



Biopolymers in Focus: A Comprehensive Review of Natural Macromolecules

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ABSTRACT

The essential components of every drug formulation consist of the active ingredient along with excipients. Excipients are substances that support the manufacture of dosage forms and enhance their physicochemical characteristics. In drug dosage forms, polymers serve as essential excipients. They exert a considerable influence on drug release and need to possess qualities including compatibility, non-toxicity, stability, and cost-effectiveness. Polymers are generally grouped into three categories: natural, semi-synthetic, and synthetic. In oral drug delivery systems, natural polymers are commonly employed as rate-controlling devices, for concealing unpleasant tastes, and for stabilizing, protecting, and encapsulating formulations. Cosmetic formulations that contain synthetic and/or semi-synthetic polymers, whether used alone or combined with natural polymers, feature an appealing design and are sensitive to heat and chemicals.

Key words: Natural Polymers, Biopolymers, Oral drug delivery system, Physicochemical Parameter, Adhesive

INTRODUCTION

Poly, meaning 'many', and Mero's, meaning 'parts', are units of high molecular mass. The word polymer comes from the Greek words.[1] Every molecule consists of a huge number of individual structural units that are bound together in some regular pattern by covalent bonds.[1] Polymers are generally large molecules of high molecular weights called macromolecules, which are formed by combination of large number of small molecules called monomers.[1] The process of combining monomers to form polymers is called polymerization.[1] Polymerization has been described as a chemical reaction wherein two or more substances combine, with or without the evolution of water or heat or any other solvent, to give a molecule of high molecular weight. [1] The product of the polymerization process is called a polymer; the initial substances from which polymers are formed are called monomers.[1]

Natural polymers

These polymers are natural and can be found in nature, for example, in plants or animals. This type includes such substances as proteins, cellulose, starch, resins, etc. [2]

Polymers that are semi-synthetic

This refers to polymers that have been created from naturally occurring polymers in a chemical process that simplifies and modifies the physical properties of natural polymers such as starch and silicones. [2]

Polymers that are synthetic

These polymers come from the polymerization of monomers carried out in a chemical laboratory, such as nylon, polyethylene, polystyrene, synthetic rubber, polyvinyl chloride, Teflon, and numerous others.[2] In pharmaceuticals, polymers are used to produce solid implants, films, beads, microparticles, nanoparticles, inhalable and injectable dosage forms, as well as viscous liquid dosage forms 2-4. [2] This shows that polymers serve many functions across range of drug dosage forms, acting as binders, matrix forming or drug release-modifying agents, film coating forming agents, viscosity increasing agents, stabilizers, disintegrating agents, solubilizing agents, and emulsifying agents. Numerous other purposes exist. Suspending agents, gelling agents, and bio adhesives. [2]

Importance of Herbal Polymers Compared to Biodegradable Synthetic Polymers

Polymers that are produced by living organisms also occur naturally. [2] They do not have any harmful effects on the environment or on humans. In contrast, synthetic polymers, which are synthesized with the help of chemicals, have adverse effects on the atmosphere and on humans. [2]

Polymers Compatibility with Living Tissue and Their Effect

From a chemical standpoint, nearly all of these plant-based materials are carbohydrates in nature, made up of repeating monosaccharide units. [3] As a result, they are non-toxic in comparison with synthetic polymers. Natural polymers are more cost-effective, and their production costs are lower than those of synthetic materials.[3] Safe and free from side effects. Since they occur in natural form, they are safe and have no side effects. [3]

Ease of availability

Natural polymers grow as herbs in numerous countries, are more economical than synthetic polymers. [3] Have no side effects; considering their wide use across many industries, they are manufactured on a large scale, so their availability is more assured than that of synthetic polymers. [3]

Disadvantages of Herbal Polymers

1.Contamination caused by microorganisms. While they are being produced, these materials are exposed to the surrounding environment, which means that contamination by microorganisms is a possible outcome. [3]

2.Differences that occur from one batch to the next.[3] When polymers are manufactured synthetically, the process is carefully controlled and the quantity of every ingredient is precisely measured; in contrast, producing natural polymers means that how much of each ingredient is present depends on the surrounding environment as well as numerous other influencing factors.

