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POLYMER-BASED BIOMATERIALS FOR WOUND HEALING: ADVANCES IN NATURAL, SYNTHETIC AND HYBRID BIODEGRADABLE POLYMERS FOR SCAR REDUCTION AND SKIN REGENERATION

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The management of skin wounds resulting from trauma and different pathophysiological diseases still presents a major challenge in healthcare, which greatly contributes to the worldwide economic burden. Recently, wound dressings based in nanotechnology and polymeric systems have emerged as a viable option to improve the healing process. Natural Biodegradable polymers, which include collagen, cellulose, chitosan (CS), and hyaluronic acid (HA), have shown high biocompatibility and efficacy in promoting wound healing. Despite these advantages, wound dressings made of biodegradable synthetic polymers provide a promising alternative by overcoming the limitations of natural polymers and displaying desired properties for skin wound treatment. The synthetic polymers include polycaprolactone (PCL), polyvinyl alcohol (PVA), poly (lactic-co-glycolic acid) (PLGA), polylactic acid (PLA), polyurethane (PU), polyethylene glycol (PEG), polyethylene oxide (PEO), and polyglycolic acid (PGA). These polymers are biocompatible, present a versatile chemical structure, and are easily modified to obtain distinct mechanical properties and degradation rates. Overall, these polymers are less expensive than natural polymers. This review outlines the optimal management and care required for wound treatment with a special focus on natural and synthetic biopolymers, drug-delivery systems, and nanotechnologies used for enhanced wound-healing applications

Keywords: *wound healing, wound management, dressings, biodegradable polymer, natural polymers, synthetic polymers*

INTRODUCTION

The skin is a complex barrier system consisting of surface keratinocytes, inter-keratinocytes, dermis, and subdermal structures[1]. It is the first line of defense to protect our bodies from external disturbances such as UV exposure, chemical and mechanical strain, and infection[2]. The skin is one of the most accessible organs of the body, with an average thickness of approximately 2.97 ± 0.28 mm. It serves as a critical barrier, separating the underlying blood circulation network from the external environment, regulating body temperature and blood pressure, and preventing physical, chemical, and microbiological attacks[3]. It is an ideal location to provide therapeutic chemicals for both local and systemic effects, but many of these drugs are frequently impermeable to the skin[4]. The human skin is composed of three layers: epidermis, dermis, subcutaneous tissues, and several skin appendages: hair follicles, eccrine glands, and sebaceous and apocrine sweat glands [5], as shown in **(Fig. 1)**.

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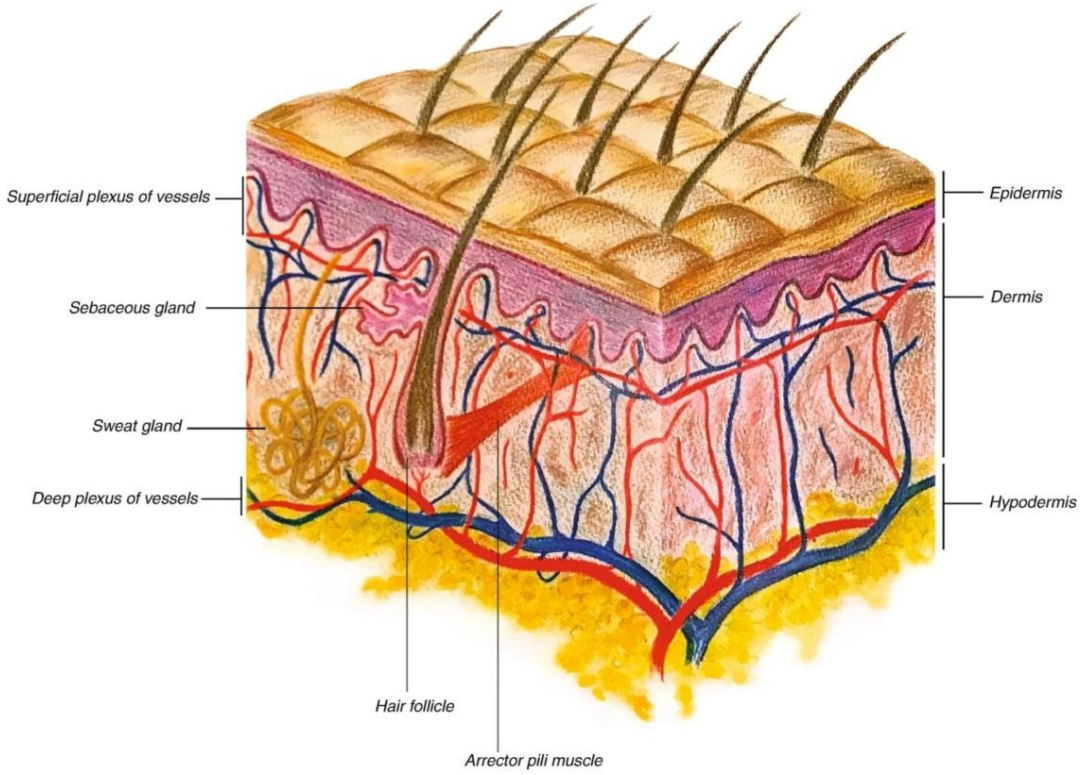


Fig.1: Schematic representation of skin layers and its appendages [6].

Epidermis

The entire outer surface of the body is covered in this continuously self-renewing, stratified squamous epithelium, which is primarily made up of two types of cells: the living, or viable, cells of the malpighian layer (viable epidermis) and the dead cells of the stratum corneum[6]. The stratum corneum is the outermost protective layer of the epidermis and is called the horny layer. It is the rate-limiting barrier that restricts the movement of chemical substances inward and outward. This layer is composed of 15–20 layers of flattened corneocytes (keratinocytes) with no nuclei or cell organelles embedded in a lipid matrix of ceramides, cholesterol, and fatty acids arranged in bilayers [7]. Viable epidermis is further classified into four different layers: stratum lucidum, stratum granulosum, stratum spinosum, and stratum basal [8].

Dermis

The dermis is the skin layer immediately below the epidermis, which is 3 to 5 mm thick, and its specialized cells (fibroblasts) oversee the production of collagen and elastin fibers, which are responsible for the strength and flexibility of the skin. It consists of a matrix of connective tissue comprising blood vessels, lymph vessels, nerve endings, hair follicles, smooth muscles, sweat, and oil glands. The supply of cutaneous blood has an important role in controlling body temperature. It also removes waste and impurities from the skin while supplying it with nutrients and oxygen. Most molecules that pass through the outer layer of the skin are quickly diluted and transported systemically by the blood because capillaries extend to a point around 0.2 mm below the skin's surface, close to the dermis-epidermis boundary. The dermal concentration of the majority of transdermal medications is kept low by this abundant blood flow, which creates a concentration gradient that runs from the exterior of the body into the skin and allows drug delivery through the skin [3].

Hypodermis

It is the innermost layer, attached to the dermis by collagen and elastic fiber, and is also called subcutaneous fat. It acts as a storage area for fat. It consists mainly of lobules of adipocytes as well as connective tissue. This layer facilitates to control of the temperature

and provides mechanical protection and nutritional support. It carries to the skin major blood vessels and nerves and may contain organs of sensory pressure. Drugs must penetrate all three layers and enter systemic circulation for transdermal drug delivery [3].

Wound Healing Process

A wound is a disruption of the integrity of the skin and underlying tissues caused by physical, chemical, or pathological factors [9]. It can be classified based on various criteria, including duration, cause, and depth [10]. Based on duration, wounds are categorized as acute or chronic; acute wounds heal within a predictable timeframe, typically 4–6 weeks, whereas chronic wounds persist beyond this period due to underlying pathological conditions such as diabetes or vascular insufficiencies [11]. Classification based on etiology includes traumatic wounds, which result from external mechanical forces such as lacerations and abrasions; surgical wounds, which arise from medical interventions; burn wounds, caused by thermal, chemical, electrical, or radiation exposure; and pathological wounds, which develop due to underlying diseases, such as diabetic foot ulcers and pressure ulcers [12]. Furthermore, wounds can be categorized by depth, with superficial wounds involving only the epidermis, partial-thickness wounds extending into the dermis, and full-thickness wounds penetrating beyond the dermis into subcutaneous tissue, muscle, or bone [13]. These classifications are critical in determining appropriate treatment strategies and optimizing wound healing outcomes.

Wound healing is a complicated process that involves the interaction of a variety of components, including immune cells (such as monocytes, neutrophils, macrophages, and lymphocytes), non-immune cells (such as endothelial cells, keratinocytes, and fibroblasts), extracellular matrix (ECM) components, and soluble mediators (such as cytokines and growth factors) [14]. The healing rate of acute wounds differs from that of chronic wounds and is influenced by the immune system. Wound healing usually happens in four stages: hemostasis, inflammation, proliferation, and remodeling [15] **(Fig. 2)**.

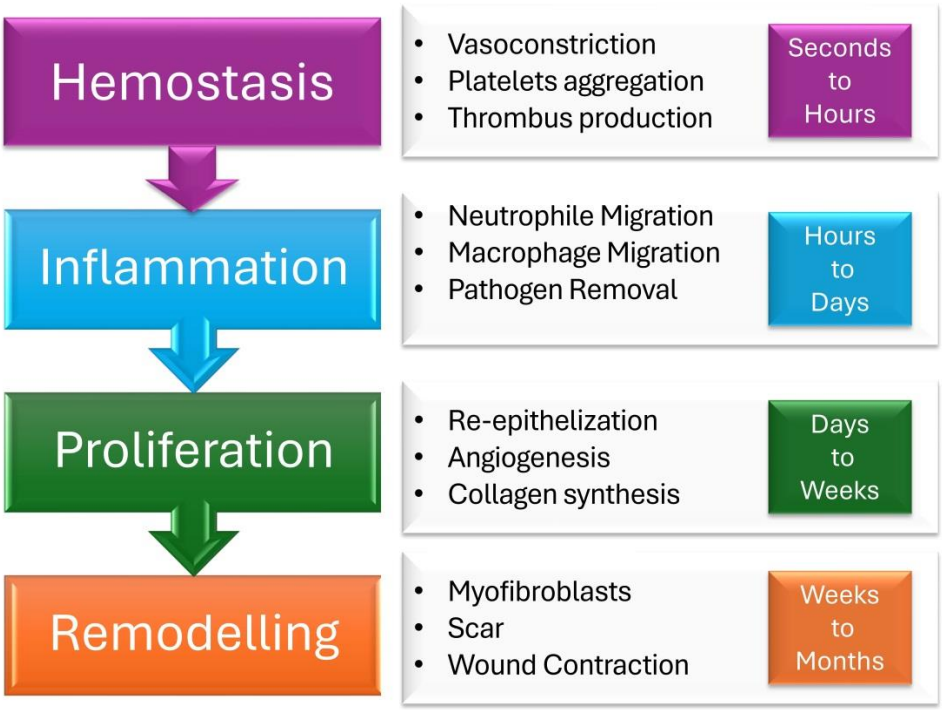


Fig.2: Wound healing phases [15].

The wound healing process begins with the hemostasis phase, during which a fibrin clot forms, serving as a protective barrier against external elements and promoting optimal moisture retention [16]. Following this, the inflammatory phase is initiated, characterized by the release of pro-inflammatory cytokines from damaged tissues. These cytokines attract circulating white blood cells, while degranulated platelets and activated macrophages release various growth factors [17]. The proliferation phase follows, marked by essential processes such as granulation tissue formation, extracellular matrix (ECM) synthesis, angiogenesis, epithelialization, and wound contraction[18]. During this phase, collagen molecules self-assemble into a triple-helical structure, are released into the extracellular environment, and form stable cross-links to enhance tissue strength and stability. Finally, the remodeling phase involves the gradual transformation of granulation tissue into scar tissue, a process that typically spans six to twelve months [19].

