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Review Article

Natural Polymers and Applications in Cancer Therapeutics

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ABSTRACT

Polymers are widely used in almost every material. To date, the importance of polymer is highly focused because of their usage in different domains of sciences and technologies. Any pharmaceutical plan contains two components, one is the dynamic, active ingredient, and other is an excipient. An excipient helps in the assembling of dose shape, and it additionally enhances the physicochemical parameters of the measurement frame. A few polymers of both natural and manufactured source have been utilized for an assortment of biomedical applications including pharmaceutical arrangements, drug targeting, imaging, drug delivery, prosthetics, and tissue building frameworks. Due to their reproducible attributes as far as their molecular weight, degradation, and mechanical properties, and engineered polymers are appealing for an assortment of the previously mentioned applications. Be that as it may, manufactured polymers from the natural point of view, engineered polymers frequently lack much-wanted bioactivity and biocompatibility, which may convert into antagonistic symptoms. Natural polymers then again are plentiful and look like the segments display in organic extracellular networks. Therefore, natural polymers are promptly acknowledged by the body and have high bioactivity and biocompatibility. This review shows the current flow status of research and clinical uses of common natural polymers as drug delivery systems for the various organizations.

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INTRODUCTION

Natural polymers are a class of polymers, sourced from nature (plants and animals). Most of the natural polymers are condensation polymers which are derived as a result of the union of monomeric units to form small molecules as by-products. Others are those which are made up to the polymer by the direct combination of monomeric units without any by-product. Based on their sources polymers which exist in nature can be grouped into six main classifications: Proteins, polysaccharides, polynucleotides, polyisoprenes, polyesters, and lignin (Atkins, 1987).

Natural polymers gain interest toward pharmaceutical industries, as they are economical, readily available, and non-toxic in nature. These natural polymers can undergo modifications chemically and are potentially bio gradable with few exceptions. Recent research on new and improved biodegradable polymers focuses on biomedical applications to solve problems with high efficacy and least pains. These natural polymers are used in the manufacture of beads, films, micro and nanoparticles, inhalable and injectable systems, implants, etc.[1-3] In these aspects, the perform roles such as matrix formers, binders, efficient drug delivery tools, thickness stabilizers, solubilizers, emulsifiers, gelling agents, and adhesives.[4]

HISTORY AND DEVELOPMENT OF POLYMERS

Many natural forms of polymers such as DNA, RNA, proteins, and polysaccharides, existed in days of life origin, played crucial roles in plant and animal life. Right from earlier times, these naturally occurring polymers were exploited as materials for providing clothing, decoration, shelter, tools, weapons, and other requirements. In the beginning of the 18th century, an English inventor, Thomas Hancock studied the effects of sulfur on rubber (vulcanization). Bakelite was the first synthetic polymer followed by synthetic fiber, rayon. The new field of polymer sciences started a century back with the pioneering contributions of Herman Staudinger with his new definition that polymers are high molecular mass compounds bonded with long covalent bonds.

CLASSIFICATION OF POLYMERS

On the basis of their occurrence in nature, polymers have been classified into three types.

A. Natural polymer: The polymers, which occur in nature are called natural polymer also known as biopolymers. Examples of such polymers are natural rubber, natural

silk, cellulose, starch, and proteins.

B. Semi-synthetic polymer: They are the chemically modified natural polymers such as hydrogenated, natural rubber, cellulosic, cellulose nitrate, and methyl cellulose.

C. Synthetic polymer: The polymer which has been synthesized in the laboratory is known as a synthetic polymer. These are also known as manmade polymers. Examples of such polymers are polyvinyl alcohol, polyethylene, polystyrene, and polysulfone.

Natural polymers, on the other hand, are further grouped into two broad categories as:

- Plant origin - cellulose, hemicellulose, glucomannan, agar, starch, pectin, inulin, rosin, guar gum, locust bean gum, gum acacia, karaya gum, gum tragacanth, and aloe vera gel.
- Animal origin - chitin, alginates, carrageenans, psyllium, and xanthan gum.