[3]

3. The rate at which hydration takes place cannot be controlled.[3] Because natural polymers are obtained from nature, the level of chemical content they contain may differ according to the season, the region, and the kind of plant involved. A large number of additional factors. [3]

Slow process

1.Acquiring natural polymers takes a considerable amount of time, since the growth of natural materials itself proceeds slowly and is influenced by a wide range of different factors. [4]

2.Contamination caused by heavy metals. [4]

Polysaccharide (Cellulose)Composition derived from plants

This substance is an organic polysaccharide that is made up of a linear chain of glucose connected by β (1 $\rightarrow$ 4) linkages, and its chain length can vary from several hundred units to more than ten thousand units, with the chemical formula (C₆H₁₀O₅).[4]

Composition Of Agar:

Agar is from two primary components: agarose and agaropectin.[4] Agarose is a type of linear polymer that is composed of repeating units of agarose monomers.[4] Agar is classified as a disaccharide, which is formed from d-galactose and 3,6-anhydroL-glucopyranose. [4] In contrast, agaropectin is a heterogeneous mixture made up of smaller acidic polysaccharides, and it has only a weak ability to form gels.[4]

Application Of Agar:

1.It serves a variety of purposes, functioning as a suspending agent, an emulsifying agent, and a gelling agent in suppositories; it is also employed as a surgical lubricant, as a tablet disintegrant, as a medium for bacterial culture, and as a laxative.[5]

2.It is utilized in the making of jellies and confectionary items, as well as in tissue culture studies and in the field of microbiology.[5]

Sources of Starches

In green plants, starch serves as the principal carbohydrate used for storage, and it is found mainly within seeds as well as in organs located underground.[5] Starch is present in the form of granules which are also referred to as starch grains.[5] A number of starches have received approval for use in pharmaceutical applications, among them maize (Zea mays) and rice (Oryza sativa) and wheat (Triticum aestivum), and potato (Solanum tuberosum).[5]

Composition

Starch, also referred to as amylum, comes from class of carbohydrates and is made up of many glucose units that are connected to one another through glycosidic bonds.[5] It consists of two distinct polysaccharides: amylose, which is an unbranched, helical polymer formed from Dglucose monomers linked by α -1,4 bonds and amylopectin, which is a highly branched polymer built from D-glucose monomers connected by both α -1,4 and α -1,6 linkages.[5]

Source of Inulin

This polysaccharide is obtained from bulbs of Dahlia, Inula helenium (Compositae) and roots of

Dandelion, Taraxacum officinale (Compositae). Burdock root, chicory roots.[7]

Source of Guar Gum

Guar gum goes by several other names as well, including guaran, cluster bean, Calcutta lucerne, Gum Cyamopsis, Cyamopsis gum, Guarini, Glucoside, and Guyarem²¹.^[7] Guar gum is produced by grinding the endosperm found within the seeds of the plant *Cyamopsis tetragonolobus* Linn. (Leguminosae).^[5]

Composition

Guar gum is a natural polysaccharide develop from galactose and mannose.^[7] It is a galactomannan: a straight-chain polysaccharide built from (1→4)-equatorially linked β mannose units, with a few single α -D-galactose side chains.²¹ Its backbone consists of β -1,4 linked D-Manno pyranoses, and on average every other mannose carries an α -galactose attached at 1→6.²²^[7]

Polysaccharides of Animal Origin: Chitin Source

Chitin, a polysaccharide derivative bearing amino and acetyl groups, is the main organic constituent of invertebrate skeletons. It occurs chiefly in molluscs, annelids, and arthropods.^[7] It also forms part of the mycelia and spores of many fungi.^[7]

Source of Xanthan Gum

Xanthan gum is a high-molecular-weight extracellular polysaccharide made by fermenting the gram-negative bacterium *Xanthomonas campestris*.^[7]

Composition

Naturally occurring cellulose derivatives consist of a cellulose backbone (β -D-glucose units) plus a trisaccharide side chain of β -D-mannose–D-guluronic acid– β -mannose, joined to the main chain at alternating glucose residues. ^[7]

Applications

- 1.Xanthan gum serves as a suspending and stabilizing agent in oral and topical formulations, cosmetics, and food. ^[7]
- 2.It has also been used to make sustained release matrix tablets.²⁸. ^[7]

Source of Psyllium

Psyllium mucilage comes from the seed coat of *Plantago ovata*, extracted by milling the seeds' outer layer.^[7] ³⁴ Proteins of Animal outer layer.³⁴ Proteins of Animal Origin Collagen Source Collagen is the first protein making up connective tissues in animals.^[7] ³⁶ Pig skin, bovine hide, and pork and cattle bones are the richest sources of collagen.³⁷.^[7]

