RESEARCH PAPER

Rationalizing Prospective of Biomaterials in Healing of Wound

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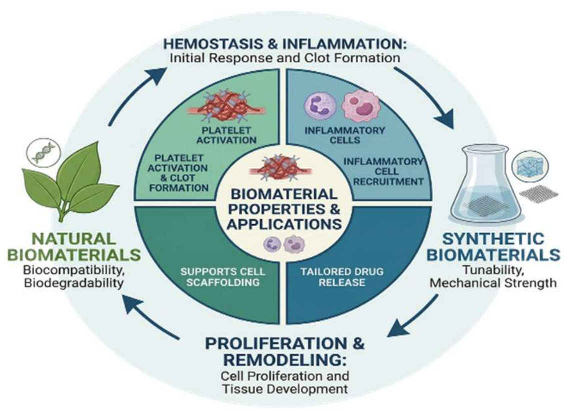
Abstract
Biomaterials are necessary for improving wound healing because they accelerate the wound healing processes and promote regeneration process of the tissue. The matrix outside of cells of cells is duplicated by the scaffold that these components, both synthetic and natural, permitting the cellular differentiation, adhesion, and proliferation process that are necessary for tissue healing. Apart from their ability to degrade naturally and their biocompatibility, alter the wound environment, biomaterials like collagen, chitosan, alginate, and hyaluronic acid have demonstrated tremendous promise. Biomaterials have been developed to address vital problems in the healing process of the wounds, like minimizing infection, moisture management, and controlling reactions that are inflammatory. They can be made functional to distribute therapeutic agents, such as stem cells, development factors, and antibacterial substances, which will improve the healing process. Advances like hydrogel-based biomaterials and nanoparticles have further enhanced the wound site's ability to control medication release, oxygen transport, and cellular interactions. Furthermore, innovative biomaterials have characteristics which encourage quicker healing of both acute and chronic wounds, reducing scarring, and avoiding complications like infections. The fusion of biomaterials with modern technology, such as three-dimensional bioprinting, has opened up new opportunities for wound care customization, offer in specialized treatments catered to the need of each patient. Therefore, biomaterials offer multipurpose solutions to maximize recovery both quickly and effectively while reducing problems, marking a promising new frontier in wound healing. To maximize their clinical applicability and accomplish all of their therapeutic potential, additional research and development are required.



Description: Figure shows the detail illustration of wound healing process.

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1. Introduction

The largest and broadest part of human body is skin, burns, illnesses, and include injuries which can more easily occur there. Skin damage from superficial, localized wounds that need to be treated is a serious illness.[1] The healing of wound is typically a long duration processes.as small wound can heal by themselves, but wound of greater size heal slowly generally takes time up to 8–12 years, in which healing may be interrupted by the presence of bacteria and dust particles. Wound healing composed of four main phases. Wound dressings are essential in wound care to prevent infection, promote faster healing, and inhibit the accumulation of harmful foreign materials.[2] Wound dressings are essential in wound management, providing a barrier which provides protection and aiding in the process of healing. Moist wound dressings have gained popularity for their capacity to produce a favorable environment for the purpose of proliferation of cells, prevent tissue necrosis, and alleviate pain. Natural and synthetic polymers, including hydrogels made from biomaterials like silk, keratin, bacterial cellulose, hyaluronic acid, and collagen, are widely used due to compatibility and similarity towards the extracellular matrix.[3] The detail illustration of wound healing phase is described in figure.1.