Wound Management

The main purpose of wound care is to reduce scarring and patient suffering while hastening the healing process [20]. The objective of effective wound treatment should be to prevent the infiltration of microbes, reduce the production of necrotic tissue, and minimize the formation of scar tissue. Recently, a variety of medications have been established and divided into two main groups: both traditional and advanced dressings. A traditional dressing is a material that is applied directly to the damaged area to maintain hemostasis protection and coverage. On the other hand, an advanced dressing is designed to provide a moist microenvironment and a steady temperature, eliminate necrotic material and exudates, and provide defense against exogenous infection [21]. The skin's ability to naturally heal minor injuries is truly remarkable. However, if the harmed skin area is large, a suitable treatment or dressing is necessary.

The primary goals of wound dressings are to facilitate optimal wound healing, protect the wound from external contamination, and manage exudate while maintaining a moist healing environment[22]. An ideal wound dressing should provide a moist environment to promote epithelialization and tissue regeneration, protect against infection by acting as a barrier to microbial invasion, and absorb excess exudate to prevent maceration of surrounding skin [23]. Additionally, wound dressings should facilitate autolytic debridement, allowing the natural removal of necrotic tissue, while also being non-adherent and atraumatic to minimize pain and tissue damage during dressing changes[24]. Depending on the type of wound, dressings may also serve specialized functions such as delivering therapeutic agents (e.g., antimicrobial, anti-inflammatory, or growth-promoting compounds), providing insulation to maintain optimal temperature, and offloading pressure in chronic wounds like pressure ulcers[25].

An appropriate wound dressing should be chosen based on three fundamental perspectives: biological, patient focused, and medical [26,27]. Biologically, it should maintain a moist wound environment, promote angiogenesis and granulation tissue formation, modulate inflammation, and facilitate autolytic debridement, all while being biocompatible and non-immunogenic[28]. Advanced formulations may incorporate bioactive agents such as growth factors or antimicrobial peptides to enhance cellular responses[29]. From the patient's perspective, wound dressings should not only be effective but also prioritize comfort, convenience, and adherence to treatment regimens [30]. One of the most critical factors is pain minimization, particularly during dressing changes, which necessitates the use of non-adherent materials that do not disrupt newly formed granulation tissue [31]. Additionally, the dressing should be breathable and flexible, allowing for adequate oxygen exchange while conforming to anatomical structures, especially in wounds located in highly mobile areas such as joints [32]. Furthermore, given the economic burden associated with chronic wound care, an ideal dressing should be cost-effective and require infrequent changes, thereby reducing financial strain and improving patient compliance [33].

According to a medical perspective, a wound dressing should be practical, versatile, and aligned with standard wound care protocols [34]. It should be easy to apply and remove, minimizing the time required for dressing changes while reducing the need for

frequent intervention by healthcare providers. The dressing should also provide effective microbial barrier properties, as infection control is paramount in wound management, particularly in immunocompromised patients or those with diabetes-related ulcers [35]. Moreover, given that wound healing is a dynamic process, the dressing should be adaptable to different wound types and healing stages, allowing for progression from the inflammatory to the proliferative and remodeling **phases [36].**

Classification of the wound dressings by physical form

Wound dressings are categorized based on their physical structure **(Figure 3)**, which determines their absorption capacity, permeability, mechanical properties, and therapeutic applications [37]. Selecting the appropriate dressing is crucial for optimizing wound healing, preventing infections, and managing exudates.

Bandages and Gauze

Bandages and gauze are traditional wound coverings composed of woven or non-woven fibres. They primarily function as protective barriers that aid in exudate absorption, wound coverage, and secondary dressing fixation. While gauze dressings are commonly used for basic wound care, they may not provide an optimal moist healing environment unless combined with advanced dressings or medicated formulations [38,39].

Hydrogels

Hydrogels are water-based polymeric dressings that maintain a moist wound environment, essential for enhancing cellular proliferation, granulation tissue formation, and autolytic debridement [40]. These dressings are particularly beneficial for dry and necrotic wounds, as they provide hydration and facilitate pain relief. They can be in the form of sheets, gels, or impregnated dressings, offering flexibility in clinical applications [26].

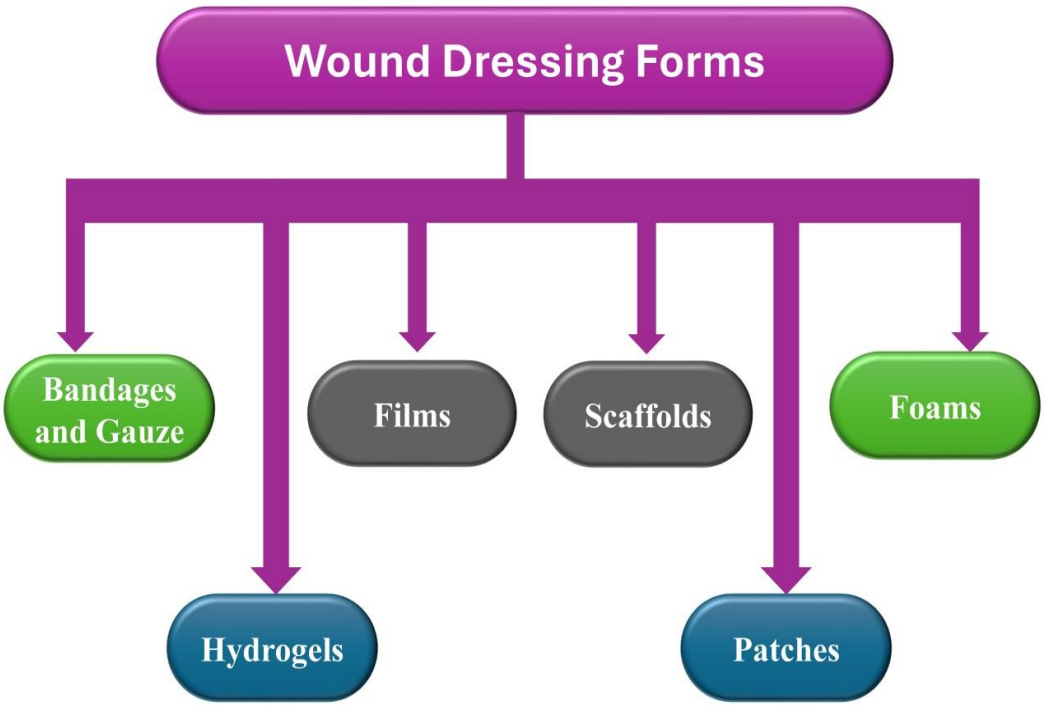


Fig. 3: Wound dressing form.

Films

Film dressings are thin, transparent, and flexible materials, usually composed of polyurethane or other polymeric substances [41]. They act as semi-permeable barriers, allowing gas exchange while preventing bacterial contamination. Due to their adhesive nature, films are best suited for superficial wounds, abrasions, and post-surgical sites. However, their limited absorptive capacity makes them less effective for moderate-to-heavily exuding wounds [42].

Patches

Patches are adhesive-based wound coverings designed for localized drug delivery [43]. These dressings ensure sustained and controlled drug release at the wound site, enhancing therapeutic efficacy. Patches are commonly employed in chronic wound care, burn management, and transdermal drug delivery systems [36].

Scaffolds

Scaffold-based dressings are three-dimensional porous matrices designed to mimic the extracellular matrix (ECM), promoting cell adhesion, proliferation, and tissue regeneration [44]. These biomimetic structures play a crucial role in chronic wound management, deep tissue repair, and regenerative medicine by supporting angiogenesis and fibroblast migration. Scaffolds are particularly beneficial for complex wounds, including diabetic foot ulcers and deep burns [45].

Foam Dressings

Foam dressings are highly absorbent wound coverings made from hydrophilic polyurethane foam[46]. They effectively manage moderate-to-heavy exudates, preventing maceration and bacterial overgrowth. Additionally, foam dressings provide cushioning, thermal insulation, and a protective barrier, making them ideal for pressure ulcers, traumatic wounds, and post-operative sites [47].

Classification of the wound dressing nanotechnology

Nanotechnology-based wound dressings represent a significant advancement in wound care, offering enhanced therapeutic outcomes through precise control over drug delivery, antimicrobial action, and tissue regeneration. These dressings can be categorized based on their composition, functional properties, and mechanism of action [48].

Classification Based on Composition

Wound dressings formulated with nanotechnology can be composed of polymeric, metal-based, or lipid-based nanoparticles. Polymeric nanoparticles, such as chitosan (CS), polycaprolactone (PCL), poly (lactic-co-glycolic acid) (PLGA), polyethylene glycol (PEG), and hyaluronic acid (HA), are widely utilized for their biocompatibility and biodegradability [49]. They enhance wound healing by providing structural support, regulating moisture, and facilitating drug delivery. Metal-based nanoparticles, including silver (AgNPs), copper oxide (CuO), zinc oxide (ZnO), and gold (AuNPs), exhibit potent antimicrobial and anti-inflammatory properties, preventing infections and promoting tissue regeneration [50]. Additionally, lipid-based nanoparticles, such as liposomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs), enable the efficient encapsulation and controlled release of bioactive agents, improving drug stability and absorption [51].

Classification Based on Functional Properties

Nanotechnology-driven wound dressings can also be categorized based on their therapeutic functions. Antimicrobial nanodressings incorporate AgNPs, ZnO, CuO, or antimicrobial peptides to prevent bacterial colonization and biofilm formation, reducing the risk of infection [52]. Additionally, moisture-regulating and absorbent nanodressings, composed of hydrogels and nanofibrous scaffolds, maintain an optimal wound environment by modulating exudate absorption and moisture retention. Some advanced stimuli-responsive nanodressings are engineered to release therapeutic agents in response to external cues such as pH, temperature, or enzymatic activity, ensuring targeted and efficient drug delivery [53].

Classification Based on Mechanism of Action

Wound dressings employing nanotechnology can also be classified based on their mode of action into passive, active, and smart nanodressings. Passive nanodressings primarily serve as protective barriers, shielding wounds from external contaminants while maintaining a suitable healing environment [54]. Examples include electrospun nanofibrous membranes and polymeric scaffolds that mimic the extracellular matrix. Active nanodressings, on the other hand, actively interact with the wound microenvironment to accelerate tissue regeneration, enhance fibroblast proliferation, and combat microbial infections [55]. These dressings often incorporate bioactive nanoparticles that promote angiogenesis and modulate inflammatory responses [56]. The latest advancements include smart and bioengineered nanodressings, which integrate biosensors for real-time wound monitoring and controlled drug release in response to wound conditions. These dressings have the potential to revolutionize chronic wound management by providing personalized and adaptive treatments [57].

Desirable Properties of Wound Dressing Materials

The critical points to consider when preparing a wound dressing to maximize healing ability are; (A) their ability to reduce infections ;(B) their ability to stop bleeding as soon as possible to minimize blood loss; (C) biodegradable; (D) biocompatible; (E) capable of absorbing wound exudates, as a moist environment promotes angiogenesis and collagen synthesis while preventing dehydration, which aids in the healing process [58]; (F) Increase blood circulation in the lesion area by promoting connective tissue synthesis and maintaining an appropriate tissue temperature; (G) should not cause any type of allergy; (H) High mechanical stability and (I) facilitate gaseous exchange between injured tissue and the surrounding environment, as wound healing requires oxygen. Oxygen is required for protein synthesis, angiogenesis, and cell proliferation and (J) has antimicrobial properties. It works at the cellular level to inhibit the growth of microorganisms [25]. (K) simple sterilization; (L) nontoxic to avoid side effects, and (M) easy application and removal from the wound. To avoid trauma during removal, the product should not adhere to the injury site **(Fig. 4)**.

