternatively connected by β -1-3 and β -1-4 glycosidic linkages. The concentration and molecular weight of the hyaluronic acid chains regulate the viscoelastic behaviour of hyaluronic acid, which is crucial for their usage as a biocompound.[24]

The production of hyaluronic acid rises during tissue damage and wound healing, and hyaluronic acid controls tissue repair, such as the immunological activity to injury, the reaction of fibroblasts and epithelial cells to injury, and the start off of inflammatory cells. Hyaluronic acid synthases are specialized enzymes that produce hyaluronic acid. These are membrane-bound enzymes that manufacture hyaluronic acid on the plasma membrane's inner surface.[25] Due to its purported pharmacological effects, which include anti-ageing, anti-inflammatories, skin restorative, tissue revitalize, and wound retrieval qualities, hyaluronic acid, a significant component of extra-cellular matrix, has been broadly used in the medicament and beauty product. At the moment, hyaluronic acid is frequently used in transdermal administration systems to improve drug penetration in the treatment of psoriasis. To improve medication pass through and into the skin for psoriasis therapy, several drug delivery technologies have been developed, including ethosomes, cryogels, microneedle patches, and hyaluronic acid-based nanoparticles. A key topical carrier for targeted delivery of medications to skin, as well as a medicament releasing agent for ocular, nasal, for the lung, injectable, and outer surface of the part of body, hyaluronic acid was developed as a result of its remarkable solubility qualities.

hyaluronic acid, functions as a mucoadhesive, keeping the medication at the intended active center. Additionally, it may alter therapeutic agent's rate of release and absorption in vivo and localize drug delivery to the epidermis. Methotrexate, tacrolimus, and corticosteroids are among the psoriasis medicaments included in these hyaluronic acid-based transmission systems; they are all first-line therapies for moderate to chronic psoriasis.[26] Depending on the size of the polymer, hyaluronan has varied effects on different types of cells. The discovery that tiny chains or oligosaccharides of hyaluronic acid but not big polymers can kill a variety of cancer cells by inducing programmed cell death while sparing natural cells is one of the more intriguing ones. When hyaluronic acid oligosaccharides are added to the treatment, even chemoresistant cells become drug-susceptible.[27]

- 5. Cyclodextrin:** A family of cyclic oligosaccharides with a lipophilic interior and a hydrophilic exterior are known as cyclodextrin (CD). Because of their size and the abundance of hydrogen donors and acceptors, CD molecules do not normally cross lipophilic membranes. CD is mainly used as a chelating agent in the pharmaceutical industry to improve the bioavailability and stability of poorly soluble drugs by making them more water-soluble. Many pharmaceutical applications use CD, especially those that increase drug bioavailability.[28] CD consists of six to eight glucose units linked together at the α -1,4 position by glucosidic bonds[11]. The parent CD is soluble in water to varying degrees, with γ -CD being the most soluble (232.0 g/L), followed by α -CD (145.0 g/L) and β -CD (18.5 g/L), is the least soluble. The strong intramolecular hydrogen bonds in β -CD are thought to be responsible for the compound's low solubility in water and its ability to inhibit hydration, thereby limiting its use, especially in injectable preparations. This problem was solved by replacing the hydroxyl groups in β -CD creating hydrogen bonds, greatly increasing its water solubility. This leads to the generation of many other water-soluble CD derivatives. Because of their torus-like shape, CDs have the unusual ability to act as molecular carriers by trapping outer molecules inside their internal cavity.[29]