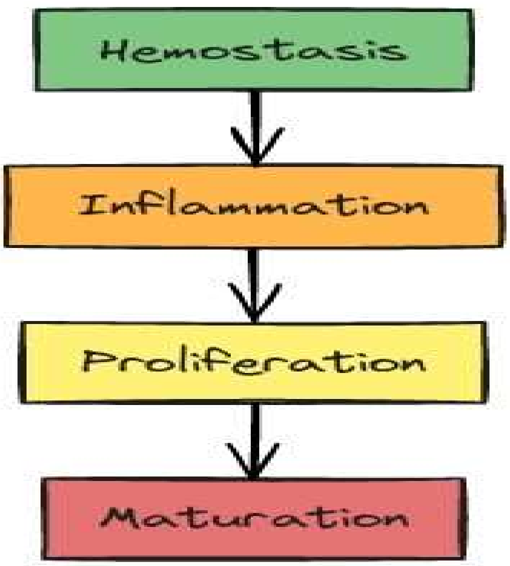

Figure. 1 Represents the phases of wound healing

These biomaterials can be mold into various shaped and into various shape which include examples such as hydrogels, foams, films, nanofibers and scaffolds to address various wound types and needs.[4] Hydrogel dressings, in particular, are beneficial for wound healing as they function like the extracellular matrix, supporting cell growth and new tissue formation. These dressings maintain a moist and acidic environment that promotes healing of wound by stimulating the process of cell proliferation and preventing infections. Hydrogel dressings based on natural polymers like chitosan and glycerol exhibit temperature-sensitive properties that enhance their efficacy in wound healing applications.[5] Recent advancements have prompted the creation of self-healing hydrogels with antibacterial properties that can be customized for on-demand dissolution, making them ideal for promoting wound repair. The diagrammatic process of wound healing phase is described in figure.2.