HEMICELLULOSE

A hemicellulose is a heteropolymer (lattice polysaccharides), for example, arabinoxylans, introduce alongside cellulose in all plant cell dividers. While cellulose is crystalline, solid, and impervious to hydrolysis, hemicellulose has an irregular, shapeless structure with little quality. Not like cellulose, hemicellulose (likewise a polysaccharide) consists of shorter chains - 500-3,000 sugar units. Furthermore, hemicellulose is an extended polymer, while cellulose is unbranched. Hemicellulose polysaccharides comprise xyloglucans, xylans, and mannans that can be extricated from the plant cell wall with a strong alkali. They have backbones comprised β-1,4-connected D-glycans. Xyloglucan has a comparable backbone as that of cellulose, yet contains xylose stretches on 3 of each 4 glucose monomers. The β-1, 4-connected D-Xylan backbone of arabinoxylan contains arabinose branches (Figure 1).

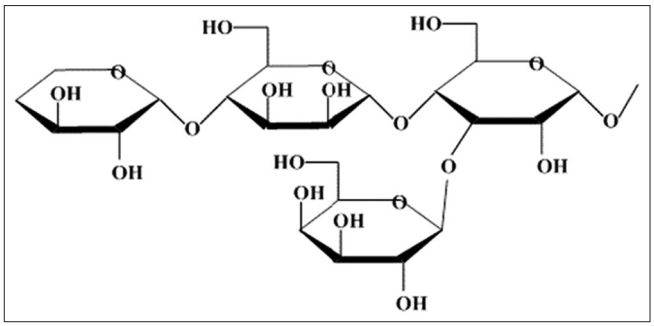

Figure 1: Structure of hemicellulose

Starch

Starch is the main carbohydrate reserve in green plants. It consists of countless units combined by glycosidic bonds. It comprises two polymers, in particular, amylose (a non-fanning helical polymer comprising α-1, 4 connected D-glucose monomers) and amylopectin (an exceptionally extended polymer comprising both α-1,4 and α-1,6 connected D-glucose monomers). The utilization of starch in pharmaceutics is broad. It is utilized as copolymer and excipient in controlled medication conveyance,[5-7] as medication bearers in tissue designing frameworks, as hydrogels and as dissolvability enhancers[8] Santander-Ortega *et al*. explored the capability of starch nanoparticles as a transdermal medication conveyance framework (TDDS). The test looked in conveying drug through these frameworks is that the skin goes about as an effective barrier for the passage of drugs and should thusly be defeated for successful medication conveyance.

Nanoparticles were appeared to encourage drug delivery without interference to the skin's integrity. The technique used to set up the nanoparticles was emulsification diffusion due to its reproducibility, higher yields, simplicity of scale-up, and control over size of particles and level of polydispersity. Maize starch altered and un-adjusted (by the addition of propyl groups) were utilized as a polymeric material to define 2 distinct kinds of nanoparticles. The modified starch nanoparticles were appeared to be non-toxic using lactose dehydrogenase and MTT assay brought about particles of uniform size conveyance while the nanoparticles planned from the local starch was not detectable. Flufenamic acid, caffeine, and testosterone were utilized as model medications, and their conveyance as model drugs and their delivery across the skin was analyzed using excised skin from female Caucasian patients who had experienced stomach plastic surgery. Permeation data obtained for caffeine and testosterone were similar for nanoencapsulated and free drugs while the conveyance of flufenamic acid utilizing the nanoparticles was upgraded by around 10 times.

Starch nanoparticles have been utilized to convey insulin by means of non-invasive courses; Makham examined the utilization of chitosan cross-connected starch polymers as transporters for oral insulin conveyance, controlling the bio-adhesive and not all that cementing properties of chitosan and carboxymethyl starch to plan hydrogels stacked with insulin. The creators anyway noticed that Insulin conveyed by this technique anyway faces the test of being broken down by proteases. The nasal course can likewise be considered as a contrasting option to the subcutaneous course of administration since it is extremely vascularized and is of extraordinary advantage in medicine delivery as medications given through this course are not subject to first-pass digestion. Anyway, for successful conveyance through this route, it is essential that obstruction to nasal drug delivery which includes the lipophilic epithelium and mucociliary choice must be prevailing over. Jani *et al*. report a size ward insulin discharge in rats from starch nanoparticles. Potato starch was utilized to plan two unique sorts of nanoparticles by cross-connecting with epichlorohydrin and phosphoryl chloride ($POCl_3$) utilizing both the gel and emulsion strategies.

