Journal of Textiles, Coloration and Polymer Science
https://jtcps.journals.ekb.eg/
Egyptian Society for Textile Science and Technology
الجمعية المصرية لعلوم وتكنولوجيا النسيج

Natural Polymers in Medical Textiles

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Abstract

In numerous biomedical applications, including pharmaceuticals, scaffolds for tissue regeneration, drug delivery systems, and imaging agents, natural polymers have been extensively exploited. They serve as templates for regeneration and dressings for either acute or chronic wounds in wound care. There are numerous natural sources of polymers, including plants, animals, and microorganisms. Natural polymer-based scaffolds are desirable for skin repair and regeneration due to their homology to the extracellular matrix, mechanical tunability, high biocompatibility, and high water-holding capacity. An overview of popular or promising natural polymers for wound healing will be provided in this chapter.

Keywords: Natural polymer, chitosan, Alginate, Collagen, medical textile.

Introduction

High molecular weight chemicals known as polymers are created by repeatedly joining small molecules.(Monomers). Examples include starch, PVC, PE, Nylon 6, and others. [1].

The Greek words poly, which means many, and mer, which means unit or part, are combined to form the word polymer. Very big molecules with a high molecular mass are referred to as polymers. These are also known as macromolecules because they are created by joining numerous repeating structural units together. The monomers, which are some basic, reactive molecules that make up the repeating structural units, are joined to one another by covalent bonds. [1].

Natural polymers have drawn interest as affordable, widely accessible, and non-toxic materials. They can undergo chemical alterations, they may degrade biologically, and with very few exceptions, they are also biocompatible. [2].

Synthetic polymers are made from non-renewable resources, whereas biopolymers are readily available from renewable sources in vast quantities. Due to their sustainability, biodegradability, and biosafety, polysaccharides represent one of the most prevalent industrial raw materials and have been the focus of extensive research. [3].

Natural Polymers

Biopolymers are created during the cell division processes of living things. They provide a range of uses that are environmentally friendly and have the benefits of traditional plastic. These materials have the benefit of being constantly available in big numbers at affordable prices. [2].

1- Cellulose

An organic polymer called cellulose is found in plant fiber walls. The most significant and interesting biopolymer is this natural polymer. Cellulose, which is utilised in a variety of applications such as composites, netting, upholstery, coatings, packing, paper, etc., is insoluble in water and the majority of popular solvents. [4-10]

2- chitin

An essential natural polysaccharide is chitin. This biopolymer, which is among the most prevalent natural polymers after cellulose, is produced by a huge variety of living things. [11]

In addition to being present in lobsters, crabs, insects, and prawns, chitin can also be produced by some fungi during fermentation processes. This biodegradable polymer is found in nature as organized crystalline microfibrils that serve as structural elements in the cell walls of fungi and

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Receive Date: 12 July 2023, **Accept Date:** 06 August 2023
DOI: 10.21608/JTCPS.2023.222699.1225

yeast as well as in the exoskeleton of arthropods. [12].

Chitosan

By deacetylating chitin, a polysaccharide called chitosan is produced. This biopolymer, which has reactive amino groups and is nontoxic and affordable, has demonstrated utility in a variety of fields as an antimicrobial compound in agriculture, a potential trigger of plant defense responses, a food additive, a hydrating agent in cosmetics, a flocculating agent in wastewater treatment, and more recently as a pharmaceutical agent in biomedicine. [2, 13-17]

Gelatin

Gelatin is a biomaterial made from animal proteins that are created by thermally denaturing collagen. It is a pure protein dietary ingredient. It has a somewhat yellow appearance and is commercially available as clear, tasteless, brittle, odorless sheets, flakes, or powder. It is soluble in hot water, glycerol, and acetic acid but insoluble in organic solvents. [18-23]

This organic polymer, which is derived from collagen, is primarily present in fibrous tissues like ligaments, skin, and tendons. Additionally, the cornea, cartilage, bone, blood vessels, gut, and intervertebral disc are all rich in it. [24].

Dextran

Dextran is a multi-chain, branching polysaccharide that has chains that range in length from 10 to 150 kilodaltons and is made up of several glucose molecules. [25] This group of polysaccharides is stored as fuel in yeasts and bacteria and is made up of monomers of the simple sugar glucose. [26-28]

Dextrans is a substance that has a wide range of essential applications due to its exceptional moisturizing qualities, a natural composition made from renewable resources, excellent biocompatibility, and clinical safety record. [29]

Collagen

Animals' bones and skin are primarily made of collagen, which is the most common protein in the animal kingdom. It belongs to the large family of extracellular Matrices. The Greek word "Kolla," which means glue, is whence the word "collagen" got its meaning. [30]

This particular natural polymer has excellent hydrophilicity, moisturizing, repeatability, and biodegradability qualities. [31]

Medical textile

Healthcare Textiles is another name for medical textiles. Because of its considerable expansion in domains including wound healing and controlled release, bandaging, implanted devices as well as medical devices, and the creation of new intelligent textile goods, advanced medical textiles are a rapidly growing industry. One of the segments of the technical textile market that is growing the fastest is medical textiles. The use of textile materials for medical and healthcare products spans from straightforward gauze or bandage materials to scaffolds for tissue culturing and a wide variety for permanent body implants. It is one of the primary growth areas within technical textiles. Textiles are used in the fields of healthcare and personal hygiene. Their use is based on a variety of standard textile characteristics, including softness, lightness, flexibility, absorption, and filtering. [32].

Classification of Medical Textiles

1- Non-implantable materials: These substances are applied externally to the body and may or may not come into contact with the skin. [33].

2- Implantable materials: These components are used to restore the body, whether it be by replacement surgery, vascular grafts, artificial ligaments, or artificial cartilage. [33].

Natural polymers

Chitosan: Deacetylation of chitin yields the polymer known as chitosan. This biopolymer, which has reactive amino groups and is nontoxic and affordable, has demonstrated utility in several industries as an additive in the food industry, as a hydrating agent in cosmetics, as an a flocculating agent in wastewater treatment, and, more recently, as a pharmaceutical agent in biomedicine. [2].

Chitin, one of the most prevalent naturally occurring polysaccharides, is the source of chitosan (1-4)-linked 2-amino-2-deoxy-D-glucopyranose (Fig. 1). The non-toxic, biocompatible, and biodegradable qualities of chitosan are well known. It also possesses several distinctive qualities, including the ability to fight off a wide range of bacteria, fungi, and yeasts, which makes it useful for usage in the biomedical industry. Additionally, it can bind toxic metal ions, which makes it useful for applications such as water and air purification. Due to the protonation of NH2-groups on the chitosan backbone, these properties are produced. [34].

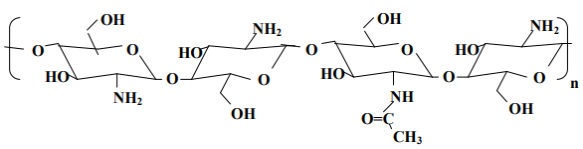

Fig. 1. Chitosan chemical structure. [35].