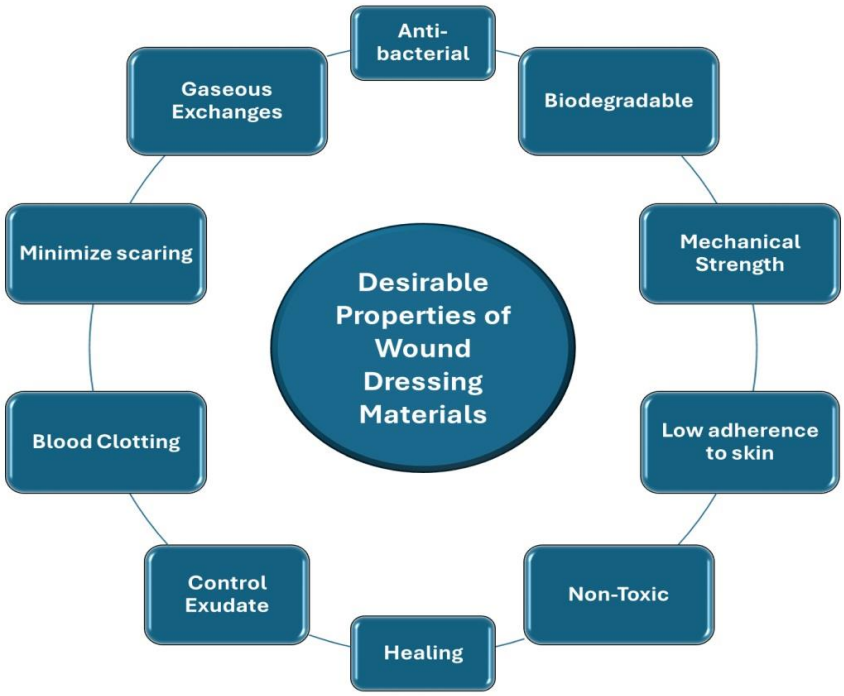


Fig.4: Desirable Properties of Wound Dressing Materials.

Mechanical Properties of wound dressing Materials

The mechanical properties of wound dressings play a crucial role at both macro- and micro-levels, influencing structural integrity, flexibility, and interaction with biological tissues[59]. At the macro level, properties such as tensile strength, elasticity, and flexibility ensure that the dressing maintains durability, conforms to the wound site, and provides adequate protection while allowing patient mobility[60]. At the micro level, the mechanical characteristics of the dressing influence cell adhesion, migration, and proliferation, directly impacting the wound healing process[36]. Materials that mimic the mechanical properties of the extracellular matrix (ECM) can enhance tissue regeneration by supporting cell attachment and growth. Furthermore, wound dressings can exhibit static or dynamic mechanical properties, where static materials provide constant support, while dynamic materials, such as stimuli-responsive hydrogels or shape-memory polymers, adapt to physiological conditions to optimize healing[61]. Achieving an optimal balance between mechanical strength, flexibility, and biocompatibility is essential for developing advanced wound dressings that enhance healing outcomes and patient comfort.

Preparation Methods for Wound Dressings

The fabrication of wound dressings involves various techniques **(Fig. 5)** that determine their physical, mechanical, and biological properties, influencing their absorption capacity, drug release profile, and interaction with tissues. The following are main preparation methods used in the development of advanced wound dressings:

Solvent Casting Technique

This method is a widely used method for preparing polymeric films and membranes. In this technique, a polymer is dissolved in a suitable solvent, and the solution is cast onto a surface or mold. The solvent is then evaporated, leaving behind a thin, uniform polymeric film. This method is commonly used for fabricating hydrogel dressings, bioactive films, and drug-loaded wound coverings [62].

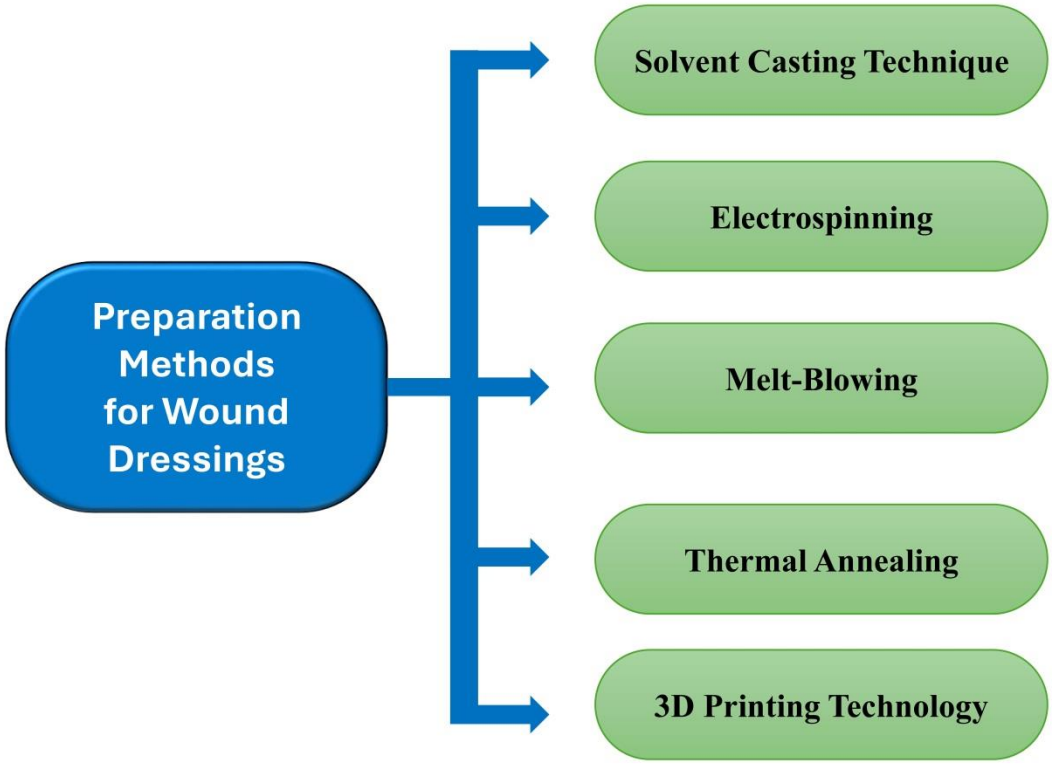


Fig.5: Preparation Methods for Wound Dressings

Electrospinning

Electrospinning is a nanofiber fabrication technique that uses a high-voltage electric field to draw a polymer solution into ultrafine fibres[63]. These nanofibrous structures provide a high surface area-to-volume ratio, mimicking the extracellular matrix (ECM) and enhancing cell attachment, proliferation, and wound healing. Electrospun dressings are highly porous and can be loaded with antimicrobial agents, growth factors, or bioactive compounds to promote tissue regeneration [64].

Melt-Blowing

Melt-blowing is a solvent-free technique that involves extruding a molten polymer through fine nozzles while applying high-velocity hot air, which stretches the polymer into micro- or nanofibers [65]. This process produces nonwoven, highly porous structures with excellent fluid absorption properties, making them ideal for moisture-regulating wound dressings, antimicrobial mats, and controlled drug delivery systems[66].

Thermal Annealing

Thermal annealing is used to modify the mechanical and structural properties of polymer-based wound dressings [67]. It involves exposing the material to controlled heating conditions, allowing polymer chains to rearrange and stabilize, which enhances durability, flexibility, and strength. This method is particularly beneficial for hydrogels, films, and electrospun scaffolds, improving their stability and biocompatibility [68].

3D Printing Technology

3D printing is an advanced additive manufacturing technique that enables the precise fabrication of customized, patient-specific wound dressings [69]. Using bioprinting or extrusion-based printing, wound dressings with complex architectures, drug reservoirs, and bioactive components can be designed. This method is particularly promising for personalized medicine, regenerative wound care, and tissue-engineered scaffolds [45].

Polymer Based Dressings

The choice of polymers for biomedical applications, such as wound dressings depend on critical properties including biodegradation, bioerosion, bioresorption, permeability [70] and molecular weight [71]. Firstly, biodegradation involves the enzymatic or microbial breakdown of polymers into smaller, non-toxic molecules, making it essential for temporary biomedical materials that do not require removal[72]. Secondary, bioerosion refers to the gradual breakdown of polymers through chemical or physical processes, including hydrolysis and dissolution, ensuring controlled degradation *in vivo*[73]. Tertiary, bioresorption describes the complete degradation and absorption of polymer byproducts, allowing for safe metabolism and excretion without adverse immune reactions, a crucial feature for biodegradable implants and scaffolds[74]. Conversely, permeability determines the diffusion of gases, liquids, or bioactive molecules through the polymer structure, playing an important role in moisture retention, oxygen exchange, and controlled drug release in wound healing and drug delivery applications [27].

On the other hand, molecular weight is a critical factor in polymer selection, as it directly influences degradation rate, mechanical strength, permeability, and processability, all of which are essential for biomedical applications [71]. Polymers are characterized by different molecular weight (MW) averages, including number-average molecular weight (Mn), which affects solubility and degradation; weight-average molecular weight (MW), which determines mechanical properties and viscosity; and viscosity-average molecular weight (Mv), which is relevant to processing and performance[75]. Lower molecular weight (LMW) polymers tend to degrade faster, making them suitable for short-term applications like resorbable wound dressings and drug delivery systems[71], whereas higher molecular weight (HMW) polymers offer greater mechanical strength and durability, making them ideal for long-term implants or scaffolds[76].

Hydrophobicity of the polymer

Hydrophobicity refers to a polymer's ability to repel water and resist dissolution in aqueous environments, significantly impacting its wettability, swelling behavior, degradation rate, and bioadhesion[77]. Hydrophilic polymers

exhibit a strong affinity for water, leading to high absorption, swelling, or dissolution, making them suitable for hydrogels, bioadhesive drug carriers, and wound dressings, where moisture retention enhances cell proliferation, drug diffusion, and tissue regeneration [27]. In contrast, hydrophobic polymers repel water and are more soluble in non-polar solvents, displaying low water absorption and slower degradation rates, making them ideal for long-term implants, protective coatings, and controlled drug release systems that require minimal moisture interaction[78]. The hydrophobic or hydrophilic nature of a polymer directly influences biodegradation kinetics, drug release profiles, and biocompatibility, necessitating careful selection based on the intended biomedical application[79]. Finally, hydrophilic materials are preferred for moist wound dressings and tissue scaffolds, while hydrophobic polymers are used in barrier coatings and extended drug release formulations[37]. Achieving an optimal balance between hydrophilicity and hydrophobicity is essential for designing biomaterials with controlled water interactions, ensuring enhanced therapeutic efficacy and clinical performance. These polymers can be classified based on their origin into natural and synthetic polymers, each with distinct properties and applications. Natural polymers, derived from biological sources, include polysaccharides (chitosan, cellulose and hyaluronic acid) and proteins (collagen), offering biocompatibility and biodegradability, making them ideal for biomedical applications[80]. Synthetic polymers, including PCL, PVA, PLGA, PLA, PU, PEG, PEO, and PGA, are artificially synthesized to achieve controlled mechanical properties, degradation rates, and drug delivery capabilities, making them essential for advanced pharmaceutical and tissue engineering applications [81].

Natural Polymers

Biopolymers, also known as natural polymers, are organic substances made by living organisms. These molecules are arranged structurally as repeating units, which join to form peptides and polysaccharides. These units are often amino acids or monosaccharides. They are derived from a variety of sources, such as animals, plants, bacteria, and fungi. Because of their distinct characteristics and diverse origins, they are applicable in a variety of fields[82] **(Fig. 6)**. The natural origin of these polymers renders them the most suitable replacements for the native skin's initial cellular environment and the ECM. Natural polymers have lower antigenicity, biocompatibility, and renewability than synthetic materials [83].