When the CD drug complex is formed, no covalent bonds are created or destroyed, and in an aqueous solution, the free drug molecules and those bound inside the CD cavity maintain their state. Equilibrium because the complex is easily soluble.. [30] CDs are not digested in the stomach or small intestine of the GI tract. They are converted by the big colonic bacteria present in the colon into minute monosaccharides, which are then absorbed from these regions. The large intestine completely digests CDs, but the small intestine only marginally degrades them.[11] CDs have been used to prevent interactions with drugs or with drug additives, reduce or eliminate unpleasant tastes, reduce or eliminate gastrointestinal or eye irritation, and even turn oil and liquid drugs into microcrystalline or amorphous powders.[30] Since most infusion formulations are aqueous, CD provides an ideal strategy to facilitate their formulation with less water-soluble drugs. Therefore, the formation of a complex consisting of a water-soluble drug-CD is very favorable as it increases the solubility of the drug, improves the stability, and also increases the bioavailability of the drug by elongation. long transit time.[29]

- 6. Chitosan:** Chitosan is an abundant natural-based polymer[32] Chitosan is a linear copolymer consisting of glucosamine and N-acetylglucosamine units linked by 2-amino-2-deoxy-D-glucan (GlcN). Water-soluble chitosan derivatives, including chitosan salts,

zwitterionic chitosan and chitosan oligomers, have recently attracted interest due to their water solubility. Chitosan has many beneficial properties but is soluble in neutral aqueous solutions. Therefore, they are both complex biomaterials and their applications in biotechnology and biopharmaceuticals are both important.[33]

It is commonly used to form polyelectrolyte complexes with polyanions for drug delivery because it is a cationic polymer with beneficial properties.[19] Several chitosan-based colloidal systems are currently promising carriers for bioactive compounds. Chitosan is a promising candidate for oral drug delivery because it is a bio-adhesive polymer with antibacterial properties.[32] It has beneficial biological properties such as adhesion, biocompatibility, non-toxicity and, above all, biodegradability.[33] The chitosan microspheres allow the delivery of specific drugs to the stomach and can stay in the stomach longer. Chitosan increases the residence time of the dosage form in the mucous membranes, inhibits proteolytic enzymes, and increases the permeability of proteins and peptides across the mucous membranes to enhance intestinal absorption. According to research, bacteria living in the colon break down chitosan. Therefore, this polymer may have a potential future in delivering specific drugs to the colon. Numerous in vitro and in vivo studies have demonstrated that chitosan is an effective medium for the transmission of non-viral genes and DNA vaccines. Due to its unique physical, chemical and biological properties, chitosan has been used in a variety of formulations for gastrointestinal drug delivery and gene transfer.[32]

- 7. Albumin:** Albumin is a predominant protein found in the blood plasma, representing 60% of the total serum protein. In the body, it functions as a means of transportation and disposal of drugs that bind to it. Therefore, albumin's extreme binding capability can help increase the delivery of drugs, which is why it is extensively used in drug delivery development.[34] Human serum albumin (HSA) is a plentiful, multifunctional, non-glycosylated, negatively charged plasma protein that has been shown to have antioxidant and enzymatic capabilities in addition to its ligand-binding and transport properties. Preproalbumin, which has an N-terminal peptide, is the form in which it is largely produced in the liver. A globular, water-soluble, and un-glycosylated serum protein is albumin.[2]
- 8. Alginates:** Alginate is commonly made by adding sodium chloride or calcium chloride after removing the brown seaweed. Sodium alginate is a typical excipient used in pharmaceuticals. ALG has a wide variety of biological applications due to its low toxicity, biocompatibility and reasonable low cost. Alginate can create a viscous, low-density gel "raft" that acts as a barrier to the low pH of the stomach, thereby reducing reflux symptoms.[34] Alginate is an unbranched binary copolymer consisting of b-D-mannuronic acid and a-L-guluronic acid monomers linked to (1-4) glycosides..[35] As a result, the physical properties of the resulting alginate and hydrogel are influenced by composition, sequence, bulk length and molecular weight. Commercially available sodium alginate has a molecular weight of 32,000 to 400,000 g/mol and is available in low, medium and high viscosity. Alginate has been studied and used as an emulsion stabilizer, tablet binder, tablet disintegrator and suspension agent. Guluronic residues in alginate can gel in the presence of polyvalent ions such as calcium or aluminium. Matrix, film, granule, pellet, microparticle and nanoparticle can be made using this crosslinking

and gel formation.[5] The fundamental drawback of employing alginate-based materials is that they cannot be degraded enzymatically by mammals.[35]