Properties of Chitosan: Chitosan's solubility in acidic solutions in its free amine (-NH2) form. Un soluble above pH 6.5Limited solubility in H3PO4; insoluble in most organic solvents; insoluble in H2SO4; soluble at pH values below 6.5. Creates viscous liquids. Shear-thinning solutions produce polyanion-based gels. [36].

Chemical properties of Chitosan: Chitosan is a reactive hydroxyl and amine group-containing linear polyamine (polymer-OF-glucosamine).Chelates a lot of metal ions in transition. [36].

Other chemical property

Biocompatibility: Biopolymers made of chitin and chitosan are organic. They are completely compatible with live tissue since they lack antigenic characteristics. They are ideally suited for application in many biological disciplines due to their anti-thrombogenic and hemostatic characteristics.

Biodegradable: Chitin and chitosan are biopolymers that degrade with time. They are broken down into oli go polymers by the enzymes chitin and chitosan, which are then processed by the metabolism. It degrades into typical bodily components.

Antimicrobial activity: It also acts as a fungistatic and has anticancer and spermicidal effects. Chitosan (D. A. = 9.9%, concentration 0.15%) has typically been shown to be mildew-free for four cultivating days. With an increase in chitosan concentration, the activity rises. [36].

Application of chitosan: Cosmetics ‹Water engineering ‹Paper industry ‹Textile industry‹ Food processing ‹Agriculture ‹ Photography ‹ Solid state batteries. Biomedical application ‹ Industrial applications. [37]

Application of chitosan in medical textile

Antimicrobial finishing

Chitosan is a polycationic biopolymer having a wide range of biological activity that has been well-documented, including anti-microbial and anti-fungal qualities. The degree of deacetylation (DD) and the quantity of chitosan rising with the number of ionizable groups are two crucial structural characteristics that affect the substance's antibacterial activity. It has been demonstrated that the rate of bacterial decrease increases with any increase in MW of chitosan. The driving reasons behind the antibacterial efficiency of chitosan, in addition to DD and MW, are the quantity and placement of the amino group, which is coupled to both parameters. Chitosan's amino groups transform into quaternary amino groups in acidic solvents, which enables it to prevent the growth of a variety of bacteria, including both gram-negative and gram-positive bacteria, by surface interference. There are two hypothesized mechanisms for chitosan's antibacterial activity, and both emphasize the significance of the quantity of active amino groups. By stacking the surface of the cell, chitosan's polycationic structure interferes with bacterial metabolism in one way. The other way for inhibiting mRNA translation involves chitosan's binding to DNA. The fibers were in the form of combed cotton slivers before being treated for 10 minutes with a 1% chitosan acidic solution (in 1% acetic acid).

Textile substrates coated with chitosan for wound care applications

Chitosan-treated cotton gauge or yarn: By oxidizing cotton thread with sodium per-iodate in water at 60°C and then treating it with a chitosan solution in aqueous acetic acid, new cotton yarn with a chitosan coating was created. The creation of Schiff's base between the chitosan and the oxidised cellulose was suggested by the infrared spectra of the cotton yarn covered with chitosan. After the series reaction, the surface of the cotton yarn with chitosan coating was somewhat altered. The cotton yarn treated with chitosan has outstanding (100%) antibacterial activity against microorganisms. Thus, this novel thread is appropriate for use in medical applications such as wound healing. [38].

Chitosan-treated cotton gauze: The chitosan-coated cotton gauze was created and its chemical, thermal, and antibacterial capabilities were assessed. The cotton gauze with chitosan coating was found to be effective against microorganisms, making it a good candidate for use as a potential wound dressing. [39].

Chitosan sponges, non-woven wound dressings, and composite dressings for use in wound care systems: Chitosan sponges: For the treatment of wounds in all stages of healing, dressing materials were based on produced polysaccharides that were used as sponges. To make the dressings, chitosan micro fibroids, and chitosan-alginate micro fibers with calcium were utilized. Sponges were made utilizing the freeze-drying procedure (Fig). Materials that had been developed had their mechanical, sorption, biological, cytotoxic, and hemostatic properties assessed. The study has shown that the chitosan sponge satisfies the fundamental requirements for the physico-mechanical and biological dressings. These sponges were discovered to have excellent sorption qualities and enough strength. [40].

This two-layer dressing has an absorber layer made of a hydrophilic polyurethane sponge. This is attached to the physiologically active layer that also contains silver salts, chitosan, sodium alginate, and calcium. Animal studies conducted in vitro and in vivo have demonstrated that the TROMBOGUARD+ dressing can stop bleeding. Additionally, they exhibit

strong antibacterial action against Escherichia coli and Staphylococcus aureus, protecting against infection without the need for or with minimal involvement from medications. [40].

Different tencel/cotton ratios were employed to create non-woven dressings made with chitosan. The immersion-precipitation phase-inversion casting method was used to create the Tencel/cotton non-woven with chitosan. First, a 3.0 weight percent chitosan solution with 1.0 weight percent acetic acid aqueous solution was added to the Tencel/cotton nonwoven, which was then frozen for three hours. The non-woven chitosan dressing was defrosted, submerged in NaOH aqueous solution for 24 hours, and repeatedly rinsed with deionized water. The samples of Tencel/cotton non-wovens treated with chitosan were then put through a quality assessment. The outcomes demonstrated that the non-woven-chitosan membrane had increased fluid drainage ability and minimized evaporative water loss. They lacked toxicity and antigenicity as well. [41].

Alginate

Alginate: A polymer called alginate is produced by bacteria from the Pseudomonas and Azotobacter genera and is found naturally in the cell walls of brown marine algae. The phrase is typically used when describing alginic acid and its salts. [42].

The linear alginate molecule (Figure) is made up of two different monosaccharide moieties, D-mannuronic (M) and L-guluronic (G) acids, which are joined by 1,4-glycosidic linkages. The two types of residues are arranged in homopolymeric blocks made up of M or G units. There are also sporadic heteropolymeric blocks with both M and G residues in the alginate structure. It is important to remember that the source of the polysaccharide may affect its structure. [43]. Different physicochemical attributes are linked to structural variations. The remaining guluronic acid is what interacts with divalent ions and creates crosslinks. As a result, when compared to compounds with a larger amount of guluronic acid, those lacking G-blocks produce softer, less rigid gels. [44]

Acetylation level and molecular mass are two further aspects of alginate that can alter its characteristics. Alginic acid is not soluble in water, however, its salts with monovalent cations show good solubility and can be dissolved in water and remain stable. [44]

Alginate has a wide range of biomedical applications as a result of the many characteristics that make this polymer ideal for protein and drug delivery systems, tissue regeneration, or wound healing. It's all because of the material's adaptable and biological qualities, which include biocompatibility, nonimmunogenicity, affordability, chelating ability, water solubility, and flexibility. These qualities allow for simple modification of the material's properties through crosslinking or grafting with other polymers. [45].