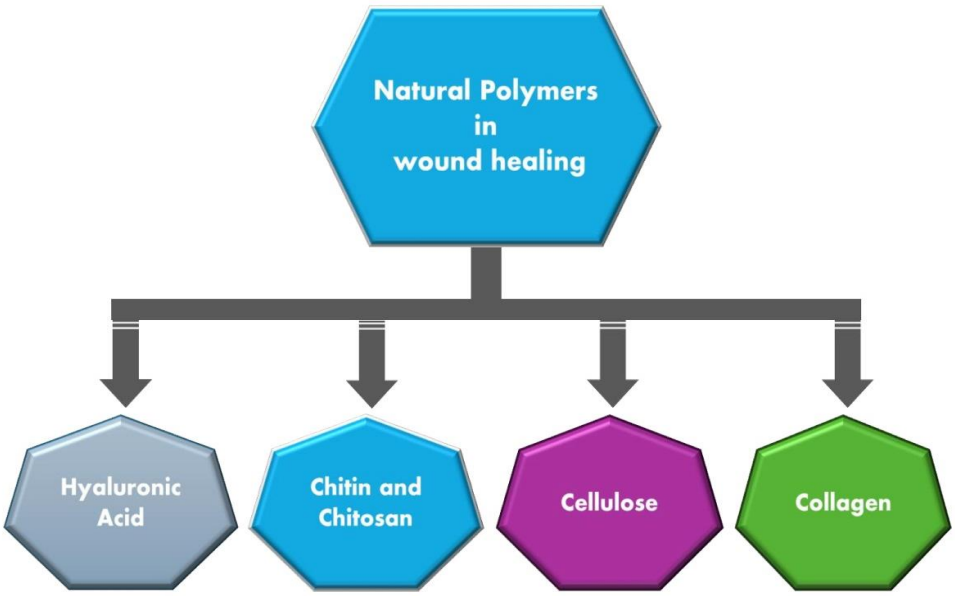


Fig.6: Natural polymers in wound healing.

Collagen

Animal connective tissue is mostly composed of collagen, which gives skin its tensile strength and is crucial to the overall wound healing process. Its effects extend to the site of injury, where it stimulates important cells such as keratinocytes and fibroblasts, which aid in re-epithelialization and encourage angiogenesis. Chemically, it consists of triple-helix fibrils, with each fibril representing a polymer of recurring amino acids linked together by peptides, as shown in **Table (1)**. It occurs in two states: its native form and gelatin, which is a denaturized version [84]. Different proteolytic enzymes are generated during the inflammatory phase, causing collagen to break into smaller pieces. The Arg-Gly-Asp (RGD) sequences found in these pieces work as mitogens for fibroblasts and as chemoattractants for macrophages. As a result, they cause granulation and encourage the growth of new tissue in the wound bed [85]. These dressings can also chemically bind matrix metalloproteinases (MMPs), which are present in the extracellular fluid around wounds. MMPs typically break down collagen, but using collagen-based dressings gives them another place to attach, allowing the body's natural collagen to be preserved for the usual wound-healing process.

Collagen cleavage produces gelatin, which, when paired with native collagen, lowers MMP activity and promotes proliferation over inflammation. By joining them with other molecules and creating scaffolds, biopolymers can have their mechanical, functional, and physical characteristics enhanced [86]. Collagen is used in the creation of delivery systems that facilitate healing, including hydrogels, films, sponges, nanofibers, and nanoparticles (NPs)[87]. Currently, it is used in a multitude of biomedical and pharmaceutical applications, such as gels for periodontal restoration, wound dressings, collagen sutures and catguts, skin injections, hemostatic agents (such as collagen sponges), and joint coatings. Because collagen is very stable and biocompatible, it is regarded as the perfect material for wound dressings. Applying and removing collagen treatments is simple. Common recommendations for the treatment of partial and full-thickness wounds with exudates are items produced from avian, porcine, or cow sources. However, collagen-based treatments are not advisable for patients with sensitive or allergic skin, or those who have experienced third-degree burns[88]. Many studies have recently reported the utilization of collagen for drug release, such as antibiotics.

Table 1: Chemical structure and properties of Natural polymers.

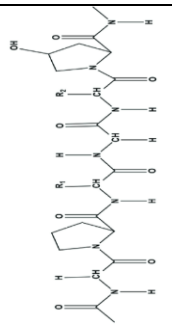
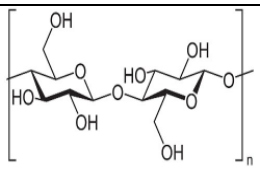
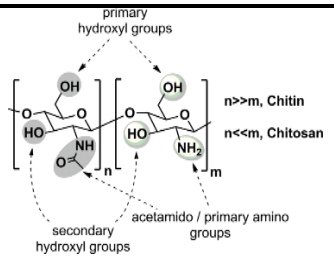
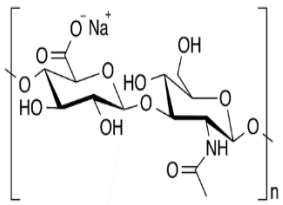
Polymer	Chemical Structure	Properties	Ref.
Collagen		• It is a necessary protein component of the extracellular matrix. • It can be obtained from a different of sources, including bovine, equine, porcine, cattle abattoir waste, and fishery byproducts. • It is an excellent biomaterial for wound healing because of its biocompatibility, biodegradability, and ability to retain a large amount of water, all of which contribute to cell health.	84
Cellulose		• It is a highly abundant, renewable, and limitless biopolymer. It has four main components: a glucose unit, a C4-OH group (non-reducing end), a C1-OH group (terminating end), and aldehydes. • The glucose subunits are connected through a β-(1,4) glycosidic bond.	94

Table 1 : Continued.

Chitin and Chitosan		• It is a naturally occurring polysaccharide consisting of glucosamine and N-acetyl glucosamine linked by a β-(1,4) glycoside bond. It can also be extracted by partially deacetylating the chitin found in crustacean shells. Its solubility in water is increased by the protonated amine group on the repeating glycoside residues, which gives it a cationic charge in acidic environments.	116
Hyaluronic acid		• It is a biopolymer that belongs to the glycosaminoglycan family of heteropolysaccharides and can be found in human vitreous humour, roosters' comb skin, joints, umbilical cord, and soft tissues. • it is produced through microbial fermentation.	132

Puoci *et al.* discovered a conjugate that acts as an antibacterial agent during wound healing by combining fluoroquinolone and collagen. The protein was covalently bonded to the antibiotic ciprofloxacin, which is used locally to treat diabetic feet. This approach focused on utilizing collagen as a biomaterial to stimulate fibroblast growth[89]. In another study, curcumin and quercetin were individually incorporated into a collagen matrix under experimental conditions. Several studies were performed on the software of diverse collagen dressing formulations for wounds and burns[90]. Furthermore, the electrospinning method has produced collagen nanofibers, that have enabled greater effective wound restoration than other fabrication techniques [91]. Another study, de la Mora-López *et al.* create nanofibrous membranes with healing properties by combining collagen, polyvinyl alcohol, CS, and honey at concentrations of 0% (PCH and PCHC), 5% (PCHC-5H), 10% (PCHC-10H), and 15% (PCHC-15H)[92].

Additionally, Deaconu *et al.* created wound dressings with a zinc-modified marine collagen porous scaffold as the host for wild bilberry (WB) leaf extract immobilized in functionalized mesoporous silica nanoparticles (MSN). The extract encapsulated in functionalized MSN demonstrated improved biological activities compared to the extract alone, including better inhibition of P. aeruginosa and S. aureus strains, higher biocompatibility on HaCaT keratinocytes, and anti-inflammatory potential demonstrated by reduced IL-1β and TNF-α levels [93]. The applications of collagen in the field of biomaterials-based wound dressings are summarized in **Table (2).**

Table 2: Applications of Natural polymer in the field of biomaterials-based wound dressing.

Polymer	Polymer-Based Dressing Type	Wound Model	Outcomes	Ref.
Collagen	Collagen hydrogel	Burn wounds	Promoted epithelialization and reduced inflammation	88
Collagen	Collagen-fluoroquinolone conjugate	Diabetic foot ulcers	Enhanced antibacterial activity and fibroblast stimulation	89
Collagen	Collagen matrix loaded with bioactive compounds	Experimental wound models	Enhanced wound healing efficiency	90
Collagen	Collagen nanofibers	Various wound models	Superior wound healing compared to conventional formulations	91
Collagen	Collagen/PVA/Chitosan/Honey nanofibrous membranes	Chronic wounds	Improved healing efficacy with honey concentration	92
Collagen	Zinc-modified marine collagen scaffold	Infected wounds	Increased antimicrobial activity, biocompatibility, and anti-inflammatory effects	93
Cellulose	OBC/CS/COL nanocomposite	Hemostatic wound dressing	Collagen improved hemostatic properties; chitosan enhanced antibacterial activity	102
Cellulose	Microbial cellulose membranes coated with CS	Wound healing	Enhanced epithelialization and faster tissue regeneration	108
Cellulose	BC films with TEMPO-oxidized cellulose & Ag nanoparticles	Antibacterial wound dressing	High inhibition against E. coli and S. aureus with good biocompatibility	110
Cellulose	BC films with sodium tripolyphosphate & Ag NPs	Antibacterial wound dressing	100% protection against E. coli and 99.99% against S. aureus	111
Cellulose	Regenerated bacterial cellulose (RBC) sponge	Antimicrobial wound dressing	Enhanced antibacterial activity and biocompatibility	113
Cellulose	Cellulose acetate-based hydrogels and nanofibers	Wound healing and skin regeneration	Improved wound healing efficiency	114
Cellulose	PU/HPMC nanofibers with mango peel extract	Antibacterial wound dressing	High cell viability and antibacterial efficacy	115
Chitosan	CS/HA polyelectrolyte nanoparticles	Topical NSAID delivery for irritant contact dermatitis	Enhanced skin penetration of etoricoxib, reduced systemic toxicity, improved healing efficacy	122
Chitosan	CS/HA nanoparticles	Acne treatment	Targeted drug delivery to pilosebaceous units, enhanced sebaceous interaction	123
Chitosan	CS-polyacrylic acid hybrid nanoparticles	Post-operative wound healing	Mechanical strength 50–120 kPa (1:1 ratio), 120–230 kPa (1:0.2 ratio)	124
Chitosan	CS-gelatin-acrylic acid film	Skin tissue engineering	Increased hydrophilicity with higher CS and acrylic acid concentration	125
Chitosan	CS gel	2nd-degree burn wounds in rabbits	Faster re-epithelialization, reduced scar formation, shorter healing time	126
Chitosan	CS/guar gum/peppermint oil hydrogel	Burn wound infections in mice	90% wound contraction on day 22, improved collagen fiber thickness and angiogenesis	127

Table 2: Continued.

Chitosan	Oleic acid-coated CS NPs	Allergic dermatitis model	Improved skin permeation of KP and SP nanoparticles, enhanced drug diffusion and therapeutic response	128
Chitosan	CS-SF-MMT dressing	Hemostatic wound dressing	Enhanced mechanical strength, rapid hemostasis, improved biocompatibility	129
Chitosan	CS-alginic acid hydrogel cross-linked with EDC/NHS	Wound healing	High swelling capacity, efficient water retention, optimal vapor permeability	130
Chitosan	Nanoparticles	Infected wounds	Sustained antibiotic release (24h vs. 2h for commercial product), broad-spectrum antimicrobial activity	131
Hyaluronic Acid	Thermosensitive HA hydrogel with maize silk extract (CSE) and silver (Ag) NPs	Bacterial wound infection model	Antibacterial activity against P. aeruginosa, E. coli, B. subtilis, and S. aureus	141
Hyaluronic Acid	Diet-loaded E-loaded polysaccharide NPs coated with cationic lipid DODMA	In vitro skin model	Improved stability and enhanced drug penetration	142
Hyaluronic Acid	Polyelectrolyte complex nanoparticles (PEC-NPs) loaded with etoricoxib (ETX)	Irritant contact dermatitis model	Reduced systemic toxicity, improved anti-inflammatory effects	122
Hyaluronic Acid	HA-CMCNa sponges	Skin wound healing model	Improved stability, enhanced skin regeneration	143
Hyaluronic Acid	VEGF-loaded HA-EDA hydrogel	Human Umbilical Vein Endothelial Cells (HUVEC) model	Induced angiogenesis, retained 50% VEGF after 5 days	144

Cellulose

It is composed of repeating molecules of β-D-glucose, which might be linked by way of β-1,4 bonds as presented in **Table (1)** and found in plant mobile partitions. It is produced by positive bacteria, like those from S. ventriculi, Agrobacterium, and G. acetobacter. The properties of cellulose are demonstrated in **(Fig. 7)**, which include its biocompatibility, crystalline nature, durability, resistance to trauma, tensile strength, and the ability to moisten the injured area while simultaneously soaking produced exudates [94]. Additionally, it is effortless to replenish with pharmaceuticals. Additionally, it prevents bacterial infection by creating a barrier between the wound and bacteria, thereby preventing their infiltration, in addition to facilitating gas exchange. In addition, it is capable of being extracted from the site of injury without causing any pain or harm to the newly produced tissue [95]. A bacterial cellulose (BC) wound dressing's optical transparency offers the potential to employ laser-based imaging diagnostics, such as optical coherence tomography, multiphoton tomography, and confocal laser scanning microscopy. As a result, the repair's progress can be monitored non-invasively [96]. BC is recognized for its noticeably high purity[97]. BC demonstrates great potential as a biopolymer, because of its capacity to alter the characteristics of wound exudate and maintain moist surroundings, which are very allied to the techniques of wound healing. However, its practical application is constrained by a lack of intrinsic antibacterial properties. It is a 3D community that synthesizes β-1, 4-glucan cellulose chains by utilizing a diverse bacterial source. BC is an optimal carrier for the controlled release of drugs such as antibiotics and anti-inflammatory agents because of its porosity and surface area[98].