Composition

Collagen comes in twenty-seven varieties, each built from distinct polypeptides composed mainly of Collagen type I, a fibrous protein formed by three interwoven amino acid chains.^[8] These chains feature recurring stretches of glycine and proline and hydroxyproline and lysine.^{36,37} A collagen chain's flexibility depends entirely on how much glycine it contains.^[8]

Applications

- 1.Collagen films serve as drug delivery systems in ophthalmology, enabling sustained release of incorporated drugs.^[8]
- 2.They also find use in tissue engineering, including skin replacement, bone substitutes, and artificial blood vessels and valves.^[8]

Gelatine

Gelatin⁴⁰ is a high molecular weight polypeptide produced through denaturation and/or physicochemical breakdown of collagen.^[8] Gelatine, a water-soluble protein, consists of 19 amino acids⁴¹. ^[8] Other animal-derived proteins include elastin, albumin, and fibrin.^[8]

Applications

These generally include the use as emulsifiers, foaming agents, colloid stabilizers, biodegradable film-forming materials, and microencapsulating agents.^[8]

2. Overview of Polymers Used in Cosmetics

Polymers play an essential role in delivering numerous features and benefits that cosmetic products offer to consumers, but how well they perform is heavily influenced by the remaining components within the formulation, including the kind of solvent, surfactant, and electrolytes used, as well as the pH level, the order in which the ingredients are combined, and the manufacturing parameters such as temperature and the speed at which the mixture is stirred. ^[6]To prevent problems that arise when a formula is unstable, including haziness and the separation of phases, it is essential to confirm that the polymer you have chosen works well with each and every raw material contained in the product. Within shampoos, polymers are behind a great number of the attributes that consumers look for in a versatile product, since beyond simply clearing away surplus oil from the hair, a shampoo is also expected to leave hair feeling reasonably soft, looking shiny, and better able to withstand damage, while also reducing the occurrence of split ends. Even a tiny

quantity of a cationic polymer, for instance polyquaternium-10 or polyquaternium-44, can assist a shampoo in providing these advantages, as such polymers form a coating over the hair and additionally influence the way the product flows and the way the lather looks .[8]It is worth pointing out that cationic surfactants, which are similarly capable of depositing onto the hair and creating films, are not able to be used in shampoos, since they do not mix well with the anionic surfactants found in the majority of shampoos, which are precisely the ingredients responsible for removing excess oil and producing that clean sensation. Once anionic and cationic surfactants are brought together, the electrical charges on the molecules cancel each other out, resulting in the formation of a compound that is unable to dissolve in water.[8] Non-ionic polymers, including guar gum and xanthan gum, are used primarily for the purpose of thickening the product and are not directly linked to any other functions. In conditioning and moisturizing products, such as conditioners and hair treatment masks, where the hair needs more intensive hydration, polymers work by boosting the softness that the cationic surfactant provides, and they additionally contribute to better combability and increased shine by means of a film-forming mechanism that is extremely similar to the **In-vitro Drug Diffusion Study Based upon these results, we have determined that the prepared topical gel NMG3 releases 83.09 % of the drug in a 24-hour period.**[8]

Immediate release dosage forms Tablets [9]

In an effort to address the shortcomings associated with traditional oral dosage forms, researchers turned to the development of modified release dosage forms as a means of overcoming these constraints.[9] For many years, polymers have served as excipients within conventional immediate release oral dosage forms and being employed or to facilitate the manufacturing process or to safeguard the drug against degradation while it is in storage.[9]

Additionally, polymers like polyvinyl-pyrrolidone and hydroxypropyl methylcellulose (HPMC) serve as binders, which play a role in forming granules that enhance both the flow properties and the compatibility of tablet blends before they undergo compression.[9] In certain cases, dosage forms require coating with a "nonfunctional" polymeric film in order to shield a drug from degradation, conceal the taste of a drug or excipient that is unpleasant, or enhance the visual appeal of a dosage form, all without altering the rate at which the drug is released [9] For materials that do not compress well, capsules offer an alternative to tablets, and they are also used to hide the bitter taste of certain drugs or, on occasion, for enhance bioavailability.[9] A large number of the polymeric excipients that are employed to "bulk out" capsule fills are actually the very same materials that are utilized in immediate release tablets.[9]As a shell material for both hard (two piece) and soft (one-piece) capsules, gelatine has been used almost exclusively.[9] More recently, HPMC has been developed and gained acceptance as an alternative material for the production of hard (two-piece) capsules.[9]