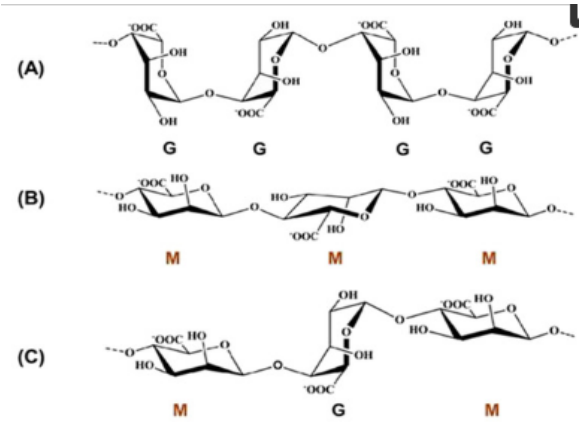

Fig. 2. (A) Homopolymeric blocks of poly-α-1,4-l-guluronic acid (GG), (B) homopolymeric blocks of poly-β-1,4-d-mannuronic acid (MM), (C) heteropolymeric blocks of alternating M and G residues.

Application Alginate in medical textile

Alginate in Wound Dressings: Instead of only covering the wound surface and serving as a mechanical barrier to keep contaminants out, modern wound dressings have been developed to offer the best conditions for healing. The dressing's primary job is to absorb excessive amounts of exudate without significantly drying the wound bed. A few types of the many dressings that are now used can be identified. It can be considered that some of them are similar to others when considering the physicochemical makeup of specific wound dressing systems. The exceptionally high absorption effectiveness of commercially available alginate dressings, however, allows for the evacuation of even large volumes of exudate. In alginate dressings, calcium alginate is typically administered in its dry state, and following The fibrous matrix is rehydrated upon contact with the moist wound bed. The resulting gel matrix offers a wet setting for healing wounds. Alginate dressings' minimal adhesion to the wound bed and ease of removal are significant benefits. Additionally, both clean and infected wounds can benefit from the use of this kind of substance. Typically, a secondary dressing overlaying alginate is required to prevent dehydration of the occurring gel, and in infected wounds, the exterior layer should be non-occlusive. [46]

Alginate has good biocompatibility and is nontoxic, both of which are crucial qualities in materials used to treat damaged skin. This polymer's adaptability is a key benefit since it may be utilised to create a wide range of dressing materials, such as hydrogels, nonporous films, porous foams, wafers, nanofibers, and micro- and nanoparticles. [47]

Alginate can also be blended with many different substances, such as polymers, herbal extracts, and antimicrobials. To enhance its mechanical properties, additional polymers are typically added. Combinations containing carboxymethyl cellulose are currently available among the products that are marketed. However, a wide range of other polymers and modification techniques, like grafting or various crosslinking techniques, are being researched. [48]

Alginate Wound Dressings Loaded with Inorganic Particles

Recent years have seen a rise in interest in the use of metal and metal oxide nanoparticles as antimicrobial agents for a variety of biomedical purposes, including the prevention of wound infections. Nanoparticles of silver, zinc, copper, gold, and their oxides, as well as titanium, magnesium, and cerium oxides, are thought to provide a viable solution to the worrying issue of rising antibiotic resistance. They have been used in a variety of biopolymeric hydrogel matrices, such as alginate polymers for wound healing, in this fashion. Research on alginate-based dressings has mostly concentrated on two types of inorganic antimicrobial nanoparticles: nanocrystalline silver (also known as AgNP) and zinc oxide (ZnONP), even though a variety of metal compounds can be employed. [49, 50]

Nanocrystalline Silver (Ag NP): Silver is one of the oldest medicines known to humankind and has been used as an antiseptic for ages. Since the Ag+ ion exerts bactericidal action, its antibacterial application has mostly relied on ionic forms (silver salt solutions, colloidal silver). It kills the bacterial cell by interfering with negatively charged protein sites (sulfur- and phosphorus-containing groups), which is comparatively more effective in the case of Gram-negative strains. Once inside the cell, Ag+ can also bind with nucleic acids, ribosome denaturation, or cytochrome inhibition. Additionally, the production of reactive oxygen species (ROS) can result in additional harm. The figure displays a multifaceted antibacterial action mechanism. Besides having antibacterial properties, Additionally, silver has been discovered to control the immune system's reaction during the healing of wounds. [50]

Clinical studies have shown that the use of alginate hydrogel dressings with ionic silver decreases the risk of wound infections and speeds up the healing process. Examples of these dressings include Algicell and Silvercel. However, the cytotoxicity of ionic silver to mammalian cells restricts the concentration of silver that can be used in wound dressings. Silver nanoparticles (AgNP) are becoming more and more popular as a substitute as a result, as they guarantee extended, sustained release of Ag+ over longer times without going above the lethal amounts. AgNP has a high surface area since their particle size is below 100 nm, which enhances their interaction with bacterial cell membranes. As a result, nanocrystalline silver exhibits more antibacterial effectiveness than ionic forms, particularly in the case of wound dressings. [51, 52].

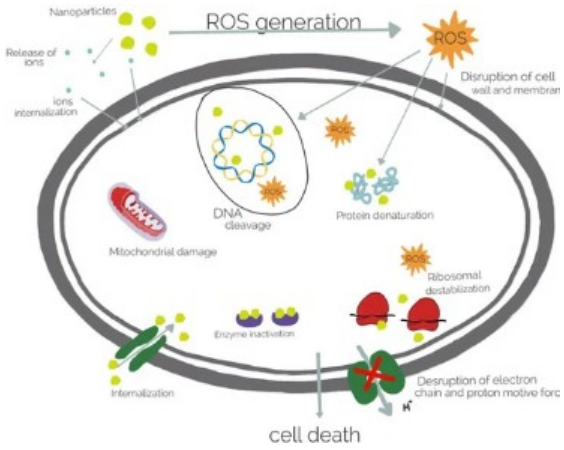

Fig. 3. Antibacterial mechanisms of metal nanoparticles

AgNP in Matrices Using Only Alginate

Alginate-based wound healing products have been described in scientific literature, however less frequently than alginate-based products that also contain other polymers. The development of AgNP in situ in sodium alginate solution (by reduction with sodium borohydride) and subsequent freeze-drying in two cycles with breaks for ionotropic Ca2+ crosslinking are two early examples. [53]

Silver nanoparticle inclusion appears to be rather common in wet-spun calcium alginate fibers. Alginate solution was added to a calcium chloride gelling bath, and then further glutaraldehyde crosslinking allowed for a 20-fold increase in hydrogel swelling (versus a 3-fold increase after ionotropic gelation alone). To carry out the ionic exchange between Ca2+ and Ag+ cations, the resultant fibers were submerged in an AgNO3 solution. They were converted to silver nanoparticles (less than 10 nm) on the fiber surface by the addition of sodium borohydride.