These techniques anyway prompted the creation of polydispersed nanoparticles. There were measurably noteworthy differences in mean sizes with the exception of an emulsion prepared epichlorohydrin cross-linked particles which were littler and of uniform appropriation. *In vitro* studies demonstrated that medication discharge took after first-order kinetics and diffusion controlled alongside burst impact, because of the nearness of left-over insulin on the surface of the nanoparticles after entrapment. Emulsion cross-connected particles discharged their medication speedier than gel cross-connected particles with 85–90% and 81% discharge in 12 h, respectively. These distinctions were ascribed to the dispersion

way length of the medication inside the particles. The littler the molecule measure, the less distance the medication will go to be discharged. Tests carried out on the diabetes-induced rats demonstrated a 50–65% decrease in blood glucose level by nanoparticles contrasted with plain insulin formulation which filled in as control and this went on for around 6 h. Penetration enhancers adjusted the hypoglycemic impact and bioavailability of nanoparticles, plasma insulin levels of little-sized nanoparticles were observed to be fundamentally higher. Conclusions acquired from the investigation anyway suggest that further work would be required to deliver a more productive carrier framework.

Simi and Abraham take note that the occurrence of hydroxyl bunches on starch improves its hydrophilicity and gives on resistance toward low dampness. This property represents a noteworthy requirement in the delivery of drug because of which it's usually important to change the polymer before it is made into nanoparticles as observed above. In their examination, starch extricated from cassava tuber was altered by copolymerization utilizing long chain unsaturated fat before the subsequent polymer was made into nanoparticles. The nanoparticles were set up by dialysis, and in this manner, cross-linked utilizing sodium tripolyphosphate. Oleic acid and stearic acid were both utilized as unsaturated fats while indomethacin was utilized as model medication. Discoveries demonstrated that medication discharge from the two kinds of nanoparticles was successfully controlled. It is anyway uncertain whether there was a critical distinction between drug discharges in the two sorts of nanoparticles. No endeavors were additionally made to plan the un-altered starch granules into nanoparticles; however, this may have been because of results got from differential scanning calorimetry which demonstrated that local starch was less process able than grafted starch. Furthermore, charged iron-oxide nanoparticles covered with starch were utilized by Cole *et al*. as a method for focusing on brain tumors.

Chitosan

This polymer is gotten from the fractional N-deacetylation of chitin found in the shells of Crustacean. It is made out of glucosamine, and N-acetyl glucosamine connected by β 1-4 glucosidic linkages and is standout amongst the most generally contemplated characteristic polymers for nanomedicate delivery. The deacetylation of chitin is both concentration and temperature dependable with an ideal yield accomplished at temperatures between 600C and 800C utilizing 50%w/w alkali.[9]

Park *et al*. 2010,[10] in a survey on chitosan portray its various applications in delivering low atomic weight drugs and outlines the explanation behind its decision being in its physiochemical and biological properties, empowering synthetic alteration and improved residence time. It has been utilized as both a composite film with collagen[11] and a cross-connected polymer for the transdermal conveyance of propranol (Figure 2).[12]

Chitosan, a linear polymer made out of conversely sorted out, deacetylated β-(1-4) - linked D glucosamine units and of acetylated N-acetyl-D-glucosamine units, is broadly utilized as a part of DDS. The sole polysaccharide polycation utilized as a polymer, chitosan ties to negatively charged moieties.

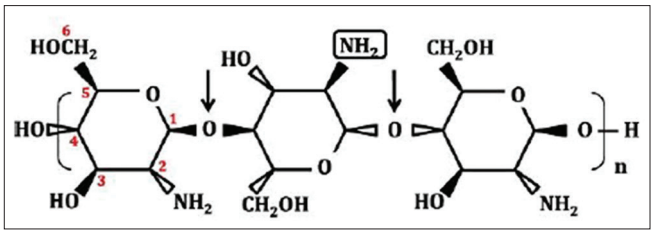

Figure 2: Structure of chitosan

As of late, Nogueira *et al*. delivered chitosan nanoparticles stacked with the anticancer operator methotrexate (MTX). This ineffectively soluble anticancer operator is to a great degree intense, however, masquerade genuine dangers of unfavorable impacts to ordinary cells, including kidney upset, neurotoxicity, and mucositis.

To conquer chitosan's harmfulness and poor solvency, Nogueira *et al*. developed chitosan-based nanoparticles embodying MTX (MTX– CS– NPs). Next, to make the chitosan-based nanoparticles pH-responsive, these scientists included the amino corrosive based amphiphile surfactant, 77KS. The consolidation of this pH-delicate moiety allowed a pH-dependent, controlled arrival of MTX. *In vitro,* explores were led in MCF 7 breast tumor cells, with promising outcomes. Future *in vivo* studies will give more data about the clinical capability of chitosan-based nanoparticles. Another promising methodology utilizing united chitosan polymeric micelles conveying two medications was produced by Nam *et al*. The chitosan subordinate O-carboxymethyl chitosan (OCMCh), with upgraded solvency, was conjugated first with α-tocopherol and framing α-tocopherol O-carboxymethyl (TOC). This chitosan polymer was then ligated with doxorubicin and a hostile to human epidermal development factor receptor 2 [HER2] target peptide, creating the last build, HPTOC– DOX polymeric micelles.