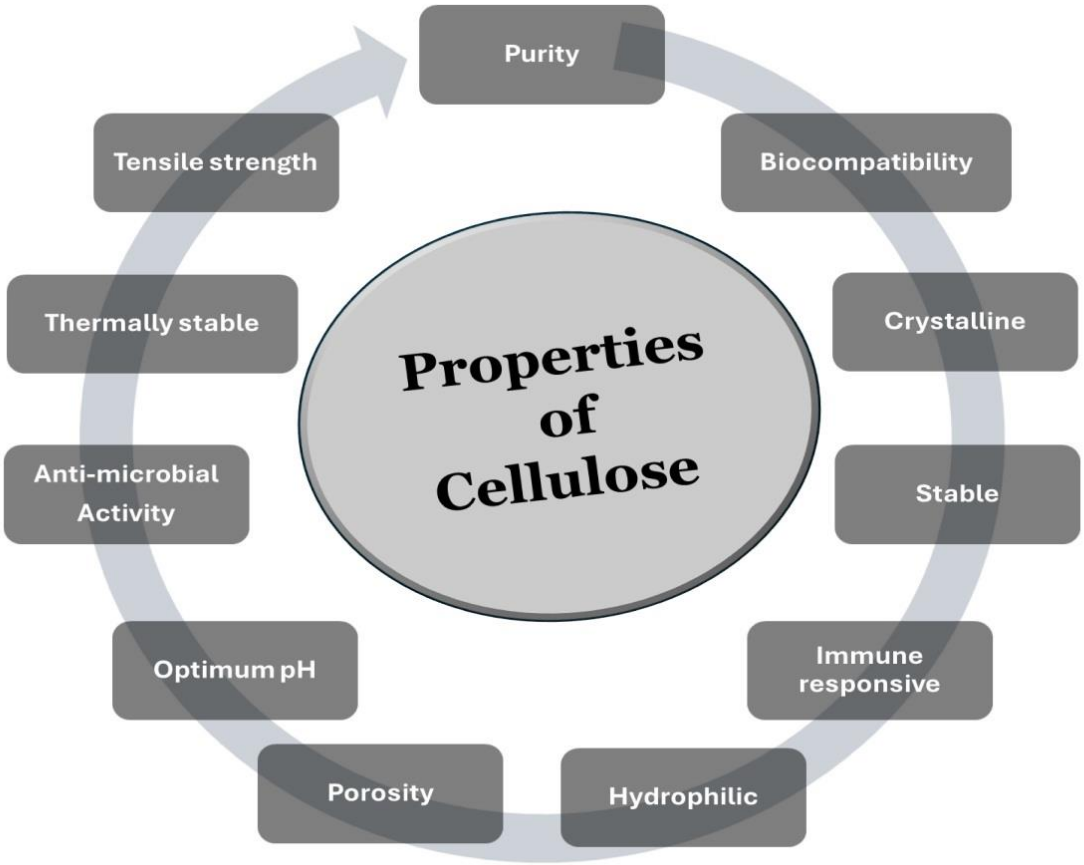


Fig.7: Properties of cellulose.

Three major strategies have been investigated to improve the antibacterial properties of BC-based fully composite wound dressings: the addition of antibiotics, the combination of inorganic and organic antibacterial sellers, and the integration of organic antibacterial marketers[99]. CS, collagen, and curcumin are natural antimicrobial agents observed as promising materials attributable to the fact that they possess a high bio-degradation index and biocompatibility [100]. From the perspective of building up the controlled release of CIP, there has been a plan for a study wherein BC is replaced by low molecular weight CS in polymeric systems. The studies indicate that CS enhanced the antibacterial action of CIP when administered alongside the compound [101]. In an examination carried out by Yuan *et al*., a special type of hemostatic nanocomposite was established (OBC/CS/COL), such as CS, collagen (COL), and oxidized bacterial cellulose (OBC)[102]. The findings indicated that the inclusion of collagen improved the nanocomposite's hemostatic effectiveness and promoted wound healing, while CS contributed to the improvement of its antibacterial properties. Current studies have concerned the use of inorganic antibacterial agents like metallic nanoparticles, metallic oxides, and nano–silicates in combination with BC toward building the antimicrobial property of a novel substance.

The purpose of this study consequently is to improve the antimicrobial performance of BC based on the properties of these inorganic marketers[103]. The nanostructure of BC provides it with desirable physicochemical and mechanical properties along with good biocompatibility and biodegradability. Additionally, its difficult porous 3-dimensional architecture, which mimics the extracellular matrix (ECM) of the skin, facilitates its use in numerous biomedical programs, mainly in enhancing tissue regeneration [104]. BC has possibilities in a lot of fields, including bioprinting, implants, drug transport, and synthetic organs [105]. To decline infections at

wound sites, cellulose may be mixed with different materials, together with antimicrobials. The incorporation of cellulose with marketers like lysostaphin [106] and silver sulfadiazine[107] has validated bactericidal residences against *E. coli* and *S. aureus*. It is crucial to observe that Lin *et al*. stated that cellulose membranes that were derived from microorganisms and lined with CS facilitated greater rapid tissue regeneration and improved epithelialization[108]. To promote tissue repair, polyvinyl alcohol/carboxymethylcellulose (PVA/CMC) composite films have been advanced, utilizing the unique qualities of each polymer combination. The properties include biodegradability, elasticity, swelling capacity, water solubility, and porosity [109]. The hydrophilic nature of carboxymethyl cellulose (CMC) permits powerful cross-linking and integration with a variety of materials, including synthetic polymers, herbal polymers, and inorganic substances. This function is instrumental in advancing the design of novel biomaterials for wound dressing programs. In numerous studies, antibacterial wound dressings evolved by combining BC with biomaterials that possess inherent antibacterial characteristics.

In an experiment, oxidized 2,2,6,6-tetramethylpiperidinyloxy (TEMPO) was used to supply and create BC films. Subsequently, these films were deposited with 16.5 nm-diameter silver nanoparticles (Ag NPs) at room temperature by using a thermal discount technique which does not involve reduction. Ag NPs and TOBCP had high bacterial inhibition against both Gram-positive E. coli and Gram-positive S. aureus and comparatively good biocompatibility for use as wound dressings as observed through experimental results by [110]. Another study prepared BC films using an in-situ immersion method presence of sodium tripolyphosphate and incorporated Ag NPs. From the properties of the film, it is revealed that the film offered 100% protection against E. coli film and 99.99% against S. aureus. However, the films offer a chance to evaluate and monitoring the wound without the need for ungearing the dressing[111].). An experiment was conducted to improve the properties of a BC composite by immersing it in an antibiotic solution containing ceftriaxone and amikacin. The BC/Ceftriaxone/Amikacin composite exhibited strong antibacterial activity against a wide range of microorganisms, including *Pseudomonas aeruginosa*, *S. aureus*, and *E. coli* [112]. In another work, *Ye et al*. immobilized amoxicillin on regenerated bacterial cellulose (RBC) to synthesize a new sponge that exhibits better antibacterial characteristics and biocompatibility. The outcomes suggested that the incorporation of RBC expanded the bacteriostasis of the sponge against microorganisms and fungi and could be employed as a replacement for the repairing dress materials of wounds [113].

In another investigation, Ndlovu *et al*. developed cellulose acetate-based hydrogels and nanofibers loaded with bioactive agents for wound healing and skin regeneration [114]. Also, Al-Naymi *et al* employed polyurethane hydroxy propyl methyl cellulose nanofibers (NFs) with different concentration ratios as well as mango peel extracts (MPE) spun through an electro-spinning process. The optimal ratio of PU90/HPMC10/20% scaffold had the highest cell viability and proliferation, relative to other samples as well as showing higher antibacterial efficiency against pathogenic S. aureus (17mm) and E.coli (11mm)[115]. The applications of cellulose in the field of biomaterials-based wound dressings are summarized in **Table (2).**

Chitin and Chitosan

Chitin is made up of units of 2-acetamido-2-deoxy-D-glucose connected by β-(1–4) linkages[116] as presented in **Table (1)**. Numerous resources contribute to its determination, such as insects, shrimps, crabs, and mushrooms. CS is a cationic semi-crystalline polysaccharide made up of N-acetylglucosamine and glucosamine monomers connected through β-(1-4) bonds[117–119]. The production of CS involves the deacetylation of glucosamine chitin units. CS and chitin personal exquisite natural trends, which include biocompatibility, biodegradability, antimicrobial pastime, non-poisonous, non-allergic, and hemostatic results. Consequently, they're appropriate for an entire lot of packages, which consist of wound recovery[120]. Furthermore, studies have demonstrated that the analgesic, anti-inflammatory, and antibacterial qualities of chitin and its

derivatives promote tissue regeneration and accelerate wound healing[118]. As a result, chitin and CS have been used as promising alternatives for treating wound packages in several forms, which encompass hydrogels, films, and fibers[121].

Abuelella *et al* create polyelectrolyte nanoparticles containing two natural biodegradable polymers, particularly CS and hyaluronic acid, to deliver the non-steroidal anti-inflammatory drug etoricoxib to the deeper skin layers to relieve any systemic toxicity and enhance its healing efficacy versus irritant contact dermatitis [122]. Another study, Tolentino *et al*. were the first to encapsulate clindamycin in hyaluronic acid or CS nanoparticles and consider the sebaceous characteristics of acne-prone pores and skin while examining the effects of these polymeric nanostructures on centralized drug delivery to pilosebaceous devices. In another investigation, hybrid nanoparticles (CS-PAA hybrid NPs) composed of CS and polyacrylic acid (PAA) were synthesized using the application of free radical polymerization (FRP) in post-operative wound healing protocols [123]. The physicochemical analysis of those CS-PAA hybrid NPs discovered that their mechanical energy and resistance ranged from 50–120 kPa for a 1:1 CS/PAA ratio and from 120–230 kPa for a 1:0.2 CS/PAA ratio[124].

In a subsequent observation, silicone/acrylic acid films have been used to immobilize CS and gelatine for wound healing and skin tissue engineering recuperation purposes. According to the findings, the hydrophilicity of the film rises as the concentration of CS and acrylic acid increases [125]. The impact of CS-based gels on 2nd degree burn wounds was studied. Six rabbits suffered first-grade burns in this study. Following that, rabbits were managed with CS gels. The conclusion depicted that CS gel enhances re-epithelialization, diminishes the formation of dermal scars, and ultimately shortens the period of wound healing [126]. In the primary observation, the backs of Wistar albino mice have been subjected to complete burns. Next, CS gel, CS/guar gum hydrogel, CS/aloe vera hydrogel, and CS/guar gum (GG)/aloe vera hydrogel (AV) were applied to the mice in that order. The results showed that, in comparison to the other treatments, the CS/GG/AV hydrogel was significantly more appropriate for angiogenesis, epithelial regeneration, and typical wound repair. In addition, during the healing process, no inflammation was observed when using the CS/GG/AV hydrogel. Thus, the CS/GG/AV hydrogel received appreciation as a highly effective burn injury dressing [126].