Modified-release dosage forms

Today, it is widely acknowledged that when many therapeutic agents are administered through immediate release dosage forms, the result is frequently therapy that falls short of optimal levels and/or the emergence of systemic side effects.[9]

Dosage forms designed for immediate release — Tablets

Over the course of many years the polymers have served as excipients within conventional oral dosage forms of the immediate-release variety, being employed either to facilitate the production process or to shield the drug against deterioration while it is being stored.[9] In tablet formulations containing highly potent drugs given at low doses and microcrystalline cellulose is frequently employed as a replacement for carbohydrates when serving as a filler.[10] Within tablet formulation, starch and cellulose function as disintegrants; upon coming into contact with water they swell, which causes the tablet to "burst", thereby enlarging the surface area of the drug that is exposed and improving the dissolution profile of the formulation.[10] The use of polymers such as a film coating of polyvinylpyrrolidone, applied to protect a drug, along with Hydroxypropyl methylcellulose (HPMC), which additionally serves as a binder that promotes granulation, enhances both the flow and the compaction properties of tablet formulations before the tableting step takes place.[10]

KINDS OF POLYMERS

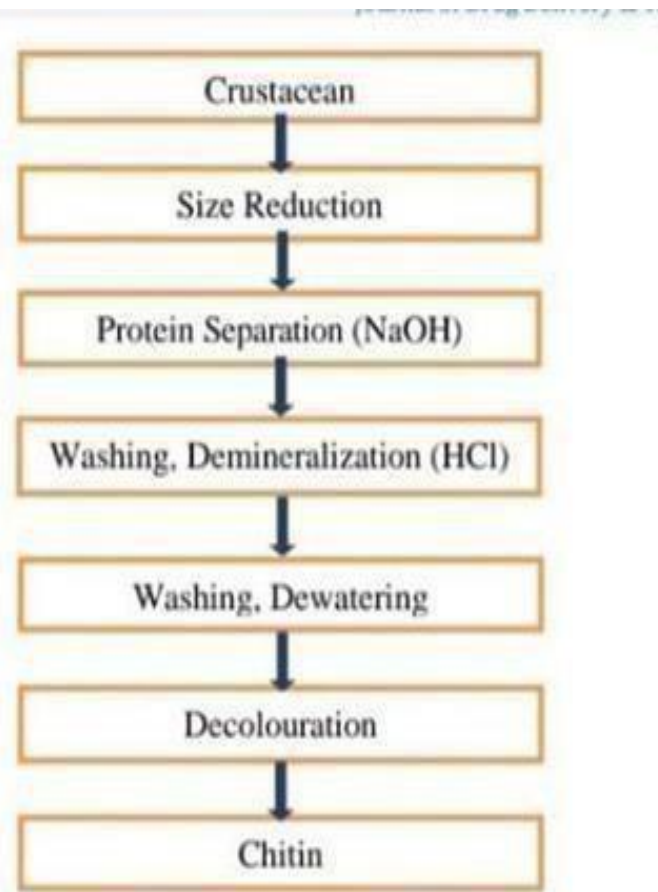
Natural polymers: - They are primarily derived from plant and animal sources such as proteins, cellulose, silk, wool, starch, resins, chitin, etc., Semi-synthetic polymers: - These are produced from natural polymers through straightforward chemical modifications that change the physical properties of natural polymers like starch and silicones.[10] Synthetic polymers: - These are fibres produced by polymerizing simple chemical molecules, for example Nylon, epoxy, polystyrene, polyethylene, synthetic rubber, PVC, Teflon, etc.[10]

IMPORTANCE OF NATURAL POLYMERS (ANIMAL SOURCES) OVER SYNTHETIC POLYMER:

The benefits that naturally occurring polymers hold over their synthetic counterparts are clear and well established: they are biodegradable, they are biocompatible, and they are non-toxic, largely because naturally occurring polymers are produced within every living organism.[10] They do not exert any toxic effects on the human body.[10] Conversely, synthetic polymers, which are for the most part manufactured with the aid of a variety of chemicals, do have a toxic effect on humans. [10] 15 Furthermore, all of these plant polymers are predominantly carbohydrates, meaning that they are composed of monosaccharides; this is precisely why they are non-toxic, in contrast to synthetic polymers.