The upsides of chitosan incorporate that it is biodegradable and biocompatible, and ready to proficiently transport polar medications over an epithelial surface. Likewise, chitosan oligomer subsidiaries of 3–6 kDa are considered generally non-toxic. Chitosan's real inconvenience is its constrained dissolvability at physiological molecules and pancreatic tumors. These microspheres (MS) can fulfill by far most of medication transporter prerequisites. Their essential use in growth inquire about is to enhance the solvency of insoluble against tumor drugs. The moderate discharge frameworks related with MS have made dextran MS the vehicle of decision for the conveyance of mitomycin C (MMC), a promising, strong anticancer specialist that capacities through bioreductive initiation. Numerous intense and also endless toxicities are related with MMC, in any case, seriously restricting its clinical application. To defeat these hindrances and accomplish focused on tranquilize conveyance to the hypoxic areas of strong tumors, Cheung and partners built up a focused on approach made out of oxidized dextran MS stacked with MMC. In an *in vitro* model of bosom disease cell-line, EMT6, these scientists connected a doxorubicin-MS treatment, trailed by an MMC-MS treatment. This consecutive use of two antitumor medications brought about a synergistically powerful mix of malignancy cell murdering.

Nanoparticles created with chitosan as copolymer were utilized by Dev *et al*., 2010, to research the controlled release of antiretroviral medicate, lamivudine. The nanoparticles were set up by emulsion and dissolvable vanishing system and described utilizing dynamic light scattering. The utilization of this technique brought about monodispersed particles with a size scope of 300–350 nm. Two plans with contrasts in rate medicate weight (3% and 6%) were made, of which tranquilize discharge rate was higher from the nanoparticles with higher medication stacking, however, both could control drug release genuinely well. Medication discharge energy demonstrated that the instrument of medication discharge was by diffusion. Conclusions came to proposed that the nanoparticles could be connected for gastrointestinal medication conveyance since sedate discharge was moderately slower at unbiased pH compared to acidic pH and furthermore slower in the acidic pH contrast with the basic pH.

Chitosan blend was additionally utilized by Menon *et al*., 2011,[13] for therapeutic drug conveyance. Nano-buildings of chitosan and polyoxometalates (POM) were tried as hostile to malignancy arrangement. Since POM's, however, harmful have indicated guarantee in being utilized as antiviral and against tumor agents, the part of chitosan was to limit the poisonous quality related with POM, by changing its surface properties. Monodispersed particles with measure 200 nm were created utilizing ionotropic gelation procedure, and the utilization of test sonication was appeared to control molecule size and dispersion contrasted with ultrasonication. *In vitro* considers demonstrated that the nanocomplex could support tranquilize discharge with upgraded hostile to tumor movement at substantially lesser measurements than the POM alone.

Chitosan combination was also used by Menon *et al*., 2011,[13] for therapeutic drug delivery. Nano-complexes of chitosan and POM were tested as anticancer preparation. Since POM's though toxic have shown promise in being used as antiviral and antitumor agent, the role of chitosan was to minimize the toxicity associated with POM, by modifying its surface properties. Monodispersed particles with size 200 nm were produced using the ionotropic gelation technique, and the use of probe sonication was shown to control particle size and distribution compared to ultrasonication. *In vitro* studies showed that the nano-complex was able to sustain drug release with enhanced antitumor activity at much lesser doses than the POM alone.

So also similarly as with starch nanoparticles, Luo *et al*., 2011,[14] utilized chitosan oligosaccharides (COS) to coat lipid-based bearers with a specific end goal to upgrade visual medication conveyance. This material is acquired from the deterioration of chitosan; however, it is more soluble in water than chitin and chitosan. Medication brought into the eye has negligible habitation times as they are immediately washed away and must be re-controlled consistently. Be that as it may, in this investigation, COS enhanced permeation and grip of the cornea. There was a 7.7-fold and 2.8-fold maintenance of the model medication, flurbiprofen by the COS covered nano lipid transporters contrasted with the phosphate cushion arrangement and uncoated nanolipid bearers which were credited to the mucoadhesive properties of COS. The utilization of COS was additionally observed to be non-chafing to the eye, a property which is of most extreme significance in the choice of a reasonable eye formulation.