On hairless mice, an incision wound healing study was conducted where AgNP-incorporating

fibres were compared to silver nanosuspension and blank alginate fibre at two doses (0.033% vs. 0.383% w/w). Surprisingly, pure AgNP suspension demonstrated greater anti-inflammatory efficacy and promoted thicker epithelium during wound healing. Without having any cytotoxic effects, AgNP alone stimulated fibroblast migration and wound healing. Alginate, therefore, had no apparent benefits for wound healing in this instance, serving simply as a support and delivery platform for silver nanoparticles. [54]

The created microfluidic spinning technique was thought to be a workable substitute for alginate electro-spinning, which requires the inclusion of a suitable polymer for a stable fiber. [55] There have been reports of nanocrystalline silver alginate dressings electro-spun with poly caprolactone (PCL) or polyethylene oxide (PEO). To speed up the healing of wounds, Hu and Lin recently created a sophisticated, multipurpose dressing that includes both silver nanoparticles and the gene that codes for platelet-derived growth factor B (PDGF-B). AgNP was mixed with PCL and PEO solution before being co-electrospun with sodium alginate-PEO solution using a dual jet system. The resultant fiber was then ionically crosslinked with Ca^{2+}.

Finally, by using the electrostatic interaction between the positively charged polyplex and negatively charged alginate, a DNA-polyethylene imine complex was adsorbed by immersion. AgNP were thus homogeneously linked to the PCL fiber component in this dressing. Silver ions were released throughout the course of 120 hours, first in a gradual, continuous release for a brief period of 24 hours. The authors claim that this release profile is very advantageous since it guarantees a rapid bactericidal effect during the early stages of wound healing and sustained, balanced exposure to Ag+ without cytotoxic consequences.

The proliferation of fibroblasts was unaffected at a successful Ag NP concentration of 30 mm. The created dressing had in vitro hemostatic and antimicrobial activities. [56] Ag NP-infused alginate-PCL dressing dramatically increased the wound closure rate by up to 67% in just 11 days. Even better outcomes were achieved with the inclusion of the PDGF-B gene, which ensured nearly complete wound healing (95%) at the same time point and increased collagen deposition and remodeling. [56]

There have also been described simpler Ag NP-alginate dressing materials made using electro-spinning. In a study by Mokhena and Luyt, Ag NP were created by reducing and stabilizing nanoparticles with chitosan at the same time. An electro-spun alginate (with PEO) fiber was then submerged in this solution, which caused Ag NP-chitosan particles to coat the fiber following the mechanism of polyelectrolyte complexation between alginate and chitosan. The fiber porosity and swelling capacity decreased as the immersion period rose, although the inhibitory zone of the G(+) and G() bacteria cultures expanded at the same time. Silver was released from the dressing in a burst manner within 1 hour, followed by a plateau, according to the observed conductivity changes.

By engaging in this behavior, 98% and 72% of Gram-positive and gram-negative bacterial colonies respectively. Even though there was no more sustained production of silver ions after 24 hours, no microbiological development was noticed. The material's water vapor permeability, however, was less than the suggested values for wound dressing materials, restricting its potential usage to specific types of wounds. It was around 1500 g/m2/day. [57]

Zinc Oxide Nanoparticles (Zn O NP)

The antimicrobial activity of Zn O is thought to depend on several mechanisms, similar to other metal and metal oxide nanoparticles (see Figure), including binding to cell membrane lipids and proteins, photocatalytic generation of reactive oxygen species, and possibly the release of Zn2+ ions and disruption of cellular metabolism. Due to the increased surface area and interaction with cell membranes, bactericidal and fungicidal actions of nanoparticles are enhanced. [58] A little amount of research has been done on the integration of ZnONP in alginate dressings, in either single or hybrid hydrogel matrix, even though it is utilized less commonly in wound treatment than nanocrystalline silver.

It's interesting to note that there aren't many ZnONP-loaded dressings. However, Loera-Valencia et al. just presented an important clinical work in this area. Human volunteers with diabetic foot ulcers received either a patch impregnated with Zn O NP or a dressing made entirely of calcium alginate. Despite the final assessed wound area (which was highly variable) showing no significant differences, the difference in healing degree in favor of the Zn O NP alginate dressing (75% vs. 71%) was statistically significant. The examined dressing encouraged healthy tissue granulation and epithelialization. In conclusion, the clinical investigation showed that zinc oxide nanoparticle-loaded alginate dressings are both safe and effective. [59]

Another study that exclusively employed alginate as the matrix created a hydrogel with Zn O NP and compared it to an alginate hydrogel with TiO2 inorganic nanoparticles. Additionally, one of the research's objectives was to contrast the two ways of making hydrogels: manually casting and 3D printing, then ionotropic gelation using calcium chloride. A more uniform lattice structure and smaller, more uniformly spaced pores were guaranteed by the more

complex technique (Figure). Because of the narrower pores and decreased ion diffusion, this also improved hydrogel stability. While the rheological study showed that manually cast hydrogels had a substantially greater elastic modulus and were stiffer, three-dimensionally printed dressings also showed higher swelling capacity. Additionally, it was shown that the addition of Zn O NP changed the rheological as well as mechanical characteristics. The zinc oxide nanoparticles improved the dressing's stability in comparison to a blank sample and a titanium dioxide-infused 3D-printed alginate hydrogel. This is likely because Zn2+ ions helped to crosslink the dressing, which is why it didn't dissolve in PBS over the course of 28 days. Not only did the alginate matrix containing 0.5-1% ZnONP outperform TiO2 hydrogel in terms of S. epidermidis activity, but it also outperformed erythromycin. There were no cytotoxic effects on fibroblasts at the same time. [60].

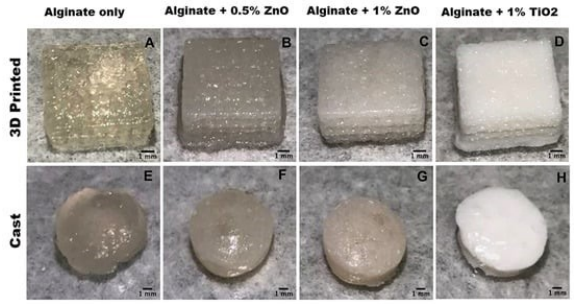

Fig. 4. (A–D) depict 3D-printed lattice structures. (E–H) portray manually casted structures. The scale bar in all images depicts 1 mm.