BIOPOLYMERS FROM ANIMAL ORIGIN CHITIN

Origin: Chitin is a derivative of polysaccharides that includes both amino and acetyl groups, and it stands as the most plentiful organic polymer present in invertebrate organisms.[10] This naturally occurring biopolymer, known as chitin, can be located in the exoskeletons of insects, on the outer layer of algae, within the shells of crustaceans, and in the cell walls of certain fungi and bacteria. [10] Its structure is made up of N-acetyl-D-glucosamine units, which places it within the category of mucopolysaccharides.



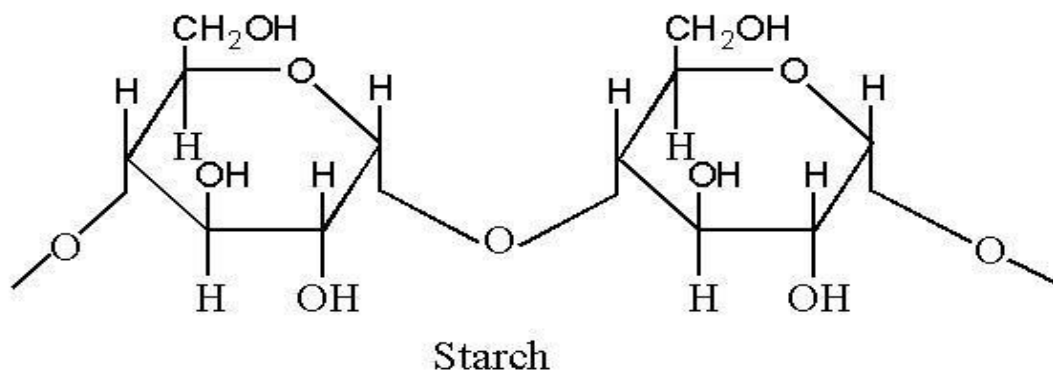
Categories of Natural Polymers

Polysaccharides are defined as polymers composed of carbohydrates, in which the monomeric units consist of saccharides.[10] These substances may be acquired either through natural means, originating from plants, animals, or microorganisms, or they may be produced through synthesis. [10] Because of the reasons listed below, they have found extensive application in drug delivery systems.[10] They are biodegradable; as a result, once the drug has been released, the polymers degrade into smaller components that the body can readily absorb or excrete. [10] Furthermore, they possess biocompatibility, which means that they do not cause toxicity in humans. Moreover, they permit binding to the target tissue, given that they contain free functional groups capable of forming noncovalent bonds with epithelial cells.[11] These characteristic guarantees extended retention at the site and, consequently, enhances drug absorption.[11] In addition, they possess particular recognition sites for receptors.[11]

This property permits non-specific protein binding, thereby enabling the polymer to be coated with a range of proteins, including those that are not specific to the targeting ligands attached to the polymers.[10] Another property it exhibits is low surface energy.[11] Its backbone contains a large number of hydroxyl groups, which enables it to carry many specific ligands.[12] Starch and Chitosan are two polymers that have been the subject of extensive research in the context of nano drug delivery.[10] For this reason, the present paper will focus its discussion on these two polymers.[12]