Pullulan

Pullulan, a characteristic polysaccharide made out of maltotriose units organized as α-1-4; α-1-6-glucan and a liver particular biopolymer is biodegradable, nontoxic, non-mutagenic, and noncarcinogenic. Its low immunogenicity and tasteful dissolvability in fluid and a few natural solvents have together prompted a scope of uses in growth sedate conveyance. Scomparin *et al*. led an *in vitro* think about with two pullulan bioconjugates. The point of their investigation was to outline an anticancer polymer restorative for focused tumor cell treatment. The gathering integrated the two pullulan subsidiaries by conjugating pullalan with (1) doxorubicin and (2) doxorubicin and folic acid, with the last utilized as a moiety for focusing on folic receptors overexpressed in some tumor cell lines (Figure 3).

To accomplish legitimate functionality, the pullulan was initiated by such further compound changes as periodate oxidation and reductive conjugation with cysteamide. The two subsidiaries, the folic acid-free subordinate and the folic acid doxorubicin-coupled subsidiary, contained a comparative doxorubicin fixation (w/w), i.e., ~6%, with 4.3% (w/w) folic acid in (FA-PEG)- Pull-(Cyst-Dox). This current gathering's *in vitro* ponder comes about indicated diminished harmfulness in the folic corrosive non-communicating receptor cell line, MCF7, yet expanded danger in the KB cell line, which has over-communicated folic corrosive receptors. This finding is evidence for the specificity of pullulan polymer bioconjugates and the enhanced pharmacokinetics of doxorubicin. In addition, Scomparin *et al*. planned for currently focus on tumors in folic corrosive over-communicating receptor tumor cell lines, offering another approach for *in vivo* investigations of this bioconjugate pullulan.

The combination of pullulan-balanced out gold nanoparticles (PAuNPs) was accounted by Ganeshkumar *et al*. for its utilization in conveying the anticancer medication 5-fluorouracil (5Fu) and folic acid. As portrayed beforehand, folic acid can be utilized for dynamic focusing of folate receptor over-communicating cell lines. 5Fu was presented in cancer clinics in 1957 as an inefficient solubilizers, yet strong medication for treating solid tumors. In spite of its guarantee as a chemotherapeutic operator, it demonstrated restricted

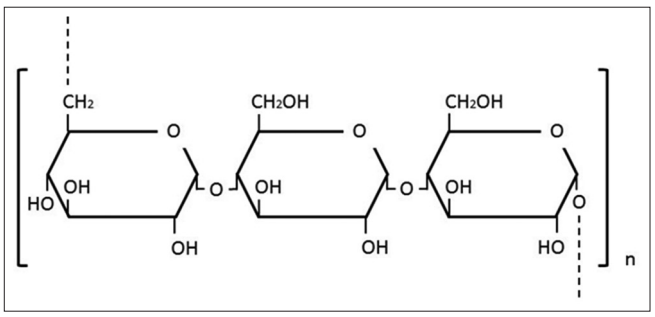

Figure 3: Pullulan structure

reaction rates of just 10–30%. Ganeshkumar *et al*. planned their 2014 examination with an end goal to build solvency, dependability, and specificity, and also to limit the reactions of this strong specialist. *In vitro* cytotoxicity tests were led in free 5-Fu and 5-Fu@AuNPs and in addition in 5-Fu@AuNPs against HepG2 cells with over-communicated folate receptors. Biodistribution ponder in male Wistar rats demonstrated no over the top poisonous quality in untargeted healthy cells. This present gathering's empowering comes about with 5-Fu@PAuNPs-Fa bioconjugates have set the basis for a novel way to deal with a dynamic liver malignancy.

Albumin

Albumin is a protein of 584 amino acids, is abundantly soluble, and has a powerful negative charge, furthermore makes out of bed partially of the routine intravascular protein dimension. Albumin has been old voguish microsphere preparation to favor lipophilic drug delivery in the direction of its prevalent availability within nature, be deficient in of toxicity along with antigenicity, next its skill on the way to prolong drug levels dressed in the general flow. One hindrance making albumin accessible to pro clinical practice is with the aim of albumin is extracted from human or animal plasma, posing the consequence of bloodborne pathogen transmission. This, however, can be avoided by high-temperature pasteurization, which might concerning attack denature the protein. However, a range of attractive properties of albumin nominates it a gorgeous artless polymer in favor of the restricted liberation of anticancer agents.