Chitosan is a well-liked complementary polymer in alginate hydrogels including ZnONP, similar to nanocrystalline silver dressings. According to a study by Nozari et al., ZnONP-loaded film dressings were created using chitosan and a gelatin matrix together with either bentonite or alginate as a binding agent without the use of crosslinking agents. This variation in composition led to several variations in the physicochemical characteristics of the substance. Alginate-prepared hydrogels had a reduced swelling capacity and were more porous, brittle, and rigid. Although all dressings containing zinc oxide were antibacterial, the alginate sample outperformed bentonite in terms of performance against S. aureus and P. aeruginosa. Both were friendly to fibroblasts. [61]

To reinforce the alginate hydrogel, Mohandas et al. added reprecipitated chitosan "pellet" to the sodium alginate solution. To create a porous, flexible composite bandage, the material was next filled with zinc oxide nanoparticles and freeze-dried (Figure). In PBS containing lysozyme, ZnONP was found to considerably slow down swelling without changing the rate at which dressings degraded. The ZnONP dressing was superior to a blank hydrogel and commercial alginate dressing at inhibiting the growth of S. aureus, E. coli, and C. albicans at 0.75%-1% loading. Additionally, the created composite bandage proved bactericidal against MRSA above 5%. The reported cytotoxicity against human dermal fibroblasts, however, would limit the use of this antibacterial potential, as even with this capability, ZnO NP cell viability was reduced to 40%–60% even at concentrations above a relatively modest threshold of 0.25%. [62].

With the use of chitosan derivatives, alginate dressings containing zinc oxide nanoparticles have also been created. In oxidized alginate solution, Zhang et al. dispersed synthesis Zn O NP, which was afterward cross-linked using the Schiff reaction and chitosan oligosaccharide. Although the oligosaccharide has antibacterial and wound-healing capabilities, it does not naturally form a hydrogel; hence, alginate support is required. The addition of Zn O NP enhanced the dressing's mechanical characteristics without impairing swelling or deterioration, and the water vapor transmission rate was comparable to that of a commercial alginate dressing (Coloplast). The produced dressing's long-lasting antibacterial activity, which was effective against G (+), G() bacteria, and yeast, was ensured by a longer release of Zn^{2+} ions. The hydrogel was blood-compatible. The developed alginate-oligosaccharide-ZnONP dressing considerably increased the rate of healing in second-degree scald wounds on rats when compared to a blank hydrogel and silver sulfadiazine. [63]

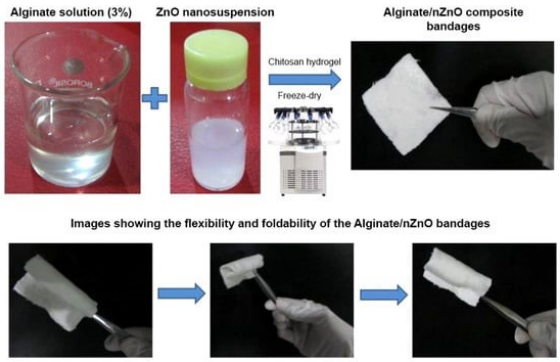

Fig. 5. Photographic representation of the preparation of alginate hydrogel/zinc oxide nanoparticle (n Zn O) composite bandages.

Gum acacia has been utilized among the natural polymers besides chitosan and its variations in alginate dressings that contain zinc oxide nanoparticles. For instance, in one work, alginate and mucilage were cross-linked with glutaraldehyde to

create oval (95 nm) ZnONP-loaded hydrogel nanoparticles (5%) that were then pelleted by centrifugation. It had better bacterial inhibitory capabilities when compared to pure zinc oxide nanoparticles. On the other hand, in a scratch test using cultivated fibroblasts, the hydrogel increased cell growth and monolayer confluence. [64]

Alginate wound dressing with honey

A brand-new and distinctive category of dressings is antibacterial honey dressings. However, there appears to be no related toxicity as with ionic silver. Active Manuka Honey (Leptospermum scoparium) has been observed to exhibit powerful and long-lasting antibacterial activity similar to that of ionic silver. This dressing has reportedly been shown to significantly accelerate healing, lower MRSA levels, and help with debridement. Additionally, it aids in maintaining the moisture balance and the smell that is frequently connected with diseased or heavily colonized wounds. Calcium alginate is used to wet honey to create a hydrocolloid-like rubbery layer. It keeps the honey in touch with the honey gel plate by forming a softer gel to absorb exudate. Antibiotic-resistant strains and other wound pathogens are blocked by alginate dressings (Calcium alginate mechanically bonded to honey) and given dressing (Advancis), which lowers the risk of infection. Osmotic activity causes an exudate flow that eliminates wound microorganisms, endotoxins, debris, and skinning. Granulation and epithelialization are encouraged in the ideal healing environment. Leg ulcers, burns, donor graft sites, and infected wounds can all be treated with this. [65]

Collagen

Animals' bones and skin are primarily made of collagen, which is the most common protein in the animal kingdom. It belongs to the large family of extracellular Matrices. The Greek word "Kolla," which means glue, is whence the word "collagen" got its meaning. It is a kind of natural polymer with excellent moisturizing, repeatability, and biodegradability qualities. [66].

Collagen structure: Collagen's fundamental structural component is made up of three polypeptide chains, two of which are similar (chain 1) and the third of which has a slightly different chemical composition (chain 2). These chains are organized in the shape of a triple helix. It is therefore a hetero polymer. Each chain is made up of 1050 amino acids that are coiled into a 300 nm long right-handed helical shape. It is around 1.5 nm in diameter and has a molecular weight of 2,90,000. Gly-X-Y is a recurring motif in its structure, with proline and hydroxyproline serving as the most common examples of X and Y among all amino acids. Glycine is essential for allowing a strong packing of the three chains in the tropocollagen molecule at each third amino acid position. Collagen is arranged to create fibrillar collagen types in hexagonal and nearly hexagonal forms. This packaging could be microfibrillar or sheet-like. [67]

Collagen sources: Both natural and artificial materials are used in the production of collagen.

Natural sources: Both animal and plant sources can provide collagen supplies. The most common animal sources of collagen are marine organisms, porcine, human, and bovine. Other landed animal sources include the sternal cartilage from domestic birds like chickens (broiler and laying hens), turkeys, quails, ducks, and geese as well as bovine skin, tendon, and bones from buffalos, lambs, equines, porcine, ovines, and rabbits. [68]

The biochemical and physical properties of marine collagen, such as that found in scale fish and fish skin, are comparable to those of swine and bovine collagen. Teleost and cartilaginous fish from freshwater and marine environments, as well as marine invertebrates, are thus valuable resources. [68].

Synthetic sources: To prevent the immunological problems produced by naturally occurring collagen, collagen supplies are increased. One of these sources is KOD, a chemical that is sold commercially. It is a synthetic 36-amino acid protein that self-assembles into hydrogels and triple-helix nanofibers.

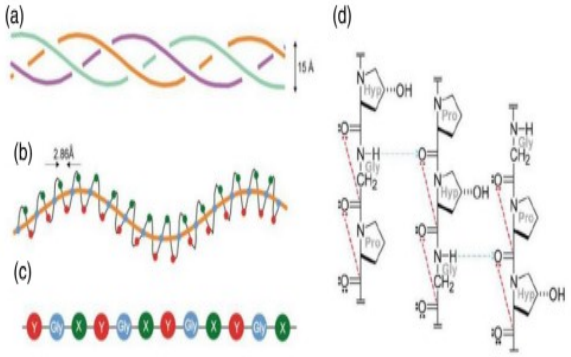

Fig. 6. (a) triple-helix of collagen. Every -chain is entangled to generate the gly-x-y repeat in (b), and (c) x and y mostly stand for proline and hydroxyproline residues. (d) collagen hydrogen bonds and n-*nteractions are shown as blue and red dashed lines, respectively. [69]

Recombinant technology has been used to generate a new synthetic collagen source that provides high-quality, animal-derived collagens devoid of contaminants. It is produced using yeast,

insect, mammalian, and plant cell cultures, among others. Recombinant technologies have drawbacks including high costs, low yields, and a lack of cofactors or enzymes in the systems. For these reasons, animal collagen is the gold standard for use in both scientific and therapeutic settings. The table lists the benefits and drawbacks of collagen from various sources.