Also, Ansari *et al.* conducted an additional study to investigate the effects of CS/guar gum/peppermint essential oil (CS/GG/PEO) antibacterial hydrogel on the healing rate of burn wound infections in mice. The results of the histopathological analysis revealed that the wound contraction, re-epithelialization, collagen fiber thickness, and angiogenesis technique were significantly better in the group that received CS/GG/PEO hydrogel (90% on 22nd day). Hence, due to having appropriate biological and physicochemical characteristics, chitin/CS can be considered as the most ideal wound dressing [127]. Shah *et al*. reported that applying oleic acid to the surface of CS NPs improved pores and skin permeation of fluorescent dye-containing nanoparticles by moving the more concentrated nanoparticles through the skin's layers and deeper pores. In an allergic dermatitis model, the skin diffusion of ketoprofen (KP) and spantide (SP) nanoparticles was improved by using an oleic acid coating, resulting in a more powerful response [128].

Furthermore, Ngo *et al.* describe a flexible hemostatic dressing for open wounds that incorporates CS for hemostasis and biocompatibility, silk fibroin (SF) for mechanical strength, and montmorillonite (MMT) for improved drug transport. CSSF@MMT dressings demonstrated promising mechanical strength and rapid hemostasis[129]. In another study, Gou *et al.* developed a composite hydrogel from carboxymethyl CS and alginic acid that was cross-linked with 1-ethyl-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC) and N-hydroxysuccinimide (NHS) and enriched with extracts from *Acanthopanax senticosus* and *Osmundastrum cinnamomeum*. The resulting hydrogel exhibited favorable attributes such as robust swelling properties, efficient water-holding capacity, and superior water vapor permeability[130]. Chitosan nanoparticles were used as drug carriers for silver sulfadiazine,

presenting continuous delivery of antibiotic over 24 h, which was higher than the delivery of commercial product (two hours). It also presented proven effectivity for Gram-positive (*Bacillus subtilis* and *Staphylococcus aureus*) and Gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa*) bacteria and Candida albicans on an infected wound[131]. The applications of chitosan in the field of biomaterials-based wound dressings are summarized in **Table (2).**

Hyaluronic Acid

Hyaluronic acid (hyaluronan) is a polymer with a linear structure made up of repeating disaccharide units joined by β-1,4-glycosidic linkages[132]. N-acetyl-D-glucosamine and D-glucuronic acid are linked by β-1,3-glycosidic linkages in each disaccharide unit[133,134], as presented in **Table (1)**. Cell signalling and wound healing/tissue regeneration [135], an assistant device in ophthalmic surgeries [136], the treatment of bone and skin inflammatory diseases, joint disease as a lubricant and/or shock-absorbing fluid[132], and many other vital functions of HA are among its many important uses[137].

Dermaplex®, Hyalomatrix®, and Hyalofill® are commercial wound care products that are derived from HA. Burns, pressure sores, ulcers, diabetic foot, and acute and chronic skin lesions are all extensively treated with HA. It is acknowledged for its adaptability, and researchers have improved its swelling, rheological, and mechanical characteristics by adding different chemical groups to the polymeric backbone[138]. Because it controls inflammation at the wound site, scavenges free radicals, and interacts with receptors on different cells involved in tissue regeneration, HA is essential for the angiogenic phase of wound healing[139]. It has been shown that the angiogenic effect of short-chain HA molecules, which range in length from three to ten disaccharide devices, is regulated by two receptors: CD44 and the receptor for HA-mediated motility (RHAMM). In response to these receptors, endothelial cells proliferate and migrate during the restoration process[140].

Makvandi *et al.* employed a novel method to create thermosensitive and injectable hydrogels by combining HA, maize silk extract (CSE), and silver (Ag) NPs. These hydrogels exhibited antibacterial activity in contrast to Gram-negative (P. aeruginosa, E. coli) and Gram-positive (B. subtilis, S. aureus) bacteria[141]. Also, Pereira *et al.* produced diet-loaded E-loaded polysaccharide NPs using hyaluronic acid and lecithin. These NPs were coated with cationic lipid dioctadecyl dimethyl ammonium bromide (DODMA)[142]. In another study, Abuelella et al made a confluent of HA and CS and their study was to synthesize polyelectrolyte complex nanoparticles. These NPs were designed for the delivery of etoricoxib (ETX) to the second skin layer to minimize systemic toxicity and improve the effectiveness of peeling in the treatment of irritant contact dermatitis [122]. L.Liu *et al*. have shown that HA-CMCNa sponges are effective in skin regeneration packages as a result of their exceptional stability[143]. Connected HA-EDA hydrogels were utilized in the study to enhance the VEGF delivery at the wound site. It has also been shown that the hydrogel induced the proliferation of Human Umbilical Vein Endothelial Cells (HUVEC) because, after incubation for five days, fifty percent of the VEGF was still retained[144]. The applications of hyaluronic acid in the field of biomaterials-based wound dressings are summarized in **Table (2).**

Synthetic Polymer-Based Skin Scaffolds

Biodegradable synthetic polymers can be created and processed to have greater control over their physical and chemical properties than natural polymers. These polymers are utilized in various applications, which include tissue engineering, wound dressings, and drug delivery [145]. The use of polymer-based wound dressings on skin wounds provides support to the wound sites and acts as a carrier for cells and growth factors. As a result, skin tissue regeneration and cell proliferation are enhanced[146]. Our subsequent discussion will focus on pharmaceutical applications of degradable synthetic polymers approved by the US Food and Drug Administration (FDA), such as PVA, PCL, PLA, PLGA, PU, PEO, PGA, and PEG [147] **(Fig. 8)**.

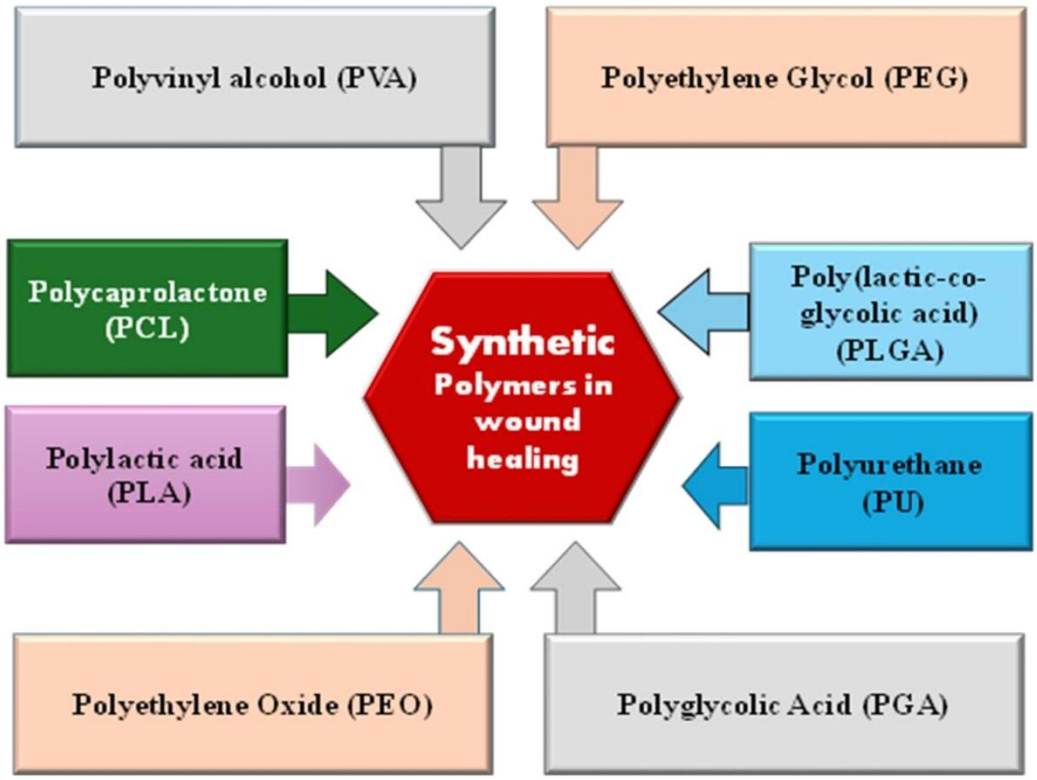


Fig.8: Synthetic polymers in wound healing.

Polyvinyl alcohol (PVA)

Polyvinyl alcohol (PVA) is a water-soluble and non-toxic polymer that is produced through the polymerization and alcoholysis of vinyl acetate[148]. It is described by the chemical formula (C2H4O) n, as illustrated in **Table (3)**. PVA's hygroscopicity is enhanced by a large number of hydrophilic groups, which facilitate biodegradation into carbon dioxide and water[149]. The use of a primate baboon model to replace diseased spinal cores demonstrated the safety of PVA implants in medical applications[150]. Natural biodegradable polymers, which include fibrin, CS, gelatine, and sodium alginate (SA), can be combined with PVA to enhance its cellular adhesion, water absorption, and wound healing properties[151]. In another study, hydrogels for wound healing advanced the usage of PVA/Pullulan/Poly-L-Lysine/Gelatine. In vitro examinations found that those hydrogels are low-toxicity and blood-well-matched. Hydrogels also promote cell proliferation, which aids wound restoration [152].

An additional study used a composite hydrogel composed of PVA, Dextran, and CS evolved as a wound dressing. According to the assessment outcomes, this hydrogel exhibited favorable characteristics together with thermal stability, antimicrobial activity, and the capacity to retain water and create moisture on the wound. As a result, the PVA/Dex/CS hydrogel is an effective wound dressing for wound recovery[153]. Another study involved modifying CS with PVA to create a PVA/CS sponge through go-linking and foaming reactions. The PVA/CS sponges exhibited incredible hemostatic performance, biocompatibility, and advanced wound healing outcomes [154].

In another experiment, Massarelli *et al.* designed a kind of wound dressing material based on CS and PVA to control the release of disinfectants, including PHMB and CHX. This component was developed as a safer chance for wound management. The PHMB-contained dressings tested appreciated cytotoxicity and infection; animal-tested dressings enhanced wound healing in dogs more than conventional treatment [155]. For example, Li *et al.* utilized a 3D printing sacrificial template mixed with freeze-drying strategies to fabricate a composite sponge manufactured from PVA and

sodium alginate [156]. The ensuing sponge exhibited a disordered porous structure along properly prepared microchannels. Compared to the ordinary PVA hemostatic sponges, the PVA/SA sponge has superior mechanical properties and a greater water absorption rate. This property has the potential to enhance the performance of advanced hemostatic sponges by allowing coagulation and integrating blood aggregation [156]. Integrating silk fibers (SF) and CS into PVA electrospun nanofibers enhanced cell adhesion, allowing for advanced mechanical properties and improved tissue regeneration. These findings provide preliminary evidence that nanofibers may be particularly useful as a skin substitute for wound healing purposes[157]. Hydrogels had been prepared from PVA/ Aloe vera (Av) and incorporated with gentamicin and curcumin. These hydrogels proved to be useful in wound healing by prompting the re-epithelialization method and raising its efficiency[158]. Therefore, many researchers are investigating the manufacture of drug-based dressings to promote wound healing.