- 9. Xanthan Gum:** Gums are polysaccharides from living organisms, including plants, algae, and bacteria. They are considered as potential carriers of attractive drugs due to their superior biocompatibility and biodegradability, swelling capacity, and ability to destroy the colonic microbiota. [36]Xantan Gum (XG) is a natural, high molecular weight anionic exo-polysaccharide with five repeating units, including two glucose units, two mannose units and one glucuronic acid unit. The structural structure of XG is similar to that of cellulose. Its terminal D-mannose is bound to D-glucuronic acid via β -(1-4) and to D-mannose via α -(1-2) in the branched chain. Depending on the strain type, the pyruvate or acetate groups are used to bind the D-mannose units in XG.[37]It has many therapeutic applications, including food, cosmetics, and pharmaceuticals. Although used to deliver non-protein drugs, XG has also been evaluated for its ability to deliver therapeutic proteins and peptides. [38] Since XG is a non-toxic substance, it does not cause skin or eye irritation. In addition, the U.S. Food and Drug Administration (FDA) approved XG for use in food products in any quantity (without any restrictions) in 1969 as a additive. safe food additives (stabilizers and emulsifiers). In addition, XG is registered in the CFR as a stabilizer and thickener. In addition, XG was approved by the European Commission (EC) in 1980 as E415 in the list of allowed stabilizers and thickeners. Since the recommended daily amount of XG was changed to the non-quantitative limit of "not specified", XG has been shown to be a safe food additive. The lack of antibacterial properties,poor workability, small surface area and low dissolution rate of XG have limited the use of XG in industrial applications. Due to these limitations, it is possible to make appropriate chemical modifications to the structure of XG to address them and make XG usable for specific drug delivery systems and wastewater treatment..[38].[37]
- 10. Inulin:** It is a polysaccharide derived from the root of the dandelion plant, *Taraxacumofficinale* (Compositae), and the tuber of the dehlia plant, *InulaHelenium* (Compositae). Many types of oligomers make up inulin, and each inulin molecule contains from two to more than 60 fructose molecules linked by β -2,1-glycosidic bonds. In the upper gastrointestinal tract, inulin resists digestion; however, bacteria in the colon will break it down. By using Eudragit® RS and highly polymerized inulin, colon-specific biodegradable membranes that can resist the digestion of gastric and intestinal juices have been created. When the mixture of Eudragit® RS and Eudragit® RL was mixed with inulin, it showed better swelling and permeability qualities in the colonic medium compared with other digestive media. Eudragits® developed as a membrane containing inulin. [39]The inherent therapeutic effects of inulin include but are not limited to tumor risk reduction, calcium ion absorption support, and anti-inflammatory and antioxidant properties. In addition, inulin is used in a variety of medical applications such as drug transporters, stabilizers, cryoprotectants, and substitutes for fats and sugars.[40]
- 11. L.Cellulose:** The most abundant polysaccharide in nature is cellulose, which is the main structural component of plant cell walls. It offers many advantages, including excellent mechanical and thermal qualities, as well as cost effectiveness, biocompatibility and biodegradability. Regarding the basic composition of cellulose, it is a simple polysaccharide with a uniform framework with no branching or substituents. The basic fibers that form the morphological hierarchy of cellulose, are grouped into larger units

called microfilaments, which are then reassembled to form fibers. There are regions of cellulose fibers that are highly organized (crystalline) and regions that are disordered (amorphous type) in terms of the arrangement of cellulose chains. Nanocrystalline cellulose is produced by extraction from crystalline regions, although different interactions between the endoplasmic reticulum and intermolecular may result in polymorphisms or allomorphisms of cellulose.[40]

