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REVIEW ARTICLE

Chitosan and PLGA Polymer a Comparative Review of Properties and Biomedical Application

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ABSTRACT
Two of the most researched biodegradable polymers are chitosan and poly (lactic-co-glycolic acid) (PLGA), each of which has special benefits for biomedical research. The natural polymer chitosan, which is produced when chitin is deacetylated, is known for its antibacterial properties, mucoadhesive properties, biocompatibility, biodegradability, and hydrogel-forming capabilities. Because of these characteristics, it is ideal for uses like tissue engineering, wound healing, colon-targeted administration, gene therapy, and vaccine delivery. On the other hand, the FDA has approved PLGA, a synthetic copolymer of lactic and glycolic acids, which is prized for its excellent mechanical and thermal stability, clinical safety, and adjustable rate of degradation. It is widely used in immunotherapy, regenerative medicine, cancer treatment, cardiovascular care, and controlled medication release. Although each polymer has drawbacks of its own, when combined to create hybrid systems, they provide synergistic advantages such as improved targeting, increased drug delivery efficiency, and the ability to create sophisticated scaffolds for tissue regeneration. This comparative analysis emphasizes the complimentary roles that chitosan and PLGA play in the development of next-generation therapeutic systems by highlighting their structural characteristics, physicochemical characteristics, biological uses, and future prospects.
Keywords: *Chitosan, PLGA, Biodegradable polymer, Drug delivery, Tissue engineering, Wound healing, Gene delivery*

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INTRODUCTION

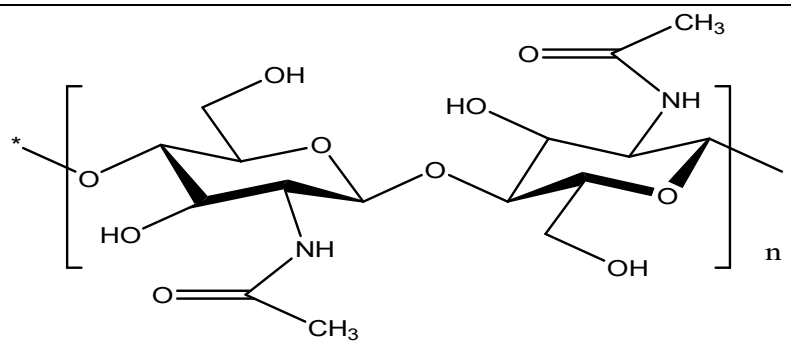
A method known as deamination is used to convert chitin into chitosan. β- (1–4)-linked D-glucosamine and N-acetyl-D-glucosamine are randomly arranged to form chitosan, a positively charged linear PS [1]. Chitosan typically has a molecular weight ranging from 3,800 to 20,000 Daltons and exhibits a degree of deacetylation between 66% and 95%. Its solubility is affected by factors such as pH, the extent of deacetylation, and the protonation state of its free amino groups [2]. Chitosan has a wide range of potential applications across various fields, including food and nutrition, biotechnology, materials science, medicine, agriculture, environmental sustainability, and more recently, gene therapy [3]. Chitosan, a chemically altered natural carbohydrate polymer derived from chitin, is present in various natural sources such as fungi, insects, crustaceans, and certain types of algae [4]. Chitin solutions treated with alkali at room temperature experience deacetylation of the molecules. This method may produce chitosan with a degree of acetylation (DA) as low as 10% following a single 48-hour treatment. It was discovered that chitosan generated consistently with a DA of around 50% dissolves in distilled water. Chitosan's solubility in neutral water is due to the equilibrium created by the random distribution of the deacetylated segments along the polymer chains [5]. Viscosity is produced when chitosan dissolves in an acidic solution. The amount of chitosan that penetrates the fabric structure depends on its viscosity. When used properly, chitosan exhibits hydrogel formation and viscoelastic behavior in liquids [6]. Because of its exceptional mucoadhesive qualities and non-toxic nature, chitosan, a cationic polysaccharide, has been extensively utilized in the development of dosage forms for transmucosal drug administration. Despite the fact that chitosan frequently has better mucoadhesive qualities than many

other water-soluble polymers, there is still a great need to enhance these qualities chemically [7]. A straight-chain polymer of glucosamine and N-acetylglucosamine, chitosan has shown promise as an antibacterial substance. Bacterial cell surface negatively charged residues of proteins, lipids, and carbohydrates may interact with positively charged chitosan in an acidic environment, preventing bacterial development [8]. Hydrogels made from chitosan can help absorb wound fluids, keep the wound moist, protect against infections, and support quicker healing. They're also compatible with the body and tend to lead to smoother scars. Because of these benefits, chitosan-based hydrogels are considered excellent materials for wound dressings [9]. As a drug excipient, chitosan's mucoadhesive qualities are being investigated for drug delivery since the polymer's adherence to a mucosal surface may lead to improved or longer drug adsorption [10]. Chitosan, when used as a coating, brings many advantages. It can increase how much drug is carried, help the drug release steadily over time, and improve how well the particles stick to body tissues, compared to those without any coating [11]. An aliphatic copolymer in biomedical applications, poly (lactic-co-glycolic acid) (PLGA) is made of lactic and glycolic acids and is both biodegradable and biocompatible [12]. It is appropriate for tissue engineering scaffolds and drug delivery systems (DDSs) due of its elasticity, mechanical strength, and low toxicity. By modifying the lactide-to-glycolide ratio, molecular weight, and crystallinity, PLGA's characteristics, including strength, swelling behavior, and degradation rate, can be adjusted. For example, PLGA 50:50 deteriorates more quickly than PLGA 75:25 or 80:20. It is easily fabricated into a variety of forms since it dissolves in organic solvents like acetone and dichloromethane [13]. The regulated and prolonged drug release capacity of PLGA lowers the frequency of doses and improves therapeutic effectiveness. Its safety and compatibility with biological systems are guaranteed by its biodegradation into non-toxic byproducts (glycolic and lactic acids). PLGA is one of the most widely utilized polymers for delivering medications, proteins, and bioactive compounds in both clinical and research contexts because of its tunable features and FDA approval [14].