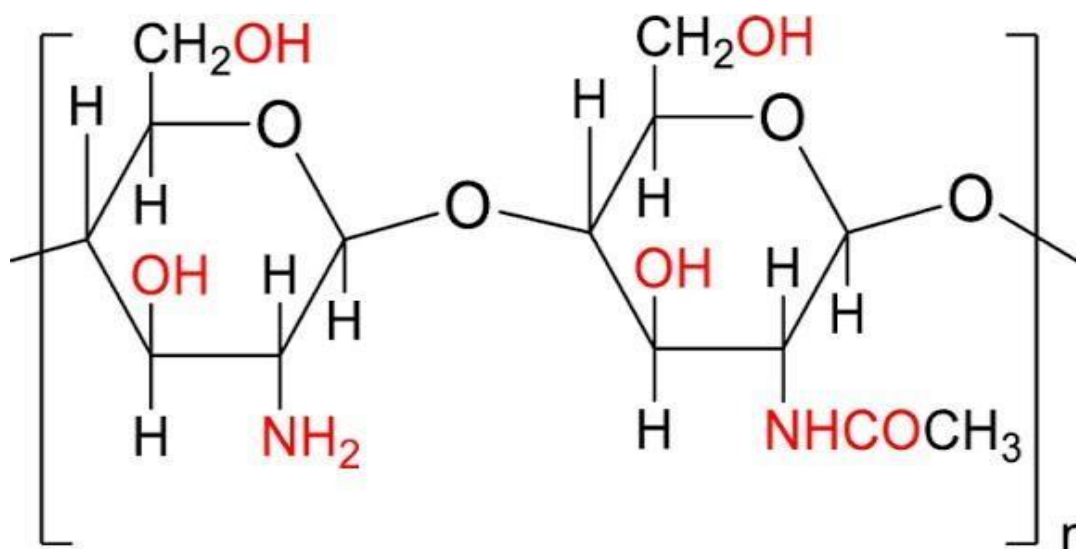
Starch

This is a method of delivery that works to maintain the integrity and natural condition of the skin. [13] Emulsification diffusion was chosen as the technique for producing nano-particles, owing to its reproducibility, its capacity to deliver higher yields, its ease of scaling up, and its ability to control both particle size and polydispersity.[13] Using two different polymeric materials, namely modified maize starch and maize starch, two separate varieties of nano-particles were successfully prepared.[13] By means of the LDH and MTT assays, the nanocarriers based on modified starch were shown to be non-toxic and to yield particles with a narrow size distribution, while the particles derived from native starch proved impossible to detect.[13] The model drugs selected for evaluation of their skin penetration were fusaric acid, caffeine, and testosterone, and these were tested on skin samples obtained from female Caucasian patients who had previously undergone abdominal plastic surgery.[13]



Chitosan's

This particular linear polysaccharide is obtained through a process in which acetyl groups are stripped away from chitin, and its structure consists of glucosamine along with N-acetyl glucosamine units that are joined together by means of β -1,4-glycosidic bonds. When considering natural polymers as a whole, this material stands out as one of the most extensively investigated options for the purpose of delivering drugs at the nanoscale level.[14] The quantity of chitosan that can be obtained from chitin is influenced by both the concentration used in the reaction and the temperature at which it is carried out; as an illustration, this can be achieved at 600C- 800 C with 50%w/w alkali .[14] In the review they conducted on chitosan, Park et al.[14] highlight the numerous different approaches through which chitosan serves as a vehicle for delivering drugs that have a low molecular weight.[15] The reason chitosan is selected for drug delivery applications is that its physiochemical and biological characteristics permit chemical modifications to be made and enable it to remain in the body for a longer period of time.[16] Chitosan has found use as a composite membrane in combination with collagen.[16], and it has also been applied as a crosslinked polymer for the transdermal delivery of Propranolol [51]. With the aim of investigating the controlled release behaviour of lamivudine, which is an anti-retroviral drug, Dev et al. [10] made use of chitosan nano-particles that were produced from a chitosan co-polymer.[16]



Nanomedicine & Nanotechnology Classes of Natural Polymers

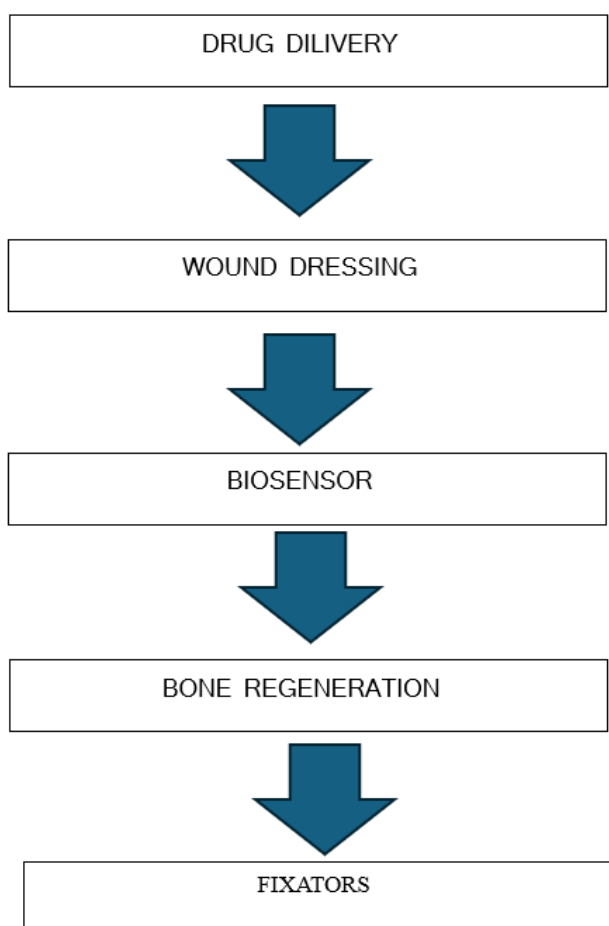
Polysaccharides are polymeric carbohydrates made up of monosaccharide monomers.[17] As polymers, they consist of lengthy chains of monosaccharides, oligosaccharides, or other carbohydrates joined by glycosidic bonds.[17] They occur abundantly in nature, coming from plants, animals, and microorganisms.[17] These compounds have seen wide use in drug delivery thanks to their many advantages .[17] They biodegrade readily, so once the drug is delivered, the carrier breaks down into constituents that are easily absorbed and excreted. Being bio-compatible, they cause no toxic effects in the body.[17] Carriers made from polysaccharides can achieve targeting because functional groups on them can form non-covalent bonds with epithelial cells. [17] This enhances the drug's residence time and, in turn, the amount delivered.[17] Recognition of specific receptors may also be achieved.[17] They also permit non-specific protein adsorption, offering a hydrophilic coating with low surface tension and many hydroxyl groups along