Özbaş *et al.* formulated a PVA-HA-carrageenan complex hydrogel dressing containing ampicillin for the healing of infected wounds [159]. Moreover, Tamahkar *et al.* developed a multi-layer hydrogel system containing ampicillin for the treatment of infected wounds and produced a dressing that can release the drug over a long time [160]. Further, Qing *et al.* prepared a hydrogel dressing prepared by a freeze-thaw method loaded with lincomycin, which showed excellent antibacterial effects without toxic side effects[161]. Another study, Sangnim *et al.* developed a clindamycin-loaded polymeric nanofiber patch composed of polyvinyl alcohol (PVA) and tamarind seed gum. Authors studied different concentrations of PVA, gum, and model drug to produce the polymeric nanofibers, adjusting the processing parameter in each case. Continuous fibers were obtained when using PVA concentrations between 10% and 15% (w/v), and fiber diameter as proportional to PVA concentration and inversely proportional to applied voltage (diameter decreased with lower concentrations and higher voltages) [162]. The applications of Polyvinyl alcohol in the field of biomaterials-based wound dressings are summarized in **Table (4).**

Polycaprolactone (PCL)

It is synthesized from the degradation of linear aliphatic polyester through autocatalyzed bulk hydrolysis and ring-beginning polymerization of ε-caprolactone monomers, as presented in **Table (3)**. It is recognized for its biocompatibility, biodegradability, nontoxicity, and FDA approval. Additionally, PCL is fairly versatile and may be readily processed into diverse shapes and forms, making it appropriate for diverse biomedical applications [163]. Electrospun PCL fibers are nicely perfect for the management of acute and chronic wounds because of their fibrous structure, which carefully mimics the extracellular matrix (ECM). However, PCL's inherent hindrance is its loss of antimicrobial properties. To address this, silver nanoparticles are integrated into the PCL matrix, improving its resistance to microbial infections. Additionally, those fibers are capable of absorbing huge wound exudates and keeping moisture, further supporting the wound recuperation manner [164]. PCL-collagen matrix activates the integrin-β1 signalling pathway, controlling fibroblast proliferation and selling wound healing [165].

In another investigation, Zahra *et al*. used a twin-nozzle electrospinning technique to optimize this fabric and create PVA/PCL/GT hybrid nanofibers. The swelling capacity of PVA and GT aided in the degradation of PCL, accelerating wound restoration, and the presence of those substances saved the wound environment moist[166]. Preclinical trying out demonstrates the potential of the amoxicillin-loaded PCL and gelatin bilayer nanofiber scaffold to heal wounds, as it is resistant to bacterial boom in disc diffusion assays [167]. In another study, the curcumin was embedded into an electrospun nanofiber scaffold composed of PCL/SF and PVA/SF to aid in wound healing by facilitating targeted shipping and biphasic release of curcumin *via* an extensive range of molecular objectives and cell pathways[168]. The applications of Polycaprolactone in the field of biomaterials-based wound dressings are summarized in **Table (4).**

Table 3: Chemical structure and properties of Synthetic polymers.

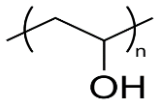
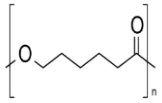
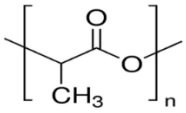
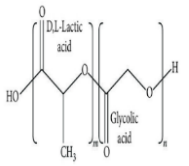
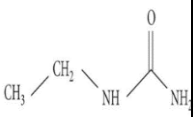
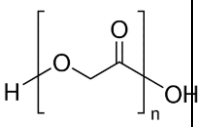
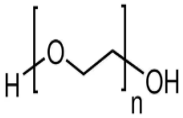
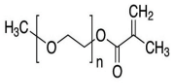
Polymer	Chemical Structure	Properties	Ref.
Polyvinyl alcohol (PVA)		• It is a water-soluble and non-toxic polymer that is produced through the alcoholysis and polymerization of vinyl acetate.	148
Polycaprolactone (PCL)		• It is synthesized from the degradation of linear aliphatic polyester through autocatalyzed bulk hydrolysis and ring-beginning polymerization of ε-caprolactone monomers. It is recognized for its biocompatibility, biodegradability, non-toxicity, and FDA approval.	163
Polylactic acid (PLA)		• It was initially synthesised in 1932 by Wallace Carothers through the condensation polymerisation of lactic acid in vacuum conditions.	169
Poly (lactic-co-glycolic acid) (PLGA)		• It is the result of the random polymerisation of lactic acid and glycolic acid which occurs through the combination of polylactic acid and polyglycolic acid. • It is characterized by a variety of important attributes such as biocompatibility, mechanical power, and ease of manipulation into desirable shapes and size. This biodegradable polymer is FDA authorized.	175
Polyurethane (PU)		• It is composed of repeating structural units of the carbamate group (-NHCOO-), which are synthesised through a stepwise polymerisation reaction of isocyanates and hydroxyl groups of polyols.	179
Polyglycolic Acid (PGA)		• It is the linear aliphatic polyester and a biodegradable thermoplastic polymer. It can be synthesised *via* glycollic acid condensation or ring-starting polymerisation.	191
Polyethylene Glycol (PEG)		• It is an amphiphilic polymer and made up of monomer units of oxide ethylene. • Because of its hydrophilicity, biodegradability, and biocompatibility, it is widely used in biomedicine.	195
Polyethylene Oxide (PEO)		• It is a polymer created *via* the polymerization of ethylene oxide. • Its shape is characterised by way of the repetitive devices of ethylene oxide, which make contributions to its precise physicochemical properties.	197

Table 4: Applications of Synthetic polymer in the field of biomaterials-based wound dressing.

Polymer	Polyvinyl alcohol -Based Dressing Type	Wound Model	Outcomes	Ref.
Polyvinyl Alcohol	PVA/Pullulan/Poly-L-Lysine/Gelatine hydrogel	In vitro wound model	Low toxicity, blood compatibility, promotes cell proliferation	152
Polyvinyl Alcohol	Composite hydrogel	Wound healing model	Thermal stability, antimicrobial activity, maintains moist wound environment	153
Polyvinyl Alcohol	Cross-linked sponge	Wound healing model	Hemostatic activity, biocompatibility, enhances wound healing	154
Polyvinyl Alcohol	Wound dressing	Canine wound model	Controls disinfectant release, enhances healing vs. conventional treatments	155
Polyvinyl Alcohol	3D-printed sponge	Hemostatic wound model	Superior mechanical strength, high water absorption, improves blood coagulation	156
Polyvinyl Alcohol	Electrospun nanofiber	In vitro wound model	Enhances cell adhesion, mechanical properties, supports tissue regeneration	157
Polyvinyl Alcohol	Hydrogel	Wound healing model	Enhances re-epithelialization, efficiency of wound healing	158
Polyvinyl Alcohol	Hydrogel dressing	Infected wound model	Antibacterial effect, promotes wound healing	159
Polyvinyl Alcohol	Multi-layer hydrogel dressing	Infected wound model	Sustained drug release, effective for long-term infection control	160
Polyvinyl Alcohol	Freeze-thaw hydrogel	Infected wound model	Antibacterial effects, non-toxic	161
Polyvinyl Alcohol	Polymeric nanofiber	Infected wounds	Optimized fiber formation with PVA 10–15% (w/v), fiber diameter inversely proportional to applied voltage	162
Polycaprolactone	Electrospun PCL fibres	Acute & chronic wound models	Mimics ECM, absorbs wound exudates, moisture retention, lacks antimicrobial properties	164
Polycaprolactone	Electrospun fibres	Infection-prone wound models	Antimicrobial activity, enhanced wound healing	164
Polycaprolactone	Matrix scaffold	Fibroblast wound model	Activates integrin-β1 signaling, enhances fibroblast proliferation, supports wound healing	165
Polycaprolactone	Electrospun nanofibers	Wound healing model	Increased swelling, enhanced PCL degradation, moist wound environment	166

Table 4 : Continued.

Polycaprolactone	Nanofiber scaffold	Preclinical wound model	Bacterial resistance, accelerated wound healing	[167]
Polycaprolactone	Electrospun nanofiber scaffold	Wound healing model	Biphasic curcumin release, targeted molecular action, enhanced wound healing	[168]
Polylactic Acid	Electrospun PLA/PCL hybrid scaffold	Murine full-thickness wound model	Enhanced cell attachment & proliferation, improved structural morphology, controlled KGF delivery, accelerated wound healing	[170]
Polylactic Acid	Electrospun scaffold	Tissue engineering	Improved hydrophilicity, enhanced cellular compatibility	[171]
Polylactic Acid	Electrospun composite nanofibers	Tissue engineering scaffold	Increased cell growth, better spinning ability, potential application in wound healing	[172]
Polylactic Acid	Sandwich-structured wound dressing	Wound healing & follicle regeneration	Exudate absorption, hair follicle regeneration, enhanced wound recovery	[173]
Polylactic Acid	Scaffold for chronic wound management	Human epidermal keratin-forming (HEK) & human dermal fibroblast (HDF) models	Reduced wound contraction, promoted skin cell proliferation, stimulated vascular growth	[174]
Poly (lactic-co-glycolic acid)	PLGA-Based Scaffolds	General wound healing applications	Biocompatible, mechanically strong, FDA-approved, biodegradable, but hydrophobic and semi-permeable (does not absorb exudates)	[176]
Poly (lactic-co-glycolic acid)	PLGA composites with antibacterial and herbal polymers	General wound healing applications	Enhanced antimicrobial activity, improved mechanical properties	[177]
Poly (lactic-co-glycolic acid)	Hydrogel	Animal model for wound healing	Scarless healing due to controlled inhibitor release	[178]
Poly (lactic-co-glycolic acid)	Hydrogel	Full-thickness skin defect model	Promoted angiogenesis, stabilized HIF-1α, enhanced healing	[178]
Polyurethane	NovoSorb® PU foam	Surgical wound healing	Supports wound healing but degrades slowly with no specific pathway	[184_185]
Polyurethane	Foam	Wound healing model	Enhanced mechanical properties, antibacterial activity, and biodegradability	[186_187]
Polyurethane	Gel	Animal wound model	Improved angiogenesis, hair follicle regeneration, reduced inflammation, self-healing properties	[189]

Table 4 : Continued.

Polyurethane	Foam	Wound healing model	ROS-responsive degradation, reduced inflammation, enhanced reepithelialization compared to NovoSorb	190
Polyglycolic Acid	Polyglycolic Acid sheets	Wound healing models	Strong, absorbent, gradually degraded by hydrolysis	191,192
Polyglycolic Acid	Polyglycolic Acid sheets	Post-surgical applications (e.g., glossectomy, fistula closure)	Prevents delayed perforation, accelerates healing	193
Polyglycolic Acid	Polyglycolic Acid sheets	Open wound coverage	Prevents liquid/air leaks, hemostatic properties, enhances tissue repair	194
Polyethylene Glycol	PEG-based hydrogels	Tissue engineering, wound dressings	Biocompatible, biodegradable, low-cost, stable activity	195
Polyethylene Glycol	PEG-based hydrogels	Wound healing applications	Improved pharmacokinetics, enhanced drug delivery	195
Polyethylene Glycol	PEG-based hydrogels	Wound healing models	Cytotoxicity concerns due to cross-linkers; research focuses on reducing toxicity	196
Polyethylene Oxide	PEO-CS composite fibres	Wound exudate absorption model	Forms a gel-like structure, accelerates healing, suitable for wounds with low to moderate exudate	197
Polyethylene Oxide	Gel	Simulated wound exudate model	Enhanced wound exudate absorption, reduced adherence to human skin with poly (dimethyl siloxane) coating	198

Polylactic acid (PLA)

It was first synthesized in 1932 via Wallace Carothers with the condensation polymerization of lactic acid performed under vacuum situations [169] as presented in **Table (3)**. According to, Kobsa *et al.* they created a PLA/PCL hybrid electrospun scaffold that exhibited superior structural morphology, improved mobile attachment and proliferation when compared to the PLA scaffold. In addition, the PLA/PCL hybrid scaffold was changed and utilized to transport a plasmid-encoding keratinocyte boom component (KGF). This amendment was discovered to enhance the precise regulation of KGF transport and speed up wound healing in a murine model with a complete-thickness disorder[170]. For example, PLA scaffolds optimized with gelatine confirmed progressed hydrophilicity and cellular compatibility [171]. After the incorporation of gelatin and SF, Yin *et al.* created electrospun PLA/gelatine/SF composite nanofibers made by Yin *et al*. show enhanced cell growth, spinning ability, and potential application in tissue engineering scaffolds [172].