STRUCTURE AND CHEMISTRY OF CHITOSAN

The physical properties of chitosan are influenced by several factors, such as its molecular weight, degree of deacetylation, the arrangement of amino and acetamido groups, and the purity of the final product. Commercially, chitin and chitosan are mainly produced from crustacean shells—like those of crabs—which are often discarded as waste in the food industry. Although it's estimated that over 100 billion tons (10 trillion kilograms) of chitin are naturally produced and recycled, only around 150,000 tons are actually made available for commercial use [15]. Chitosan is generally produced by treating α-chitin with a 40–50% aqueous alkali solution at temperatures ranging from 100 to 160°C for several hours. This procedure yields chitosan with a degree of deacetylation (DD) as high as 0.95. By performing this alkaline treatment multiple times, complete deacetylation can be accomplished. Chitosan usually has a degree of acetylation (DA) that is lower than 0.35, making it essentially the N-deacetylated variant of chitin. This copolymer is made up of glucosamine and N-acetylglucosamine units. Its physical characteristics are influenced by factors such as molecular weight (which can range from 10,000 to 1 million Daltons), DD (between 50 and 95%), purity, and the specific arrangement of amino and acetamido groups [16]. fig 1. shows the chemical structures of chitin and chitosan, two natural polysaccharides derived mainly from the exoskeletons of crustaceans and insects, and from fungal cell walls [17].

Chitin



Chitosan

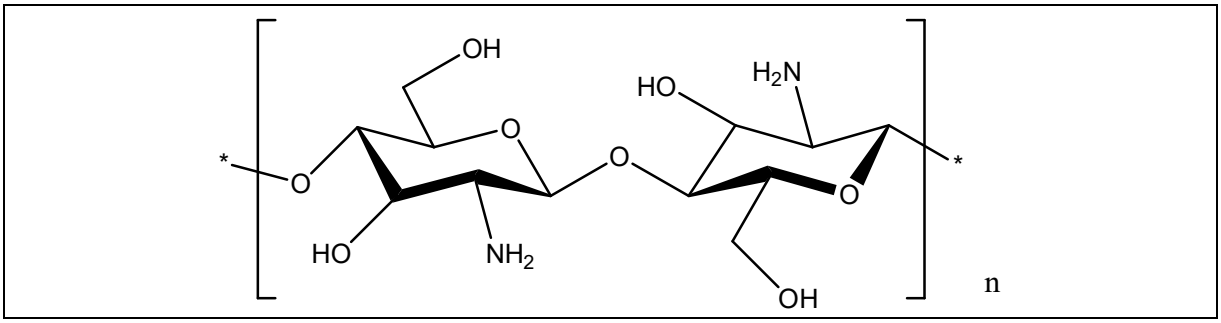


Fig. 1: Chemical structures of chitin and chitosan[17]

Chitosan's monomer has key functional groups, such as primary amine (NH2) and both primary and secondary hydroxyl (OH) groups. This allows chemical modifications to be made without changing the polymer's overall chain length [18]. The physical and chemical changes made to chitosan that improve its mechanical qualities, antibacterial activity, ability to absorb exudate, biomedical uses, solubility, regulation of biodegradability and biocompatibility, shaping, and health advantages [19]. Grafting reactions are a common method to form covalent bonds and chemically modify chitosan. This process attaches side chains to the main polymer backbone, enhancing the material's properties such as mechanical strength, antibacterial activity, swelling behavior, and thermal and physical stability [20].

METHOD OF CHITOSAN EXTRACTION AND PRODUCTION

Demineralization and deproteinization are two of the most widely used procedures for removing chitin from exoskeletons. Deacetylation must be carried out in order to transform retrieved chitin into chitosan. While deproteinization is accomplished by the action of the enzyme protease, demineralization is accomplished by the activity of bacteria that produce organic acids [21]. Fig 2 illustrates the conversion of chitin to chitosan through both chemical and biological methods, highlighting the structural differences and processing steps involved [22].