Collagen

Collagen is the primary structural protein in all vertebrate. Due to its substantial riches in the human body and high biocompatibility, collagen has been utilized for quite a long while in suturing materials and has current across the board application in tissue designing. In confined chemotherapeutic applications, collagen has been under-investigated, one issue being that collagen has poor mechanical properties, experiencing quick degeneration soon after implantation. As of late, Ye *et al*. (2008) built up a collagen film stacked with polylactic acid MS containing epirubicin for intratumoral implantation. Intratumoral implantation in a murine liver disease show brought about impressively more prominent tumor hindrance than intratumoral organization of the epirubicin MS alone. Preceding this examination, the main other utilization of collagen for confined chemotherapeutic conveyance found in the writing goes back to 1995, when Davidson *et al*. (1995). assessed a collagen grid for restricted conveyance of cisplatin following tumor resection, which totally averted tumor repeat in every test creature, while administration of cisplatin arrangement prompted massive tumor recurrence. The viscous collagen matrix was able to contain the drug at high levels in the resection site for 7 days, leading to prolonged local exposure while sparing healthy tissues.

Gelatin

Gelatin is gotten from the breakdown and hydrolysis of collagen, got from the connective tissues, bones, and skins of creatures. It is known matrixing specialist tranquilize conveyance. Bajpai and Shoubey, 2005,[15] portray a procedure for the controlled release of sulfamethoxazole utilizing 2 diverse gelatin nanoparticles (Type A [porcine skin] and sort B gelatin [bovine skin]) and cross-connected with glutaraldehyde; nanoparticles of shifting gelatin concentrations were set up by dissolvable dissipation systems and drug release kinetics evaluated using appropriate kinetic models.

Discoveries from this framework propose that this framework could be useful in focused drug delivery, for example, colon drug delivery where P_H is an imperative though. Medication discharge was found to build following expanded swelling of the nanoparticles. Moreover, the swelling was additionally upgraded by an extension in P_H with more prominent medication discharge occurring at P_H 7.5 than at P_H 1.8. The nanoparticles were additionally not corrupted in recreated gastric liquid along these lines demonstrating their dependability under acidic conditions. An expansion in the concentration of the crosslinker prompted an increment in swelling and medication discharge up until a specific concentration (10.6 mM) when swelling started to decrease. This connection between the measure of crosslinker and the polymer has additionally been accounted by Das *et al*., 2011.[16] For their situation, nanoparticles made out of gelatin mixed with montmorillonite were stacked with the anticancer agent paclitaxel. These nanoparticles were set up by a similar strategy of solvent evaporation and created comparable outcomes. Increase in glutaraldehyde concentration was accounted to build swelling and therefore tranquilize discharge up until a specific point when additionally increase in concentration of the crosslinker prompted diminished swelling and medication discharge. There was likewise an aggregate increase in drug discharge with increased P_H. 80% of the medication was discharged within 8 h at P_H 7.4 while there was under 44% medication discharge within 4 h at P_H 1.2. Increase in the concentration of the stacked medication prompted an increase in the drug discharge.

The utilization of proteins as nano transporters is additionally utilized in gene therapy. Viral and non-viral vectors are utilized for the transfection of DNA into cells, in light of the fact that, the infusion of bare DNA into living tissue brings about enzymatic degradation and lessened cell take-up because of aversion between the contrarily charged DNA and cell film. In this area, Coester *et al*., 2000,[17] utilized avidin altered gelatin nanoparticles for the conveyance of biotinylated peptide nucleic acids in other to examine their utilization as antisense treatment. Zwiorek *et al*., 2004,[18] recommended that gelatin nanoparticles can possibly be utilized for powerful non-viral gene delivery and are a more secure contrasting option to the utilization of viral vectors. A two-stage desolvation process was utilized to plan cationized particles of uniform size spreading and low polydispersity and examinations between polyethyleneimine-DNA edifices and the gelatin particles demonstrated that the last is powerful in encouraging quality articulation and has less dangerous and better endured.