Collagen applications in medical textile

1 - Wound healing

In contrast to other biomaterials, collagen possesses special biological qualities that enable it to heal wounds. Collagen has a significant part in wound healing as it is a main component of the second layer of human skin (dermis). Collagen can give fibroblasts a comfortable place to rest to enhance wound proliferation and a faster pace of wound healing. Collagen is helpful throughout the hemostasis, inflammation, and remodeling stages of wound healing in addition to proliferation. [70]. Collagen sponges with controlled porosity, in particular (see Figure), have proven effective at absorbing tissue exudate when applied to wounds, ensuring a moist environment and preventing the formation of infectious processes and mechanical damages. With a larger surface area, the porosity facilitates the movement of cells and nutrients while also promoting cell adhesion, development, and migration..

Table 1. Comparison of advantages and limitations of collagen from different sources.

Source	advantages	limitations
mammalian and marine tissue	High yield	• Interspecies disease transmissions • Restrictions based on religion
Recombinant collagen is produced using genetically engineered microorganisms, animals, and plants	No batch-to-batch variation	• Low yield • Low thermal stability • Lack native post-translational modification mechanism
Synthetic collagen formed with collagen-mimicking sequences (Gly-X-Y)	Tailorable biofunctionality	• Lacking self-assembling capabilities

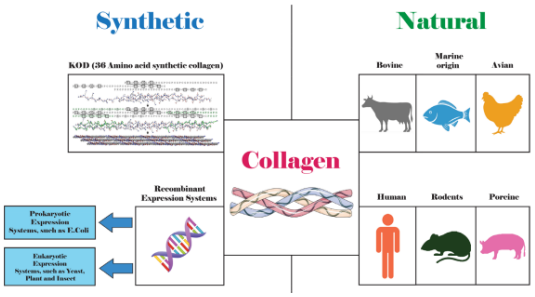

Fig. 7. The sources of collagen

By offering soft tissue sutures and growth templates for new tissues, sponge implants into burn sites can hasten skin recovery.17 Type I collagen sponges are distinguished by their fibrillar structures, which speed up the healing process and raise the tensile strength of exposed skin wounds. Due to their streamlined and uniform construction, these membranes are widely utilized in wound healing and dressings since they can facilitate both preoperative and after-surgical procedures. Currently, a variety of commercial dressings are used to heal ulcers and preserve burn wounds. [69].

ponges for burns/wounds

Collagen helps in the development of biomedical applications because of its unique characteristics, including porosity, meshwork and sponge-like structure forming capacity, high biocompatibility, and surface qualities. This kind of collagen is used to treat skin conditions like burns and ulcers. By encouraging wound contraction and the creation of scar tissue, epidermal growth factor (EGF) placed in collagen sponge matrix aids in the establishment of the dermal matrix and increases the mechanical strength of wounds. [71] For the control-led release of medications to achieve prolonged release activity, succinylated collagen manufactured as a bilayer dressing material when loaded with chemotherapeutic agent such as ciprofloxacin is used. When loaded with therapeutic chemicals like cytokines and growth factors, collagen sponge promotes the growth of keratinocyte and fibroblast donor cells. [72]

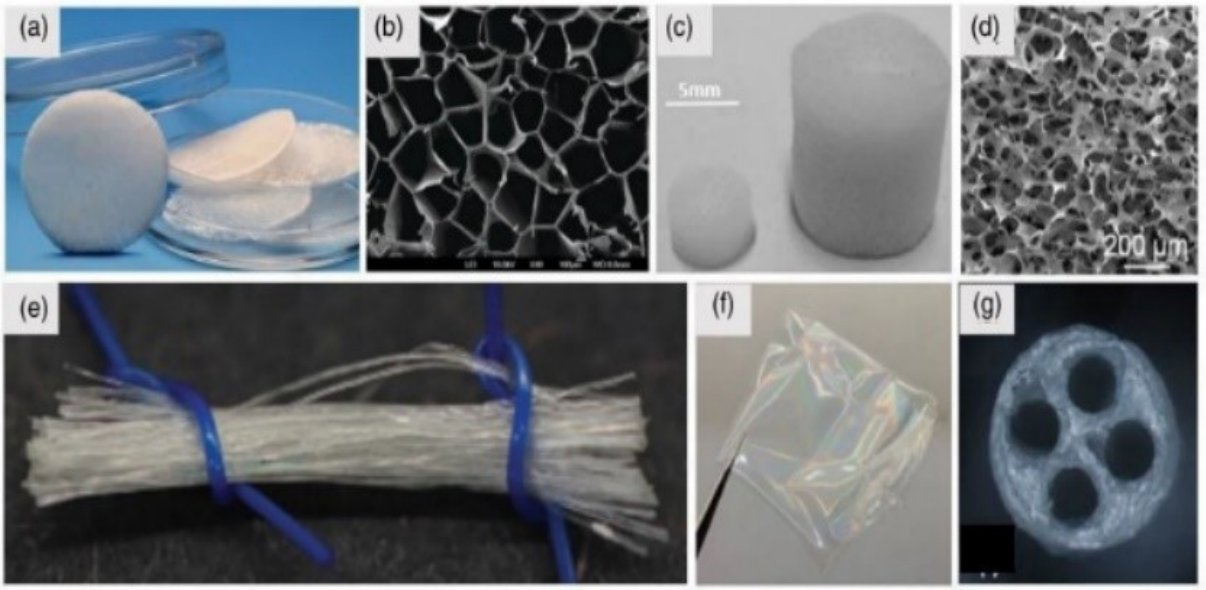

Fig. 8. Type I collagen-based collagen sponge discs (Sponge Col) in (a) and (b) scanning electron microscopy (SEM) images of the porous network structure. (c) Scaffolds of various sizes, and (d) an SEM view of a collagen scaffold made from jellyfish. (e) A group of type I collagen fibers that were extruded. (f) A collagen-type I translucent film. Neural conduit is made of several channels of type I collagen9. [73].