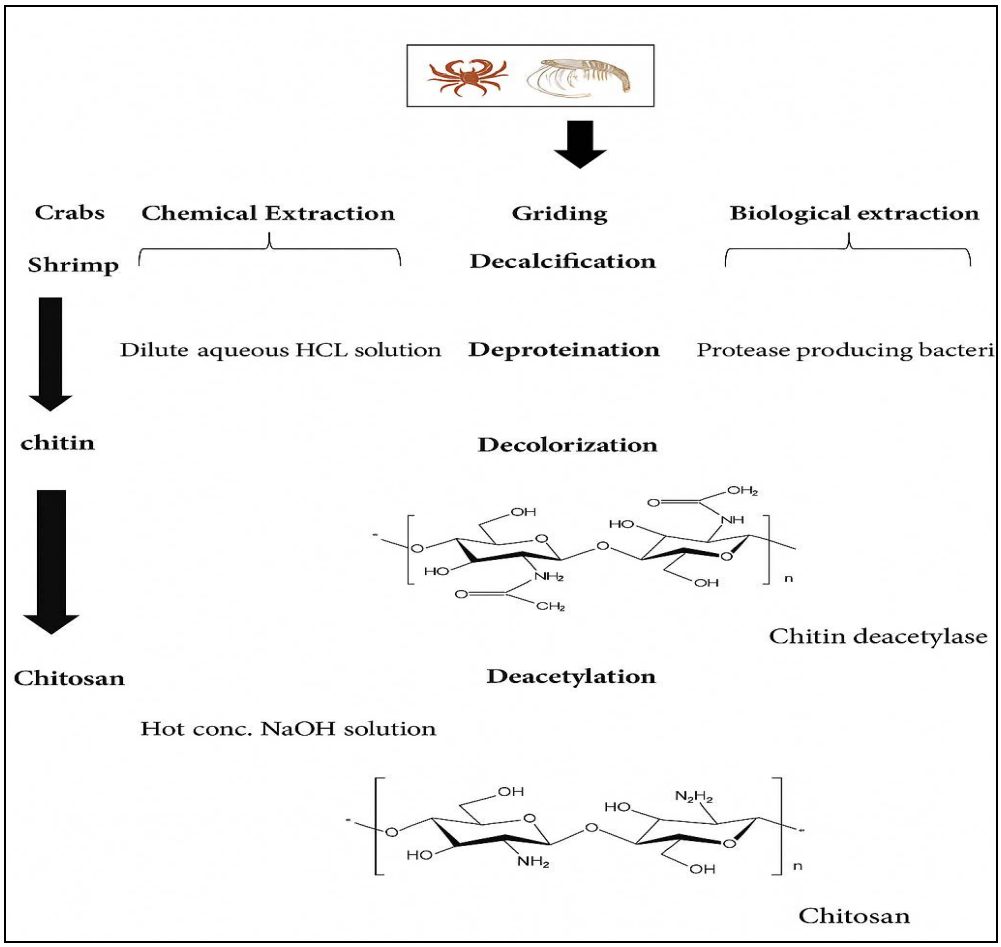


Fig. 2: Chitin and Chitosan Chemical and Biological Process [22]

Adding an alkaline solution deproteinizes the raw material, treating it with an acidic solution demineralizes it, and treating the finished product with an alkaline solution discolors it [23]. Enzymatic or chemical methods can be used to transform chitin into chitosan; however, the chemical conversion is recommended because it is less expensive and feasible for large-scale production [24].

PHYSICHOCHEMICAL PROPERTIES OF CHITOSAN

Solubility

Chitosan easily dissolves in weak acidic solutions with a pH lower than 6.0, while chitin stays insoluble in a majority of organic solvents. This distinction occurs because chitosan's primary amino groups have a pKa of approximately 6.3, which designates it as a strong base. Due to these amino groups, the charge and characteristics of chitosan vary greatly depending on the pH [25]. Several important factors greatly influence chitosan's solubility. These include temperature, the concentration of alkali, the duration of deacetylation, the methods used to isolate chitin, the ratio of chitin to alkali solution, particle size, and more [26]. A 1% acetic acid solution at around pH4 is the most commonly used solvent for chitosan. While chitosan does not dissolve in phosphoric or sulfuric acids, it is soluble in 1% hydrochloric acid and in more dilute nitric acid. However, using acetic acid at high temperatures and concentrations can cause chitosan to break down[27]. Chitosan's molecular weight and degree of deacetylation both have a major impact on its solubility and general characteristics [28].

Viscosity

In chitosan solutions, factors like ionic strength, pH, and the type of counter ions play a big role in determining viscosity. As the pH rises, the viscosity decreases for solutions with the same molecular weight, but the viscosity can increase depending on other conditions. Also, chitosan solutions stored at 4°C tend to maintain a fairly stable viscosity over time [29]. In alkaline conditions, the decrease in viscosity seems to be caused by the counter ions' (Na^+) screening action, which restricts swelling at pH 9–13. Certain pharmaceutical formulations, such as suspensions and gel formulations, are appropriate for a polymer solution with high apparent viscosity and pseudoplastic properties [30].

Hydrophobicity

There are many options for chemical modification, including the addition of hydrophobic groups, because chitosan units include two hydroxyl groups and one amino group. A very interesting strategy is to add hydrophobic substituents to chitosan. The range of applications for chitosan as a drug carrier is expanded by these substituents, which create hydrophobic domains that may absorb medications that are poorly soluble in water. Furthermore, the efficacy of chitosan as a gene delivery vehicle may be increased by hydrophobic substituents, which may boost transfection [31]. Furthermore, the dynamic and rheological behavior of this polymer should be significantly influenced by chitosan's hydrophobicity. Chitosan has several uses in industry, medicine, and biotechnology and is soluble in water at an acidic pH [32].

Degree of Deacetylation

The degree of deacetylation (DDA) influences a number of chitosan's characteristics, such as its electrostatic characteristics, biodegradability, inclination to self-aggregate, ability to absorb substances, ability to bind metal ions, and acid-base behavior [33, 31]. The degree of deacetylation (DDA) influences a number of chitosan's characteristics, such as its electrostatic characteristics, biodegradability, inclination to self-aggregate, ability to absorb substances, ability to bind metal ions, and acid-base behavior [33]. The degree of chitosan's deacetylation (DD) is ascertained using a variety of techniques. These consist of the following: enzymatic assays, nuclear magnetic resonance (NMR), the ninhydrin test, colloidal and linear potentiometric titrations (LPT), UV and first derivative UV spectrophotometry (1DUVS), infrared (IR) and near-infrared (NIR) spectroscopy, and circular dichroism analysis [34].