Transfection with the guide of gelatin nanoparticles was likewise utilized by Xu *et al*., 2008,[19] for the delivery of DNA plasmids encoding for insulin development like factor 1 (IGF-1)

into chrondrocytes. With a specific end goal to fuse the plasmids into the gelatin nanoparticles, complex coacervation was utilized in light of the fact that it is a simple, quick and especially helpful strategy for the joining of extensive atoms. The writers demonstrated that cationized gelatin particles were of littler sizes than non-cationized particles, this they credited to the buildup of the cationized particles. Fluorescence spectroscopy demonstrated that the cationized gelatin nanoparticles were effectively transfected and communicated the quality while the invert was the situation for the non-cationized gelatin particles. This is likely because of improved endocytosis, take place because of communications between the positive charge on the former and the negative charge on the cell membrane. A five-fold increase in development factor generation was seen in cells containing these nanoparticles. Discoveries additionally demonstrated that over-articulation of the quality was kept up consistently for up to 2 weeks when they were developed in collagen (Type II) - glycosaminoglycan platforms in 3D culture. Since a delayed and confined arrival of IGF-1 was accomplished in this examination, and IGF-1 is known to advance development in skeletal muscle, ligament and bones and various different tissues in the body tissue, this approach demonstrates potential applications in quality gene therapy and tissue engineering.

Alginate

Alginate is a characteristic straight anionic heteropolysaccharide comprising rehash units of β-D-mannuronic acid (M) and its C-5 epimer, α-L-guluronic acid (G) consolidated by 1,4-glycosidic linkages. Alginates are extricated from dark brown seaweed and are perceived for their absence of lethality as confirm in pre-clinical investigations. This polymer has extraordinary potential for applications in drug delivery, attributable to its mind-boggling flexibility. For example, both neutral and charged gels can be made relying on the pH of the planning medium, taking into account maintenance of medications with an extensive variety of physicochemical properties. However, likewise, with different polymers extricated from normal sources, numerous pollutions are coextracted with alginates including endotoxins, substantial metals, and proteins. Pyrogenicity can be controlled, yet not totally disposed of, if ultrapure evaluations of alginates are utilized. Along these lines, local delivery frameworks shaped from alginates are still in the pre-clinical improvement phase.

As of late, Abe *et al*., 2008,[20] explored a local delivery system for paclitaxel as hydroxyapatite-alginate composite globules for treatment of metastatic spine malignancy in a rodent. Creatures in the control (medicate free globules) created hind limb loss of motion (paralysis) at 11th day and kicked the bucket within 16 days. Creatures treated with intratumoral injections of the paclitaxel-stacked beads demonstrated a 140–150% prolongation in sickness free survival contrasted with controls. Furthermore, critical restorative impacts were not found in creatures dosed with up to 30-fold higher intravenous dosages of paclitaxel solution, featuring the upgraded impact of localized delivery. The measure of adipic dihydrazine utilized as a part of the detailing was adjusted to control the rate of medication discharge, which could be shifted from days to a long time because of ionic interactions between the medications and the polymer. The formulations can effectively load and discharge MTX, doxorubicin, and mitoxantrone at the same time or individually. An alginate embed to encapsulate endostatin-secreting cells for the treatment of harmful glioblastoma was additionally created by Read *et al*., 2001.[21] Sustained local release of endostatin from the embed was found to effectively diminish vascular thickness and distance across, hindering glioma cell attack, and diminishing tumor volume. The counter angiogenic action of endostatin was tumor-specific, as vessels from solid, healthy tissues shaped over the embed. The creators analyzed the biocompatibility of the framework subcutaneously and intracranially, both of which hinted at no signs of an invulnerable response.

Hyaluronan

Hyaluronan (also referred to as hyaluronic acid) is an anionic, non-sulfated glycosaminoglycan composed of D-glucuronic acid and D-N acetylglucosamine, connected passing through discontinuous β-1,4 and β-1,3 glycosidic bonds, in addition to that is scattered far and wide all through connective, epithelial, and neural tissues. Hyaluronan in addition to its derivatives includes been industrial having the status of topical, injectable, as a consequence implantable vehicles in favor of the approach of purely involved molecules correct headed for their biocompatibility, exclusive viscoelastic nature, afterward non-immunogenicity. However, their use in the development of localized delivery systems of anticancer agents has been noticeably limited. Recently, Al-Ghananeem *et al*., 2009,[22] reported next to story paclitaxel-loaded cross-linked hyaluronan nanoparticles on behalf of the native healing of breast cancer. Intratumoral executive of the drug-loaded nanoparticles in female rats showed inhibition of tumoral growth in the whole treated rats above 50 days. Concerning the set of circumstances of the complimentary paclitaxel-treated group, the mean tumor volume increased linearly to a size that was 4.9-fold larger than the baseline volume at 57 days post-drug administration (Figure 4).