In an additional study, a sandwich-established wound dressing was produced by combining hydrophilic zinc silicate bioceramics (ZnCS) with PLA [173]. Due to the synergistic effect of the released Zn and SiO_3^{-} (ZnCS), the Janus membrane revealed exudate absorption, hair follicle regeneration, and wound recovery capabilities [173]. In another

study, Ibuprofen was incorporated into PLA nanofibers to produce scaffolds for the management of acute and chronic wounds [174]. Scaffold is utilized to reduce wound contraction in vivo and stimulate the proliferation of human pores and skin cells. Human epidermal keratin-forming (HEK) cells were added to the upper layer of the scaffold to simulate pores and skin patterns while the lower layer was laden with human dermal fibroblasts (HDF). This process has been credited for vascular growth so potential programs may be developed in wound healing [174]. The applications of Polylactic Acid in the field of biomaterials-based wound dressings are summarized in **Table (4).**

Poly (lactic-co-glycolic acid) (PLGA)

It is the result of the random polymerization of lactic acid (LA) and glycolic acid (GA), which occurs through the combination of polylactic acid (PLA) and polyglycolic acid as presented in **Table (3).** Some of the outstanding attributes include biocompatibility, mechanical power, and the ability to be shaped in forms and sizes that are preferable. The FDA has approved this type of biodegradable polymer[175]. PLGA-based Scaffolds are hydrophobic and semi-permeable, which means they no longer take in exudates or create a wet microenvironment when used as wound dressing substances, regardless of their advanced nature[176].

On the other hand, PLGA can be combined with other bioactive components, such as antibacterial species and herbal polymers, to provide high-overall performance PLA composites [177]. In another investigation, Zhang *et al*. used an animal model to create hydrogel drugs that released TGFβ inhibitors at specific intervals, leading to scarless recovery. Besides silver ions, copper ions have additionally been discovered to stabilize hypoxia-inducing elements (HIF-1α), imitate hypoxia, and sell angiogenesis [178]. Based on this, a PLGA bioactive glass dressing was loaded with copper ions and located efficient control of complete-thickness pores and skin defects. The applications of Poly (lactic-co-glycolic acid) in the field of biomaterials-based wound dressings are summarized in **Table (4).**

Polyurethane (PU)

It is composed of repeating structural units of the carbamate group (-NHCOO-), which are synthesized through a stepwise polymerization reaction of isocyanates and hydroxyl groups of polyols [179] as presented in **Table (3)**. Because of its high biocompatibility, it has a wide range of applications in medicine[180]. In 1960, Braunwald became the first to implant a PU heart valve into a human being[181]. The use of PU as a biomaterial for cartilage and bone repair dates back to the late 1990s[182]. The potential of PU-based wound dressings has been demonstrated in recent years due to their availability of the required biological, mechanical, and physicochemical properties [183].

NovoSorb®, a polyurethane foam, has been commercialized to support wound healing during surgery[184]. However, PU degrades slowly in the body and lacks a specific degradation pathway [185]. In comparison to the separate polyurethane (PU) materials, the incorporation of natural polymers, such as lignin, enhances their mechanical properties and biodegradability[186]. In another investigation, Li *et al.* selectively functionalized the phenolic hydroxyl groups in lignin to reduce silver ions and cap them hence enhancing the antibacterial properties of the scaffold. Wound healing efficiency results revealed that the lignin polyurethane/Ag composite foam showed significantly higher wound healing efficiency. During the degradation of PU, the formation of negatively charged molecules such as carboxyl, phenol, and aldehyde groups leads to the generation of negatively charged ions or other entities that contribute to the acidification of the environment[187]. PU can be combined with natural polymers to reduce the adverse impacts of acid. Hyaluronic acid has been shown to reduce inflammation by regulating the body's environmental balance and inhibiting free radical production[188].

In the current study, Wang *et al.* produced a hyaluronic acid waterborne polyurethane (HA-PU) gel that improved angiogenesis and hair follicle regeneration, decreased immunological inflammation, and had positive self-healing characteristics[189]. Furthermore, Patil *et al.* used polythioketal (PTK) to degrade PU foam dressings in a reactive oxygen species (ROS)-established way without generating

acidic byproducts. As such, the wounds treated by employing this scaffold yielded better rank in wound healing and also pinned-down inflammation level, and better reepithelialization compared to NovoSorb [190]. The applications of Polyurethane in the field of biomaterials-based wound dressings are summarized in **Table (4).**

Polyglycolic Acid (PGA)

It is the linear aliphatic polyester and a biodegradable thermoplastic polymer. It can be synthesized *via* glycolic acid condensation or ring-starting polymerization, as presented in **Table (3)**. It's a biodegradable resin with excellent mechanical strength. Because of its high molecular weight, PGA can now be produced at a lower cost than before, and it has been used in a variety of applications to capitalize on its properties[191]. Currently, PGA has been employed in wound healing as a result of evidence that it is involved in the formation of neo-epithelium and irritation approaches in a few studies[192]. PGA has been employed to save from delayed perforation, near a fistula in open and endoscopic surgery, and cowl wounds following partial glossectomy[193]. PGA and fibrin glue have also been used to cover an open wound area. PGA sheets are strong and absorbent materials, but they are gradually degraded by hydrolysis. Fibrin glue is a biological agent that is biodegradable and absorbent. It is utilized in tissue repair to prevent liquid, or air leaks and possesses hemostatic properties. The use and application of these adhesives have previously been documented[194]. The applications of Polyglycolic Acid in the field of biomaterials-based wound dressings are summarized in **Table (4).**

Polyethylene Glycol (PEG)

It is an amphiphilic polymer defined primarily by its molecular weight and made up of monomer units of oxide ethylene, as presented in **Table (3)**. Because of its biocompatibility, hydrophilicity, and biodegradability, it is commonly utilized in biomedicine. PEGs are appropriate for a variety of medical applications since they are non-toxic and non-immunogenic. They can functionalize their surfaces, which is useful for tissue engineering. PEGylation is the covalent conjugation of PEG polymers to pharmacological targets, such as oligonucleotides, peptides, and proteins, or to improve the pharmacokinetic characteristics of medicinal medicines [195].

In recent years, PEG has been increasingly utilized in the preparation of hydrogels for tissue engineering and wound dressings, owing to its availability, biocompatibility, biodegradability, stable activity, and low production cost. However, the usage of cross-linking agents in PEG-primarily based hydrogel dressings has raised issues regarding cytotoxicity. Consequently, contemporary research has focused on minimizing the toxicity related to those hydrogels[196]. The applications of Polyethylene Glycol in the field of biomaterials-based wound dressings are summarized in **Table (4).**

Polyethylene Oxide (PEO)

It is a polymer created *via* the polymerization of ethylene oxide. Its shape is characterized by the repetitive devices of ethylene oxide, which make contributions to its precise physicochemical properties as presented in **Table (3)**. Numerous articles discuss using CS with PEO. Specifically, they demonstrated its ability to absorb the exudate *in vitro*[197]. In the current study, Szymańska *et al*. created porous nanoparticles incorporated into fibers with PEO and medical-grade CS. When exposed to simulated wound exudate, this composite material formed a gel-like structure, which is an important property for accelerating the healing process. This formulation demonstrated great potential as a dressing for wounds with low to moderate exudate levels after extensive *in vitro* studies focused on wound exudate absorption. Significantly, the substance showed less adherence to surfaces of removed human skin after being coated with poly (dimethyl siloxane), further increasing its suitability as a wound dressing[198]. The applications of Polyethylene Oxide in the field of biomaterials-based wound dressings are summarized in **Table (4).**

Techniques for Quality Control of Biomaterial-Based Wound Dressings

Ensuring the quality, safety, and efficacy of biomaterial-based wound dressings requires

comprehensive *in vitro* and *in vivo* evaluations. Various techniques are employed to assess the physicochemical, mechanical, and biological properties of these dressings, ensuring their suitability for clinical applications.

Functional Analysis

This analysis involves evaluating absorption capacity, permeability, swelling behavior, degradation rate, and drug release kinetics[199]. These properties are critical for determining the dressing's ability to maintain a moist wound environment, provide controlled drug delivery, and support tissue regeneration[27].

Histological Examination

Histological techniques, including light and electron microscopy, are used to analyze the microstructure, porosity, and cellular interactions of the dressing. This allows researchers to assess tissue integration, cell adhesion, and inflammatory responses, ensuring the biomaterial is biocompatible and non-toxic [200].

Biomechanical Testing

Mechanical properties, such as tensile strength, elasticity, and flexibility, are crucial for ensuring the dressing can withstand external forces and physiological stresses [201]. Biomechanical tests evaluate the material's durability, stretchability, and mechanical stability, which are essential for wound coverage and patient comfort [202].

***In Vitro* Cytotoxicity and Biocompatibility Tests**

Cell culture studies assess the dressing's impact on cell viability, proliferation, and migration[203]. Cytotoxicity assays, such as 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and live/dead staining, help determine whether the biomaterial induces adverse cellular effects, ensuring its safety for human application[204].

***In Vivo* Evaluation**

Animal models are often used to evaluate the real-time wound healing efficiency of the dressing. Key assessments include wound contraction rate, epithelialization, angiogenesis, and inflammatory response [205]. These studies provide critical insights into the biodegradation, biointegration, and therapeutic effects of the dressing under physiological conditions [206].

Conclusion

The appearance of skin plays a critical role both psychologically and physiologically. Since skin is frequently exposed to injuries that can lead to scarring, it is essential to explore innovative strategies to improve the healing process, reduce scar formation, and promote rapid and effective skin regeneration. In this context, polymer-based biomaterials have emerged as promising candidates for wound treatment, serving as wound dressings and regenerative scaffolds due to their ability to support tissue repair and regeneration efficiently. Natural polymers have specific properties such as biocompatibility, biodegradability, and biological activity. On the other hand, synthetic polymers are biocompatible, present a versatile chemical structure, and are easily modified to obtain distinct mechanical properties and degradation rates. Overall, these polymers are less expensive than natural polymers. This review presents a detailed description of the polymers from natural polymers, synthetic polymers, or a combination of both, and the newer strategies to improve wound healing treatment.

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المواد الحيوية القائمة على البوليمرات لعلاج الجروح: تطورات في البوليمرات القابلة للتحلل الحيوي الطبيعية والاصطناعية، والهجينة لتقليل وعلاج الجروح وتجديد طبقات الجلد

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علاج الجروح الجلدية الناتجة من الصدمات والأمراض الفيسيولوجية المرضية المختلفة لا تزال تمثل تحدياً كبيراً في الرعاية الصحية، مما يساهم بشكل كبير في العبء الاقتصادي العالمي. أظهرت البوليمرات الطبيعية القابلة للتحلل الحيوي، والتي تشمل الكولاجين، السليلوز، الكيتوزان، وحمض الهيالورونيك، توافقاً حيوياً عالياً وفعالية في تعزيز شفاء الجروح. وعلى الرغم من هذه المزايا، توفرت البوليمرات الاصطناعية القابلة للتحلل الحيوي بديلاً واعداً من خلال التغلب على سلبيات البوليمرات الطبيعية وعرض الخصائص المطلوبة لعلاج الجروح الجلدية. تشمل البوليمرات الاصطناعية كلاً من بولي كابرولاكتون، بولي فينيل الكحول، بولي (حمض اللاكتيك-كو-حمض الجليكوليك)، حمض اللاكتيك، بولي يوريثان، بولي إيثيلين جلايكول، بولي إيثيلين أوكسيد ، وحمض الجليكوليك. وتستعرض هذه المراجعة الرعاية المطلوبة المثلى لعلاج الجروح مع التركيز بشكل خاص على البوليمرات الحيوية الطبيعية والاصطناعية وأنظمة توصيل الأدوية والتقنيات النانومترية المستخدمة لتعزيز تطبيقات شفاء الجروح.