FUNCTIONALISATION AND MODIFICATION

Chitin and chitosan have undergone a variety of chemical modifications. Some of the most promising techniques include nitration, phosphorylation, sulfation, xanthation, acylation, hydroxyalkylation, Schiff base formation, alkylation, and graft copolymerization. These methods open the door to creating new hybrid materials by combining synthetic and natural polymers for a wide range of applications [35]. Chitosan particles at the nanoscale have been produced as possible anticancer agents and tested against several cancer cell types *In vitro.* Sun et al. created magnetic chitosan nanoparticles that deliver photosensitizers for photodynamic therapy for cancer and offer magnetic resonance imaging of tumors for photodynamic therapy targeting diagnosis and monitoring [36].Graft copolymerization is an effective way to modify the chemical and physical properties of chitin and chitosan. Synthetic polymers like polyvinyl and polyacrylic compounds are commonly grafted onto these polysaccharides. Key redox initiators used to start the grafting process include Fenton's reagent, potassium or ammonium persulfate, and ceric ammonium nitrate. Using radiation techniques helps address problems such as chitosan

degradation and unwanted homopolymer formation [37]. Chitosan is most commonly functionalized with other polymers or small molecules through acylation that results in amide bonds when coupling agents or anhydride substrates are present with regard to the majority of biological events, the resultant conjugates exhibit remarkable stability [38]. At low temperatures, chitosan was phosphorylated using phosphorous pentoxide dissolved in methane sulfonic acid, which acted as both the solvent and catalyst. This process produced compounds with a high degree of substitution that are highly water-soluble. The enhanced water solubility and strong metal-binding ability of phosphorylated chitosan and its derivatives have made them especially valuable [39].Various cross-linking agents have been used to modify chitosan for adsorption purposes because they readily bond with its accessible amino and hydroxyl groups. Common cross-linkers such as epichlorohydrin, tripolyphosphate (TPP), and glutaraldehyde help adjust the modification process. Cross-linking is an essential step that enhances chitosan's mechanical strength, boosts its stability under extreme pH conditions, and reduces its hydrophobic nature[4].Next, improved chitosan-based hydrogels were created using chitosan derivatives. The primary amine groups of chitosan reacted nucleophilically with chloride-terminated PEG, forming a chitosan-g-PEG graft copolymer that produced a stable physical hydrogel [40].This chemical modification process involves replacing the amino group (-NH2) in chitosan with a quaternary ammonium salt, or alternatively, introducing quaternary ammonium or quaternary phosphonium groups through a chemical reaction. This type of N-substitution is widely used because it is straightforward to perform and results in chitosan derivatives with significantly improved biological activities and enhanced water solubility. The key reason behind these improvements is that the polymer's backbone acquires a permanent positive charge, which influences its interaction with biological systems and solvents. By either converting the amino groups into quaternary ammonium salts or chemically attaching quaternary ammonium or phosphonium moieties, the substitution is effectively achieved, making this a highly favored approach in modifying chitosan for advanced applications [41]. Fig 3. illustrates the key physicochemical and biological properties of chitosan, a natural cationic polysaccharide obtained by the deacetylation of chitin. These properties are responsible for its wide range of applications in pharmaceutical and biomedical fields[42].

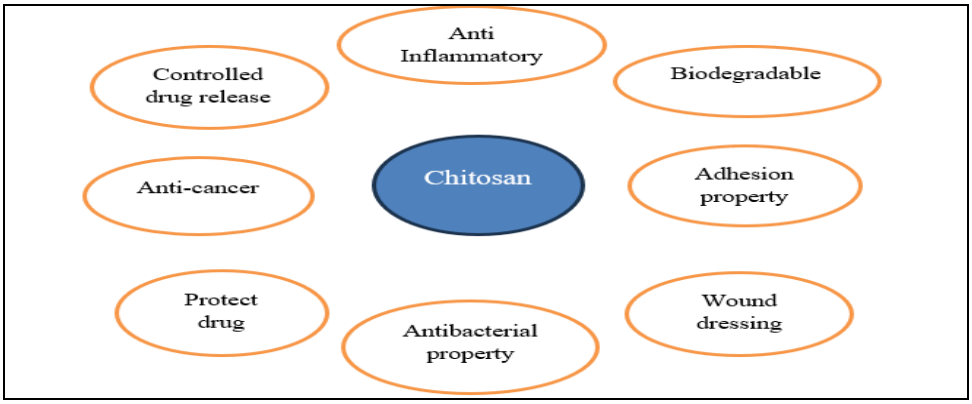


Fig. 3: Properties of Chitosan [42]

APPLICATION OF CHITOSAN POLYMER

Controlled Drug Release

Naproxen, which is an anionic drug, is formulated to be released slowly over time by using chitosan as its carrier matrix. The interaction between chitosan and the drug becomes stronger when polyanionic medications like naproxen are involved. This results in the formation of stable complexes through ionic cross-linking, enabling a controlled and sustained drug release over an extended duration [43]. Chitosan hydrogels are utilized in the biomedical field to administer various medications over an extended period of time. Their three-dimensional porous hydrophilic structure does, in fact, permit the incorporation of pharmaceuticals while preventing their release by forming a diffusion barrier. Nevertheless, keep in mind that it can be quite difficult to incorporate hydrophobic medications into the hydrophilic structure of chitosan hydrogels [44]. Moreover, to make a more homogeneous and cohesive combination, chitosan can be combined with negatively charged polymers such as carrageenan, hyaluronic acid, alginate, pectin, or polyacrylates. Drugs can be held in these dense, stable complexes and released gradually over time, primarily through slow erosion and diffusion mechanisms [45].