Agar

Agar or agar-agar is the dried coagulated substance gotten from *Gelidium amansii* (Gelidiaceae) and a few different types of red, green growth such as grailaria (Gracilariaceae) and Pterocladia (Gelidiaceae).[23] Agar comprises a blend of agarose and agaropectin. The dominating segment, agarose, is a straight polymer, made up of the rehashingmonomeric unit of agarobiose. Agarobiose is a disaccharide made up of D-galactose and 3,6- anhydro-L-galactopyranose. Agaropectin is a heterogeneous blend of littler acidic atoms that gel

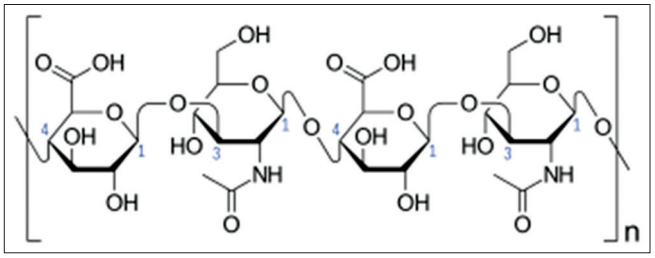

Figure 4: Hyaluronic acid

inadequately. Its incredible gelling power in a watery condition enables it to frame gels which are more safe (stronger) than those of some other gel-forming agent, expecting the utilization of equivalent fixations. It can be utilized over an extensive variety of pH, from 5 to 8, and at times past these limits. It withstands warm medications extremely well, indeed, even over 100°C which permits great sanitization. A 1.5% fluid arrangement gels between 32°C and 43°C and does not soften beneath 85°C. This is an interesting property of agar, contrasted with other gelling operators. Agar gives gels without enhance and does not require the increments of cations with solid flavors (potassium or calcium) it can be utilized without issues to gel sustenance items with delicate flavors. Its gel has brilliant reversibility enabling it to be more than once gelled and dissolved without losing any of the first properties. Agar is utilized as suspending specialist, emulsifying operator, gelling operator in suppositories, careful ointment, tablet disintegrants, medium for bacterial culture, and diuretic (Figure 5).

ADVANTAGES OF NATURAL POLYMERS

Biodegradable

As the natural polymers are produced by living organisms, they do not show any adverse effects on the environment or humans.

Cost-effective

Natural polymers are cheaper and their production cost is economic.

Easy availability

The availability of natural product is ensured, as they are produced in bulk quantities in the form of herbs in many countries.

Safe and no side effects

As these are found in its natural forms, they are considered to be safe with no side effects.

Biocompatible and nontoxic

As all the plant materials are composed of chains of monosaccharides, there exists a zero toxicity.

DISADVANTAGES OF NATURAL POLYMERS

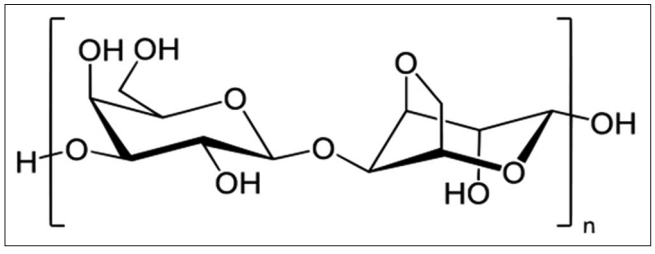

Figure 5: Structure of agar

Variations in its composition

As the natural materials are collected at different seasonal, climatic condition and from different regions, species, the percentage of chemical constituents may get varied (Grish *et al*., 2009).

Maximal variations

The natural polymeric production is dependent on the biotic and abiotic environmental factors; there occur wide variations.

Microbial contamination

The natural polymers during production, exposed to the external environment were prone to microbial contamination.

Slow rate of production

As their production is dependent on the environmental factors, they have a very slow rate of production.

Heavy metal contamination

They have a potential chance of heavy metal contamination.

CONCLUSION

Polymers assume an essential part in the drug delivery. Thus, the choice of polymer assumes a critical part in drug manufacturing. In any case, while choosing polymers care must be taken with respect to its toxicity, drug compatibility, and degradation pattern. By this survey, we can state that natural polymers can be great substitute for the manufactured polymers and a significant number of the negative reactions of the manufactured or synthetic polymers can be trounce by utilizing natural polymers.

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