the chain. [18] The flexibility of polysaccharides also allows various ligands to be incorporated. [18] Starch and Chitosan are among the natural polymers studied extensively for nano-drug delivery, and are reviewed below. [18] Starch is a polysaccharide found abundantly in nature.[18] It occurs mainly in plants, where it serves as a storage polysaccharide.[18] It consists of alpha D-(1,4) glucopyranose chains and yields glucose monosaccharide upon hydrolysis (Helle et al., 1990). [19] In pharmaceuticals, starch serves various purposes: as a copolymer and excipient in controlled drug delivery (Wang et al., 2015; Chauhan et al., 2017) and as a drug carrier in tissue engineering scaffolds (Hollister et al., 2006). [19] It also finds use as a hydrogel (Li et al., 2017) and a solubility enhancer (Li et al., 2015). [17]

ROLE OF POLYMER IN PHARMACEUTICAL DRUG

For a great many years now, polymers have been incorporated into ordinary immediate-release tablets that are swallowed, serving either to simplify the production process or to safeguard the drug throughout its period of storage. [19] Whenever a tablet is formulated with a highly potent drug given in only a small dose, manufacturers tend to select Microcrystalline Cellulose as the filler rather than opting for sugars.[19] Within tablets, Starch and Cellulose serve as disintegrants; as soon as they come into contact water, they swell up and cause the tablet to "burst", which exposes a greater portion of the drug's surface area and thereby allows the formulation to dissolve more effectively.[19] A number of other polymers, including polyvinyl pyrrolidone and hydroxypropyl methylcellulose (HPMC), function as binders, since they assist in forming granules that enable tablets to flow and be compressed together more readily .[20]

ROLE OF POLYMER



CONCLUSION

Biopolymers derived from animal sources have attracted considerable attention within the pharmaceutical industry, largely because they are being applied in innovative ways to deliver drugs and to support the maintenance of good physical health in people. [20] Biopolymers obtained from animals are strongly favoured over those produced synthetically, given that they are non-toxic, simple to source at a low cost, effective even in very small quantities, and naturally extracted from nature so that they can be utilized as a nutritional supplement.[20] Biopolymers sourced from animals accelerate the release of drugs from tablets and reduce the amount of time required for those tablets to dissolve and disintegrate, and on top of that they serve as binders, super

disintegrants, and diluents. During the manufacture of drugs, choosing the appropriate polymer is extremely important, since polymers play a central role in determining how drugs are delivered within the body.[20] Polymers must be selected with great care, taking into account how compatible they are with the drug, the manner in which they break down, and the level of toxicity they carry.[20] Therefore, it is concluded that polymers originating from natural sources represent a powerful alternative to synthetic ones, as they address the numerous harmful effects that tend to accompany synthetic polymers.[20] At present, bio-based polymers are steadily replacing conventional polymers, and their applications span everything from everyday consumer goods to sophisticated instruments, a shift that is being driven forward by advances in biotechnology as well as by a public that is increasingly aware of these issues.[20]

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