Colon Drug Delivery System

Chitosan is an essential component of many of the medication delivery systems being developed especially for targeted release in the colon. It works particularly well because it can shield sensitive bioactive substances from the severe conditions of the upper digestive system. The medicine is released gradually at the desired location once the colon's natural gut microbiota breaks down the glycosidic linkages in chitosan [46]. Specifically, a novel chitosan-based delivery system has been created to target medications to the colon. This method consists of a layer with evenly distributed chitosan powder within a water-repellent polymer, around a drug-containing core. Controlling the drug's release is made easier by this design. The inclusion of an extra outer enteric coating was made to prevent the drug from being released too soon in the stomach, where chitosan degrades readily in an acidic environment. The system is kept intact until it reaches the colon by this barrier [47].

Tissue Engineering

The unique benefits of chitosan-based scaffolds make them perfect for tissue engineering applications. Chitosan is broken down gradually inside the body, mostly via enzyme action. A scaffold's capacity to deteriorate over time is a critical component of its long-term performance since it directly affects vital biological functions like tissue repair, cell proliferation, and the body's reaction to the implanted material as a whole [48]. Moreover, chitosan exhibits potential in promoting skin healing and restoration following trauma or burns. The membranes made from this material did not exhibit any toxicity to L-929 cells during the 24-hour culture period, even when cross-linked with silica particles (SiO_2) and utilized in conjunction with a porogen agent. Excellent cell adhesion and proliferation were noted after 24 and 48 hours, indicating that the scaffold's macroporous structure promoted robust cell attachment and growth. According to these findings, this chitosan-based substance may be a good fit for skin tissue engineering [49]. Another well-known use of chitosan is as a supplement to scaffolds used in the regeneration of soft tissue, cartilage, ligaments, and bone tissue. Chitosan might be utilized alongside other materials such gelatin, alginate, β-tricalcium phosphate bioactive glass, hyaluronic acid, or silk fibroin scaffold for improved tissue regeneration by vascularization and cell proliferation [50].

Wound Healing

Chitosan stimulates fibroblasts, macrophages, and inflammatory cells, which speeds up the inflammatory phase and wound healing. This approach speeds up the proliferative phase of wound healing and decreases the inflammatory phase. the activation of fibroblasts, macrophages, and inflammatory cells during the inflammatory stage of wound healing. By lowering inflammation, this technique accelerates the proliferative stage of wound healing [51]. Hydrogels based on chitosan have many advantages when used on wounds. They assist the regular creation of collagen, stimulate the establishment of new blood vessels, improve the generation of natural hyaluronic acid, and raise the activity of fibroblasts, all of which help promote better and faster healing with fewer scars. By reducing inflammation, regulating cell activity, and directing the release of healing elements, these hydrogels also aid in the creation of the ideal healing environment. They can also be soft on the skin, absorb excess wound fluid, keep the wound moist, and prevent infections. These characteristics make hydrogels based on chitosan superior materials for wound treatments [52]. N-acetyl glucosamine (NAG), which is present in chitin and chitosan, is one of the primary dermal tissue constituents required for scar tissue regeneration. Because of its positive surface charge, it can efficiently increase cell proliferation and promote surface-induced thrombosis and blood coagulation [53].

Gene Delivery

Chitosan is an inexpensive, non-toxic, biocompatible, and biodegradable cationic polymer that combines with DNA to generate polyelectrolyte complexes. Consequently, chitosan and its derivatives could be effective and safe cationic carriers for gene delivery[54]. The gene was transported using trimethyl chitosan (TMC), whose cytotoxicity rises with the level of trimethylation. Later, trimethyl chitosan-g-poly(N-isopropylacrylamide) was created to accomplish minimal cytotoxicity, thermally controlled gene transfection. In order to transfer genes into the liver by bile duct and portal vein infusions with less severe liver damage, polyethylene glycol (PEG)-grafted chitosan/DNA complexes were created [55].

Antimicrobial activity

Chitosan contains antibacterial properties by nature. It functions by using its own positively charged molecules to target the negatively charged surfaces of bacteria. The bacterial membrane is damaged by this interaction, becoming more permeable and eventually leading to the bacteria's decomposition. These positive charges on its NH3+ groups are used by O-quaternary ammonium N-acyl thiourea chitosan, a modified version of chitosan, to enhance membrane damage and efficiently kill bacteria [56]. Numerous elements, such as chitosan's molecular weight (MW), concentration, and the kind of bacteria it targets, affect how effective it is as an antibacterial agent. Lower molecular weight chitosan is often more efficient

against bacteria than higher molecular weight chitosan, particularly when applied at quantities greater than 200 ppm. Particularly, chitosan that has molecular weights between 20 and 30 kDa and approximately 11 kDa is most effective against Gram-negative bacteria. The ability of increased molecular weight chitosan to combat Gram-positive bacteria, however, is stronger. Surprisingly, chitosan is more efficient against E. coli as its molecular weight rises, whereas it is more effective against Staphylococcus aureus when its molecular weight is less than 300 kDa [57].

Chitosan as coating material

Drug delivery frequently uses chitosan as a coating because it adheres to mucous membranes well and creates a smooth layer. When medications are coated with chitosan, they carry more of the drug, release it gradually over time, and adhere to biological surfaces more effectively than particles without the coating [58]. Chitosan is utilized to make hybrid structures called chitosomes because it attaches to cell membranes readily. For coating tiny liposomes—particles smaller than one micrometer—chitosan derivatives are frequently utilized. When soluble chitosan is combined with negatively charged liposomes, it adheres to their surface and alters the stability of the mixture as well as the liposomes' surface characteristics [59].