To make cellulose more processable and to create cellulose derivatives (cellulosic) like carboxymethyl cellulose, methylcellulose, hydroxyethylcellulose, etc. that can be specially made for certain commercial purposes, chemicals are added to cellulose. Cellulose has a many range of uses in the beautifying, medicinal, hygiene, food, and pharmaceutical application. While the intermolecular links allow the straight polymers to form sheet shapes, the intramolecular bonds stiffence the polymer chain. This biopolymer can be a promising nanoscale reinforcing material for polymers because it is readily available in nature, inexpensive, and biodegradable. [41]

Table 1: Various natural polymers and their applications

Polymer	Source	Applications	References
Agar – agar	Gelidium amansii, grailaria, and pterocladia	Emulsifying agents, tablet disintegrants, suspending agents	[10]
Cellulose	Found in cell wall of flora, algae and Oomycetes	Mucoadhesive delivery system, and in the monolithic matrix system	[42]
Tamarind	Tamarinds indicia	Hydrogels,ocularmuco adhesive drug libration	[43]
Pectin	Citrus aurantium	Beads, floating pellet, colon drug release, agglomiration	[43]
Gum arabic	Acacia trees	Matrix microencapsulating agent	[44]
Xanthan gum	Xanthomonascampestris	High thickening capacity	[45]
Carrageenan	Extracted from edible sea weeds	Thickening properties Stabilizing properties Binding property	[42]
Starch	Maize, rice, wheat, potato	Dis-integrant, binder	[46]
Gum acacia	Acacia senegal	Suspending and expanding agent	[47]
Alginates	Brown seaweed and algae	Matrixing agent	[48], [49]

Table 2: List of medicine and natural polymer combinations used in drug distribution

Drug	Polymer used	References
Furosemide	Guar gum, pectin, xanthum gum	[50]
Atenolol	Xathum gum, Guar gum	[50]
Cinnarizine	Chitin and chitosan	[51]
Metformin hydrochloride	Fenugreek seed mucilage	[51]
amoxicillin trihydrate	chitosan	[52]
Nimesulide	Locust bean gum	[51]
Ciprofloxacin Riboflavin	Ovomucin	[32]
Silver saccharinate (AgS)	Alginate	[32]
Ornidazole	Chitosan	[43]
Venlaflexine	Beeswax, carnauba wax	[53]
Indomethacin	Egg albumin	[54]
zidovudine	chitosan	[55]
Scopolamine, broxaterol	Soybean lecithin (Epikuron 200)	[56]
Metoclopramide	starch	[57]
Metronidazole	pectin	[58]
Bromazepam, ibuprofen	Cyclodextrin	[30]
Famotidine	Xanthum gum	[59]

VI. IMPLEMENTATION OF NATURAL MACROMOLECULES IN DRUG RELEASE SYSTEM

- 1. Tablets:** Polymers have long been employed as an excipient in both the traditional and instant-release oral dose formulation. Either it help with a formulation process or to keep medicine from deteriorating while it is being stored. The powder particles in dump mass, such as gelatin, starch and alginic acid etc., are bound by the polymers as a binder. In formulations of tablet, starch is employed as a disintegrant. When these tablets come into contact with water, they burst and expand the surface area of the medicine by enhancing dissolving properties[53]
- 2. Capsules:** Gelatine has been employed only as a shell material for hard (two-piece) and delicate (one-piece) capsules. [60] There have been created capsule shells with a range of formulation. These shell formulation may contain one type of polymer, like chitosan or simple protein, or a composite of various types of natural polymers, like Bovine serum