Collagen Hydrogel Formation Mechanism and Modification

Collagen serves as the primary base component in the preparation of collagen-based hydrogels. When aqueous solvents are present and certain conditions are met, collagen molecules can spontaneously form collagen fibers. In the body, collagen has good mechanical stability, flexibility, thermal stability, and enzymatic stability. However, properties like mechanical strength, thermal stability, and resistance to enzymatic degradation are significantly reduced when removed and used, calling for modification for future biological uses. Processing collagen-based hydrogels is based on collagen's ability to self-assemble. The self-assembly of collagen molecules can be affected simultaneously by changes in the solution environment, the addition of exogenous additives, and physical or chemical crosslinking, as schematized in Figure. This can alter the final structure and property evolution of collagen-based hydrogels. [74].

Solution Condition: One of the elements affecting collagen-based hydrogels is the solution condition, which includes the collagen content, polymerization temperature, and polymerization pH. The self-assembly of the collagen base and collagen concentration are causally related. [75] It has been demonstrated that collagen concentration and the mechanical properties of collagen-based hydrogels are positively associated and that as collagen concentration rises, the pore size of collagen-based hydrogels decreases, making them less favorable for cell inoculation and survival. The temperature is intimately related to the collagen hydrogel preparation process. [76]. Although 25 °C has also been employed, it has been observed that physiological temperature (37 °C) is where most gelation occurs. Additionally, the gelation process has been carried out in cryo-environments, or at extremely low temperatures.

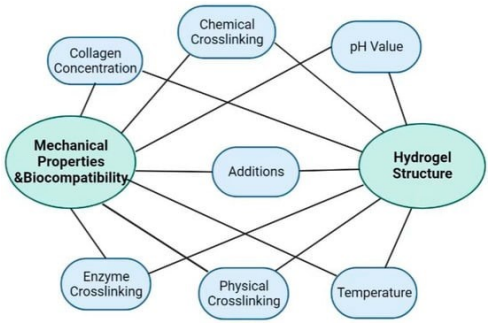

Fig. 9. Collagen hydrogel formation mechanism (produced using Bio Render). [74]

Higher temperatures cause collagen molecules to denature and speed up their self-assembly behavior, which results in a loss of collagen fibers' ordered structure and eventually has an impact on the structure of the hydrogel. Collagen-based hydrogels' mechanical characteristics have been discovered to positively correlate with pH. The pH range of 7.4 to 7.8 is where cells thrive the best. As that range approaches the alkaline side of the ideal pH range

(and more gradually towards the acid side), cell proliferation abruptly decreases. [77]

Addition of Ingredients

A second component, often referred to as co-blending modification, is added to collagen-based hydrogels to enhance performance. This component makes up for the shortcomings of the collagen material by using the benefits of other materials. Although less biocompatible, synthetic polymers like polyethylene glycol and polyvinyl alcohol when combined with collagen enhance the dressing's mechanical qualities. Meanwhile, the mechanical qualities of the dressing are improved and made more biocompatible when natural polymers like chitosan and hyaluronic acid are combined with collagen. The mechanical properties of collagen scaffolds are enhanced by the addition of natural polymeric materials, which also raise the compressive strength and swelling rate while lowering the degradation rate. [78]

Crosslinking physically: Physical crosslinking, which creates a three-dimensional network structure and a viscoelastic gel system, is the cross-linking of collagen under the physical influences of UV light, -ray irradiation, heating, and freeze-drying. This can alter the mechanical properties and microstructure of collagen hydrogels without introducing any potentially harmful chemicals into the patient's tissue. Collagen is easily cross-linked using the dehydrothermal (DHT) procedure, which exposes the molecules to high temperatures (>90°C) in a vacuum. However, collagen deformation results from DHT crosslinking, and denaturation gets worse with exposure duration and temperature. The DHT-induced crosslinking reaction can also take many days. In residues of aromatic amino acids like chromic acid and phenylalanine, ultraviolet exposure can result in the creation of unpaired electrons. Collagen crosslinking may develop as a result of the ions that the irradiation of nearby collagen molecules produces.

However, UV light can damage collagen. Collagen deterioration is caused by too high temperature and prolonged exposure. However, when exposed to UV radiation, crosslinking and denaturation processes collide. The final mechanical characteristics and degradation of collagen biomaterials are influenced by the balance of these two processes. Crosslinking's intricacy makes it challenging to precisely alter it, therefore the interaction of physics and chemistry has drawn the interest of numerous researchers. The photosensitizer and UV light interacts in this method to create intra- and intermolecular linkages inside the collagen fibers. Collagen crosslinking caused by UV-riboflavin or UV- GelMA is frequently utilized to treat skin tissue. [79-81]

Crosslinking by Chemicals

Chemical crosslinking with synthetic chemicals is the most popular method for enhancing the properties of biomaterials. The polymer chains are crosslinked to generate the appropriate collagen hydrogel through chemical crosslinking, which is the modification and reaction of functional groups like carboxyl and amino groups in collagen by the choice of suitable crosslinking chemicals. With this technique, a hydrogel can be created quickly, but even after washing, the crosslinking agent may still be present. [82]. Due of its strong reactivity and low cost, glutaraldehyde (GA) was the first crosslinking agent used. To bind the collagen, the two glutaraldehyde aldehyde groups can form Schiff bases with two main amino groups from the same or distinct molecules. Even after numerous washings, the material's byproducts and unreacted compounds remain. There are replacements for glutaraldehyde that are substantially less harmful to cells, such as 1-ethyl-3-(3dimethylaminopropyl) carbodiimide (EDC), N-hydroxysuccinimide (NHS), genipin, and dialdehyde starch (DAS). EDC-NHS is a "zero-length" crosslinking agent that can help amide bonds form by joining the amino group of collagen to the carboxyl group of glutamic or aspartic acid. EDC is not released into the collagen matrix during the crosslinking process but rather is changed into water-soluble urea derivatives. EDC/HNS greatly improves the physicochemical properties of collagen while having low cytotoxicity. [83].

Genipin is a substance that is taken out of the fruit of Gardenia jasminoides. It has a range of active groups, including hydroxyl and ester bonds, which can directly interact with proteins or amino acids and help to preserve the collagen scaffold's fundamental structure while enhancing its biological stability. Natural starch and periodate react to produce dialdehyde starch (DAS), a macromolecular aldehyde. As a poly aldehyde polymer, it can cause a crosslinking reaction with collagen's amino and imino groups. DAS has been utilized to crosslink collagen to change its mechanical characteristics because of its extremely low toxicity, biodegradability, and antiviral action. [84].

Collagen-Based Hydrogel for Skin Wound Healing

The hydrogel mats for wound care can be categorized into one of three groups, depending on whether they are made of pure collagen, natural and/or synthetic polymers, or bioactive.

Pure Collagen: To boost their biological effects, collagen can be loaded with therapeutic agents, however in some cases, they are used as plain collagen without bioactive agent integration. Collagen in its purest form is safe; nevertheless, the

incorporation of bioactive compounds might result in dangerous reactions. Collagen-based hydrogels are reportedly great choices for use as scaffolding for wound dressings. A novel hydrogel wound dressing with 10 mg/mL PSC was created by extracting collagen from tilapia skin (PSC). [85]. PSC hydrogels are suitable for use on wounds, as evidenced by the good biocompatibility shown by NIH-3T3 cells after three days of cultivation with the gels.