In vaccine delivery

When administered throughout the body, chitosan is frequently used as an adjuvant to increase the efficacy of vaccines. Following absorption, chitosan has the ability to activate macrophages, which are essential for the immunological response. The function of chitosan in DNA vaccines administered through mucosal membranes has been extensively studied. Illum and associates, for instance, created a DNA flu vaccine based on chitosan, and when mice were administered it via the nose, they showed a robust antibody response [60]. Chitosan polymers have dual uses as vaccination antigen delivery systems and immunostimulant adjuvants. Chitosan can be a potent adjuvant system that strongly stimulates humoral and cell-mediated immune responses. In their capacity as delivery systems, they (i) prevent the mucociliary clearance of free vaccine, which is followed by effective cellular uptake; (ii) prevent the enzymatic (proteases/nucleases) breakdown of loaded vaccine antigens; (iii) extend vaccination exposure; and (iv) deliver vaccines specifically to APCs [61].

PLGA POLYMER

SYNTHESIS OF PLGA

Typically, the production of PLGA involves two stages: the ring-opening copolymerization of lactide and glycolide, followed by the ring-opening polymerization of 3-methylglycolide. These lactone intermediates are most frequently found in lactic acid (LA) and glycolic acid (GA) and their derivatives. However, this process makes PLGA synthesis difficult and time-consuming, which frequently results in a lower yield. Additionally, these intermediates need to be recrystallized several times in order to produce higher molecular weight PLGA, which is time-consuming and necessitates the massive usage of organic solvents. Researchers are looking into different approaches as a result of these difficulties, like a straightforward one-step procedure that uses LA and GA for direct solution polycondensation. This process is far simpler than the conventional ring-opening polymerization technique [62]. Poly (lactic-co-glycolic acid) (PLGA) is a copolymer made by randomly combining two distinct monomers: lactic acid (1,4-dioxane-2,5-diones) and glycolic acid cyclic dimers. Through ester bonds, these monomers are joined. Both D and L stereoisomers may develop throughout the procedure because lactic acid contains an asymmetric ß-carbon. Consequently, D, L, or a racemic mixture of both can make up the polymer. At temperatures of about 175°C, the polymerization usually occurs over two to six hours, with stannous chloride or stannous octoate being employed as catalysts. The arrangement of the lactide and glycolide units and their molar ratio affect the unique physical and chemical characteristics of PLGA [63].

PHYSIOCHEMICAL PROPERTIES OF PLGA

PLGA is incredibly adaptable; it can be shaped into nearly any size or form and can hold molecules of different sizes. Numerous common solvents, including acetone, tetrahydrofuran, ethyl acetate, and chlorinated solvents, can dissolve it. The ester bonds in PLGA break away upon hydrolysis in water. Higher lactide content PLGA copolymers are less water-attracting, absorb less moisture, and disintegrate more slowly than PGA because PLA's methyl groups make it more hydrophobic. The degree of crystallinity of a polymer is impacted by its mechanical strength, swelling characteristics, hydrolysis behavior, and rate of biodegradation. This degree is governed by the kind and ratio of monomers in the copolymer chain [64]. PLGA that contains a larger percentage of lactide units often degrades more slowly in water. The polymer degrades more quickly, however, since a higher concentration of glycolide units makes it more hydrophilic [65]. PLGA endings can have acid or ester groups; the latter offer greater resistance to degradation caused by water. Furthermore, the molecular weight (Mw) of PLGA is a

significant factor in both its rate of disintegration and drug release capabilities. Greater mechanical strength and slower degradation are characteristics of polymers with higher Mw. Various synthesis and purification methods are frequently employed by different manufacturers, which may lead to differences in the monomer sequence as well as the kinds and concentrations of leftover solvents. Manufacturers can customize the properties of the polymer by varying elements such as the terminal groups, molecular weight (Mw), LA/GA ratio, and the circumstances used during PLGA synthesis. These modifications may have an impact on the polymer's mechanical strength, flow characteristics, thermal properties, rate of degradation, and water absorption and release [66]. When establishing the unique characteristics of PLGA, such as its melting temperature, the LA:GA ratio is crucial. The melting point of polylactic acid (PLGA) drops as the amount of glycolic acid (GA) in the polymer increases. Because it makes it possible to create a wide range of structures, this is beneficial. Although PLGA's solubility is also influenced by the LA:GA ratio, it typically declines as the GA concentration increases [67]. Similarly, the ratio of LA to GA affects the glass transition temperature (Tg) of PLGA. A Tg of about 50°C, which is greater than the physiological temperature of the body, influences the mechanical strength and stiffness of the polymer. Glass transition temperature (Tg) of PLGA increases with increasing molecular weight and lactic acid (LA) content[67]. In general, PLGA is amorphous as opposed to crystalline. The mechanical strength of crystalline polymers is often substantially higher, but amorphous polymers are nonetheless very useful in medicinal applications, particularly in drug delivery systems. Inherent viscosity of the polymer can range from 0.082 to 1 dL/g, depending on the composition and LA:GA ratio of the commercial PLGA. Furthermore, there is a strong correlation between PLGA's viscosity and molecular weight, with higher molecular weight resulting in higher viscosity [68].

STRUCTURE OF PLGA

Fig 4. represents the chemical structures of PLGA and its individual monomers — lactic acid and glycolic acid — and shows how they combine to form the copolymer backbone. PLGA is a biodegradable and biocompatible polymer widely used in drug delivery systems [69].