albumin-alginate polymers implemented by other materials, like inorganic nanoparticles, functionalizing polymers, antibodies, and a various other materials. These shells have different core materials enclosed inside them, either directly made of the solid or liquid active pharmaceutical cargo. Depending on the sort of core desired, a solid core made of different natural and synthetic polymers, metallic particles, and composition has been constructed the precursor materials' moieties and the demands based on the application. Additionally, liquid cores of various aqueous media, oils, and organic solvents have been created to distribute either hydrophobic or hydrophilic pharmaceutical cargo. Additionally, natural polymer-made hollow/porous capsules have also been produced. The cargo may be distributed or dissolved in the liquid or solid core acting as a reservoir, It may be implanted inside the shell of the capsules with a liquid, solid or hollow core, depending on biomedical uses. The encapsulated cargo may include pharmaceuticals, growth factors, stem cells, progenitor cells, probiotic bacterial strains, nutritional compounds, hormones, and a variety of other substances, depending on the desired applications[8]

- 3. Emulsions:** Natural polymers can create films with a high tensile strength that can be proof against coalescence among the beads and equilibrate emulsions due to their interfacial absorption. [61]
- 4. Topical Delivery:** Families of sulfated polysaccharides called carrageenans, which are obtained from red marine algae, are frequently used in pharmaceutical industry for the reason that they can create gels that are relatively stiff and thermally reversible.[4]
- 5. Transdermal Drug Delivery:** The use of chitosan gel as a drug reservoir and different natural polymers with varying crosslink capacities as drug allow to leave from the membranes for the administration of propranolol hydrochloride have been conducted.[4]
- 6. Gastro Retentive Dosage Form:** An alternate method for generating an extended-release profile is to use gastro retentive dosage forms. In this method, the pharmaceutical product will stay in the stomach for prolonged period, delivery of the medication is in situ. The drug will then dissolve in the liquid contents and steadily travel into the small intestine.[62]
- 7. Polymers as Floating Drug Delivery systems:** Polymers are frequently used in floating drug delivery systems to direct medication administration to the stomach, a specific area of the gastrointestinal tract. Chitosan, pectin, xanthan gum, guar gum, gellangum, psyllium, starch, husk, alginates, and other natural polymers have all been investigated for their intriguing potential in stomach-specific medication release. [63]
- 8. Fast Dissolving Tablets:** Based on established biocompatibility and safety, the application of natural polymers is advantageous. Because of their affordability and regulatory approval, natural gums are broadly used hydrophilic polymers. To target the delivery of drugs to the specific site in the gastrointestinal tract, namely the stomach, polymers are typically used in floating drug delivery systems. These polymers can also be chemically modified and formed into gels, and they are secure, nontoxic, and safe.[51]

9. Ocular delivery: Chitosan accompanied an excellent film forming capacity make chitosan satisfactory for the development of ocular bandage lenses.[4]

10. Wound – Dressing: Recently, a newly developed porous crystalline polymer, especially nanoscale covalent organic structures and metal organic structures, has attracted special attention for applications. effective wound dressing. These highly ordered porous materials possess many desirable properties, including high specific surface area, high porosity, excellent thermal stability, simple functionalization, good biocompatibility. and promising biodegradability. These include inorganic metal ions and organic ligands. In the biomedical field, this new line of multifunctional porous materials holds promise for drug release, high loading capacity, and multiple small-molecule drug loading..[64]

VII. CONCLUSIONS

Because they are non-toxic, easily accessible, cheap, and naturally extracted to offer dietary supplements, natural polymers are chosen over synthetic polymers. Faster medication dissolution and greater bioavailability are characteristics of natural super disintegrants, which contribute to more effective therapy and better patient compliance. Polymer plays a significant function in medication delivery. Because of the degree of toxicity, pattern of degradation, and nature of polymer incompatibility with pharmaceuticals, polymer selection is essential for the manufacturing of pharmaceutical products. The review's final analysis shows that natural polymers are useful in the formulation of pharmacological dosages. The bioavailability and residence time of the medicine at the specific site are enhanced by natural polymer. Additionally, it helps to promote the use of advanced natural polymers in drug delivery systems.

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