Collagen Blends with Natural Polymers

The primary component of the ECM and the simplest glycosaminoglycan (a type of negatively charged polysaccharide) is hyaluronic acid (HA). Throughout the healing process, it actively takes part in tissue remodeling, migration, and proliferation. An increase in the HA ratio, which encourages water absorption, leads to a change in pore size. [86]. reported employing covalent crosslinking to create ECM-like collagen and hyaluronic acid (Col/HA) hydrogel. The Col/HA hydrogel's swelling ratio was noticeably higher than that of a single Col hydrogel. It was suggested that hyaluronic acid, principally because of its high water absorption capacity, could enhance the swelling features of the Col/HA hydrogel. When the scaffold was tested in vivo, the Col/HA hydrogel-treated wound produced granulation tissue that was the thickest, measuring about 1300 m, which was 300 m thicker than the other groups. It has been shown that HA crosslinking can slow down the breakdown of Col/HA hydrogels while only mildly inflaming the tissue. As shown by the quick wound healing seen when it was applied to a lesion, this hydrogel actively encouraged the formation of the vasculature, epithelium, and collagen fibers. [87].

Collagen Blends with Synthetic Polymers: Synthetic polymers lack bioactive moieties, however, they do have the benefits of excellent reproducibility, ease of customization for the required applications, and minimal immunogenicity. PVA, a polyvinyl alcohol, has remarkable mechanical qualities. Hydrogels were made using PVA and collagen. [88]. They found that the PVA addition improved the hydrogels' tensile mechanical characteristics. The stress of mixed hydrogels increased considerably from 6 to 33 kPa at a 40% strain compared to pure collagen hydrogels, showing that PVA was principally responsible for the hydrogels' enhanced mechanical characteristics by forming sophisticated network entanglements. According to experiments on permeability, scanning electron microscopy (SEM), and water retention, the mixed hydrogels' microstructure was solid and made up of close-knit meshes, which is compatible with the results of tests on their mechanical properties. created a brand-new composite hydrogel for a wound dressing using sodium alginate (SA), PVA, and HLC. The quickest hemostasis time was 17.33 s, demonstrating the hydrogel dressings' outstanding hemostasis activity. In a rabbit model of full-thickness wounds, they saw that the PVA/HLC/SA hydrogels achieved wound closure on day 10. Their findings demonstrated the hydrogel's significant promise as a dressing for skin wound healing by demonstrating its ability to stimulate wound healing and the production of new skin while also accelerating the contraction of full-thickness wounds. [89].

Collagen Blends with Bioactives: To increase the therapeutic efficacy of wound dressings, a variety of bioactive substances can be added. Bioactive chemicals include things like antibiotics, metal nanoparticles (like silver and copper), plant extracts (like curcumin), growth factors, and microorganisms. Some of these therapeutic substances can significantly improve the properties of hydrogels, and their ability to distribute drugs makes them perfect for treating wounds.

A unique method for strengthening and stabilizing collagen tissues involves blending with functionalized nanoparticles. By directly attaching to the side-chain substance of collagen, metal oxide nanoparticles crosslink collagen, enhancing the mechanical properties of collagen-based scaffolds. In response to the rapid rise in antibiotic resistance in recent years, the worsening of infections brought on by drug-resistant bacteria, and the sluggish rate of wound healing, metal nanoparticles are being used to impart the properties of metal ions to crosslinked scaffolds, including broad-spectrum antibacterial properties, scavenging of free radicals, and reducing inflammation.

created a hydrogel with collagen as the foundation and added chitosan, and silver ions (COCAg), which have outstanding antibacterial properties. The hydrogel also exhibits injectability and self-healing properties as a result of the Schiff base reaction. Additionally, a double-network crosslinked composite hydrogel was created using photocrosslinking and a Schiff base reaction to improve the low stability of hydrogels. The COCAg group was shown to contain the fewest microorganisms in the in vivo experiments (Figure). On day 14, the COCAg group's wounds had fully recovered, whereas those in the COC and gauze groups were still open. The COCAg hydrogel offers a lot of potential as a dressing for infected wounds, according to this. [90].

created nanocomposites of collagen and silica that can transport two antibiotics. They inserted silica nanoparticles containing gentamicin and rifamycin into collagen hydrogels to test the efficacy of the composite hydrogels as a drug delivery system for the avoidance of chronic wound infections. They discovered that the presence of a collagen network could slow down silica nanoparticle disintegration.

As a result, the nanocomposite's steady release of gentamicin for more than a week provided good antibacterial action. The collagen hydrogels' structure is altered by rifamycin-loaded silica particles at high silica concentrations, and the rifamycin that is released is adsorbed on the surface of the positively charged collagen fibers, which results in a lack of antibacterial effectiveness in the composites. The in vivo performance of these materials for use in wound healing was then examined, as well as their biocompatibility and potential inflammatory reactions. In vitro testing revealed a 2-log drop in the amount of bacteria present in the wound, and the ensuing inflammation subsided. Histological analysis of albino rabbit skin revealed that following treatment, M1 inflammatory macrophages were not present in the wound bed. The ability of these composite hydrogels to function as biological dressings that carry antibiotics is significantly influenced by the complex interplay of interactions between medications, silica, and collagen. [91].

Conflicts of interest

There are no conflicts to declare

Funding sources

There is no fund to declare

Acknowledgments

The authors are gratefully-grateful to acknowledge the Faculty of Applied Arts, Benha University. Furthermore, the authors are gratefully grateful to acknowledge the Central Labs Services (CLS) and Centre of Excellence for Innovative Textiles Technology (CEITT) in Textile Research and Technology Institute (TRTI), National Research Centre (NRC) for the facilities provided.

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البوليمرات الطبيعية في المنسوجات الطبية

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الملخص

في العديد من التطبيقات الطبية الحيوية ، بما في ذلك الأدوية والسقالات لتجديد الأنسجة وأنظمة توصيل الأدوية وعوامل التصوير ، تم استغلال البوليمرات الطبيعية على نطاق واسع. إنها بمثابة قوالب للتجديد والضمادات للجروح الحادة أو المزمنة في العناية بالجروح. هناك العديد من المصادر الطبيعية للبوليمرات ، بما في ذلك النباتات والحيوانات والكائنات الحية الدقيقة. تعتبر السقالات الطبيعية القائمة على البوليمر مرغوبة لإصلاح البشرة وتجديدها نظرا لتماثلها مع المصفوفة خارج الخلية ، والضبط الميكانيكي ، والتوافق الحيوي العالي ، والقدرة العالية على الاحتفاظ بالمياه. سيتم تقديم نظرة عامة على البوليمرات الطبيعية الشائعة أو الواعدة لالتئام الجروح في هذا الفصل.

الكلمات الدالة: البوليمر الطبيعي ، الشيتوزان ، الجينات ، الكولاجين ، المنسوجات الطبية.