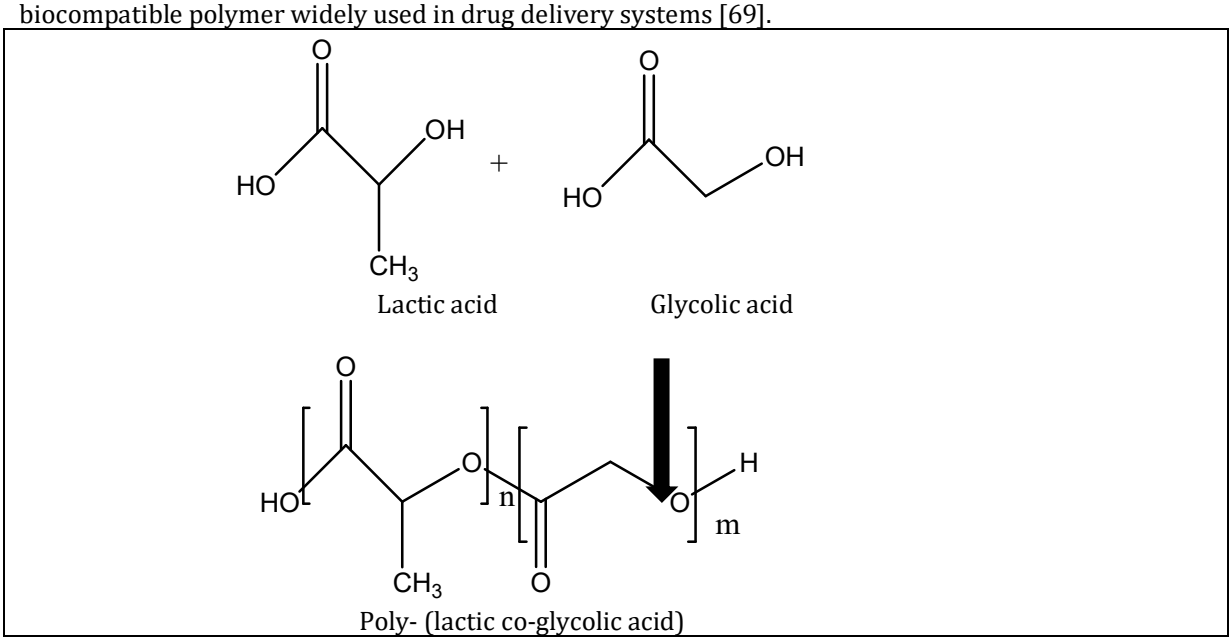


Fig. 4: Chemical structure of poly (lactic-co-glycolic acid) and its monomers [69]

Table 1: explained the application of PLGA polymer

Application	
PLGA in drug targeting	When it comes to drug targeting, PLGA polymer serves as a biodegradable carrier that encapsulates medications and releases them at the target site under controlled conditions. It minimizes systemic side effects, improves medication stability, permits surface modification for active targeting, and provides accurate delivery to infected regions [70-72].
PLGA in Vaccines	In vaccines, PLGA polymer serves as a biodegradable carrier that shields antigens from deterioration and ensures their prolonged release, boosting immune response. It improves vaccine efficacy while lowering toxicity and the necessary adjuvant dose by enabling the regulated delivery of antigens and adjuvants to dendritic cells or macrophages [73-75].

PLGA in Anti-cancer drug delivery	The purpose of PLGA in anticancer drug delivery is to serve as a biodegradable nanocarrier that protects and encapsulates anticancer medications, allowing for their targeted and regulated release at tumor locations [76]. It can improve treatment efficiency and safety by preventing premature drug degradation, increasing tumor accumulation through the EPR effect, enabling surface modification for active targeting, and stimulating immune system activity through interactions with immune cells and macrophages [77].
PLGA in Tissue Engineering	PLGA is a common synthetic polymer used in tissue engineering for 3D scaffolds because it is non-toxic and biocompatible, which makes it perfect for bone regeneration. It closely resembles genuine bone in that its composition and bioactivity encourage the production of new bone [78]. PLGA is frequently altered to create an apatite-like surface, which improves tissue integration and cell adhesion, or it is mixed with bioactive glass or ceramics to improve performance. The combination of hydroxyapatite and surface functionalization produce osteoconductive and osteoinductive qualities that greatly increase the success of bone regeneration [79].
PLGA in Tumor Immunotherapy	In tissue engineering, PLGA polymer serves as a scaffold that promotes tissue regeneration, cell adhesion, and proliferation while progressively breaking down into non-toxic byproducts. It is perfect for supplying growth factors that support healing and tissue repair as well as for rebuilding bone, cartilage, and vascular tissues because of its adjustable mechanical strength and degradation rate, which enable controlled tissue growth and medication release [80].
PLGA in Wound healing	In wound healing, the PLGA polymer serves as a biodegradable matrix that progressively releases lactate, encouraging tissue regeneration and angiogenesis [82]. PLGA is a potential material for regenerative and tissue-repair applications because its regulated disintegration promotes cell proliferation, collagen production, and blood vessel expansion, all of which speed up wound healing [83].
PLGA in cardiovascular diseases	In cardiovascular disorders, PLGA polymer serves as a biocompatible and biodegradable carrier that permits targeted and regulated delivery of drugs or genes to heart tissues. It improves cellular absorption, promotes vascular healing, and prevents restenosis in PLGA-coated stents and nanoparticles. Its sustained-release qualities guarantee longer therapeutic efficacy and less systemic side effects in cardiovascular treatments [84].

Table 2: Explained the Comparison between Chitosan & PLGA Polymer

Properties	**PLGA Polymer**	**Chitosan Polymer**
Glass Transition	45 and 55°C	203°C
Chemical Formula	(C6H8O4) m (C4H4O4) n	$[C_6H_{11}NO_4]$ m $[C_8H_{13}NO_5]$ n
Biodegradation	Both auto-catalytic and hydrolytic breakdown occur in an aqueous environment when ester linkages along the polymer backbone are randomly hydrolyzed.	Biodegradation is done by two methods either chemical or enzymatic degradation. 1- In chemical degradation include acid catalyzed degradation, oxidation-reduction depolymerization & free radical degradation 2- In Enzymatic degradation include lysozyme, chitosanase, chitinase.
Molecular Weight	85,000 Da	3800-20,000 Daltons
Specific gravity (g/ml)	1.30-1.34	1.35-1.40
Tensile strength (psi)	6,000-8,000	4,000-12,000
Color	White- Light Gold	Off-white to pale yellow
Synthesis	1)Lactic and glycolic acid monomers are directly polymerized in the direct polycondensation method. 2)Ring opening 3)Enzymatic	Deacetylation is carried out in order to transform retrieved chitin into chitosan
Melting Temperature	220-260°C	It degrades thermally rather than melting, often beginning around 280-350°C
Solubility	Soluble in solvents including tetrahydrofuran, dichloromethane, chloroform, ethyl acetate, benzyl alcohol, acetone etc.	Chitosan solubility in acid aqueous media its pka value is approximately 6.5
Nature	Amorphous	Partially crystalline
Viscosity	0.16-0.24 dl/g	9.40 dl/g
Monomer	Equal no. of lactic acid glycolic acid	Primary amine (NH2) & primary and

	monomers (50:50) ratio	secondary hydroxyl group (COOH)
Storage temperature	2-8°C	4°C Refrigeration
Application	Cardiovascular disease, cosmeceuticals, dentistry, drug targeting	Controlled released system, antibacterial, colon targeting, gene delivery

RECENT PATENTS ON CHITOSAN POLYMER

Table III explained the recent patents data since 2020-2025

Table 3: Patent update on Chitosan Polymer

S.No.	Name of Patent	Patent Number	Country
1	Process for the preparation of microcapsules [85]	US20200406218A1	United States
2	Water- soluble, high- molecular-weight chitosan powders [86]	US 2020/0255631 A1	United States
3	Chitosan containing compositions [87]	US 2021/0145861 A1	United States
4	Chitosan and applications thereof [88]	US 2022/0220227 A1	United States
5	Chitosan containing formulations and methods of making using the same [89]	US 2022/0370680 A1	United States
6	Enhancing the Antimicrobial activity of biocides with polymers [90]	US 11,666,050 B2	United States
7	Chitosan – derived compositions91	US 2022/0017647 A1	United States
8	Alginate chitosan nanoformulation of OMPA- A shigella protein subunit [92]	US 11,298,415 B2	United States
9	Chitosan nanofiber composition, composition modified chitosan and method of use [93]	US 11,878,088 B2	United States
10	Antimicrobial tailored chitosan [94]	WO 2020/225255 A1	WIPO (PCT)
11	Treatment composition with chitosan-based delivery particles [95]	WO 2024/118693 A1	WIPO (PCT)
12	Modified chitosan, preparation method thereof, and additive for tile adhesive and use thereof [96]	EP 3 981 798 B1	European patent office
13	Chitosan-containing nanoparticles for delivery of polynucleotides [97]	US 2024/0216531 A1	United States
14	Delivery systems for control of gastrointestinal bleeding [98]	US 11,564,673 B2	United States

RECENT PATENTS ON PLGA POLYMER

Table IV explained the recent patents data since 2020-2025.

Table 4: Patent update on PLGA Polymer

Sr.No.	Name of Patent	Patent Number	Country
1	Sustained release compositions [99]	WO 2021/234731 A1	WIPO (PCT)
2	Mucoadhesive PLGA nanoparticles [100]	US 2024/0374705 A1	United States
3	PLGA microparticles, a sustained release formulation thereof and a production method thereof [101]	US 2022/0133632 A1	United States
4	Sustained release microparticles and process for the preparation thereof [102]	EP 4 529 921 A1	European patent office
5	Drug comprising PLGA nanoparticles loaded with cape targeted with angiopep-2 peptide [103]	US 2023/0225983 A1	United States
6	Drug delivery system for targeted cancer treatment [104]	US 2025/0049933 A1	United States
7	A vaccine comprising a nanoparticle encapsulating epitopes and adjuvant for neutraliying virus infection [105]	WO 2020/231788 A1	WIPO (PCT)
8	Drug delivery agents for prevention of treatment of pulmonary disease [106]	US 2021/0106536 A1	United States
9	Drug delivery agents for prevention or treatment of pulmonary disease [107]	US2023/02270681 A1	United States
10	Method for treating cancer [108]	WO 2023/225204 A1	WIPO (PCT)
11	Conjugate targeting cardiovascular disease [109]	US 2025/0090683 A1	United States
12	Composite scaffold for the repair, reconstruction, and regeneration of soft tissues [110]	US 2021/0161645 A1	United States
13	Ocular implant made by a double extrusion process [111]	US 2024/0238312 A1	United States
14	Methods for the preparation of hybrid polymeric nanoparticles [112]	WO 2023/119222 A1	WIPO (PCT)

CONCLUSION

PLGA and chitosan are two extensively researched biodegradable polymers that work well together and have a wide range of uses in medicine. Originating from chitin, chitosan is prized for its superior biocompatibility, biodegradability, mucoadhesive properties, antibacterial properties, and hydrogel-forming potential. Because of these qualities, it is very useful for tissue engineering, gene and colon-targeted medication delivery, and wound healing. However, PLGA, a synthetic copolymer of lactic and glycolic acids, is well-known for its robust mechanical qualities, FDA-approved clinical use, and tunable rate of breakdown. Controlled medication release, cancer treatment, vaccine formulations, tissue healing, and cardiovascular medicines have all benefited from its use**.** When combined, PLGA and chitosan form hybrid systems that lessen the drawbacks of each material while combining their advantages. Targeted treatment approaches, regenerative medicine techniques, and drug delivery systems all benefit from this combination. Together, these polymers offer a strong basis for the creation of next-generation biomedical technologies and have enormous potential to improve contemporary healthcare, whether used singly or in combination.

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