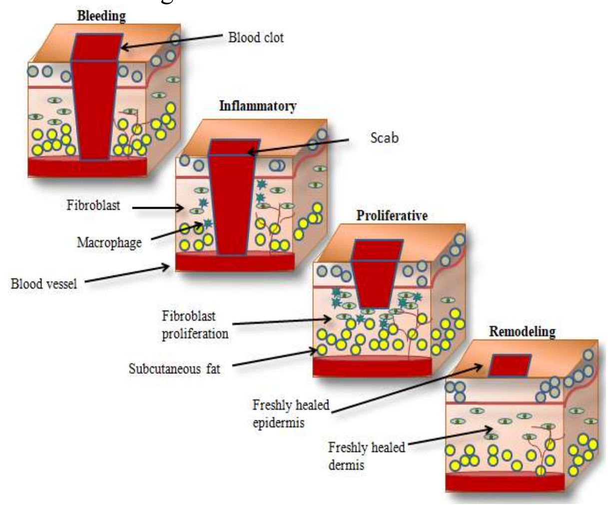

Figure. 2 Describe the phases of wound healing

These dressings not only protect the wound but also release antibiotics to combat infections, thereby expediting the healing process.[6] Incorporating bioactive substances like collagen, alginates, and hydrocolloids in wound dressings shown to directly impact wound healing, underscoring the importance of selecting the appropriate dressing for optimal outcomes. In conclusion, the utilization of biomaterial-based hydrogels with advanced features such as self-healing, antibacterial activity, and stimuli-responsiveness has significantly enhanced wound management.[7] These dressings not only offer protection but also create an environment conducive to faster healing, making them indispensable in modern wound care. Biomaterials do not exhibit any pharmacological effect it just enhances can take the place of biological tissues' or organs' functions. [8] These materials are designed to interact with bodily fluids and tissues for extended periods with minimal to no negative side effects. They play a crucial role in tissue engineering applications, where they are used to treat, augment, or replace tissues, organs, or bodily functions. Biomaterials are expected to seamlessly integrate with the body's tissues, particularly during the inflammatory response phase, to facilitate tissue repair and the process of regeneration.[9] Various biomaterials have been developed for different applications, such as soft tissue augmentation. For instance, collagen matrices of porcine origin are commonly used for soft tissue augmentation. Additionally, biomaterials like hydrogels derived from decellularized porcine adipose tissue have shown promise in promoting the survival of adipose tissue transplantation, making them suitable for soft tissue augmentation procedures. Furthermore, biomaterials based on elastic proteins have been explored for soft tissue augmentation and generation, highlighting the diverse range of materials used in this field. Biomaterials are employed to assist the body during process of wound healing, encouraging the process of growth and the process of the cells migration and the creation of the new tissue formation.[10] As biomaterial mechanical properties create their ability to support these processes. Significant amount of Porosity, structure, biodegradability, mechanical strength, flexibility and biocompatibility are characteristics of biomaterials for regeneration process of the skin are characteristics of biomaterials for skin regeneration. While flexibility enables the material to take on the shape of the wound, approximate tensile strength lets the material to exhibit the mechanical stress without losing its shape. A biomaterial's mechanical characteristics should be customized for a certain site of the wound, taking its location and size into consideration. Biomaterials are employed to assist the body during the process of healing as to accelerate the growth process and migration of cells for the creation of new tissue. It acts as scaffolds for skin tissue engineering process and can be made of composite biomaterials, synthetic and natural biomaterials.[11] A class of materials known as biomaterials works with the collaboration of biological systems, which include living cells, tissues, and body systems. They are crucial to a wide range of pharmacological, biotechnological, and medicinal applications. Biomaterials are primarily used to replace or enhance biological activities, most commonly found in the human body.[12] Recently, there has been a surge in the therapeutic use of biomaterials in wound healing, with items undergoing clinical trials. In tissue engineering, the primary function of biomaterials is to give structural support and weight transfer as to promote cell adhesion, growth, and division while controlling the shape and dimensions of the repaired tissue. Furthermore, biomaterials—also referred to as scaffolds—have the ability to precisely and spatially emit signals, which is essential for adjusting cell productivity and performance as well as promoting the best possible tissue regeneration. As of right now, there are a lot of ways to build a specific biomaterial that will be used as a scaffold.[13] Biomaterials that are synthetic, organic, or composites consisting of several components[7]. Biomaterials are used to help the body repair wounds by promoting migration of cells and growth as well as the production of the formation of new tissue. The mechanical properties of biomaterials employed in healing of wound are critical for their ability to support these processes. Suitable porosity, structure, mechanical strength, flexibility, biodegradability, and biocompatibility are characteristics of biomaterials for skin regeneration. The Sufficient tensile strength allows the material to endure mechanical strain without deteriorating, its form, but adaptability permits the material to conform to the shape of the wound.[14] It acts as a scaffold for the engineered tissue and can be made of synthetic origin, natural origin, or composite types of biomaterials. A class of biomaterials known as aliphatic polyesters, which are flexible, readily processed, nontoxic, and possess high mechanical strength, are among the synthetic biomaterials that are most frequently utilized in the tissue engineering areas. These biomaterials have the potential to be nonbiodegradable various types of polymers as polyglycolic acid and polylactic acid (PLA and PGA) are examples of synthetic biomaterials that contain repeating units produced from nonaromatic hydrocarbons.[15] These polymers are known as aliphatic polyesters. These biomaterials are nontoxic and have a high mechanical strength. They have been effectively employed for the purpose of healing process of the wound and as a delivery mechanism for the factor which are involved in growth to promote skin. Natural biomaterials composed of gelatin, fibrinogen, silk, and collagen. Their similarity to native extracellular matrix has been shown to enhance skin healing renewal process. Most commonly used is collagen which is a natural biomaterial among the others. Collagen is abundant in the skin and throughout the body, which may be the reason behind this. Animal byproducts which are composed of bovine serum albumin, shown to enhance skin healing and eggshell membrane can also be found in natural biomaterials.[16] Polymers are essential in various medical applications, such as the development of tracheal tubes, kidney and liver parts, and facial prostheses. These polymers can also be used to coat other materials, altering their functionality. Common biomaterials for artificial devices include polyester, polytetrafluoroethylene, and polyurethane, which satisfy biocompatibility requirements established by the existence of various types several authorities that regulate of the US food and drug administration.[17] The biocompatibility of synthetic biomaterials is evaluated by observing the response of body to them in vivo, including the creation of a capsule which is fibrous in nature and breakdown by inflammatory cells. Hydrogels, a type of polymer, are often preferred for medical applications due to their nonreactivity with biological tissues, nonirritating nature, and ability to degrade into harmless by products.[18] Factors including the substrate's roughness, the polymer and substrate's surface energy, and the polymer and substrate's viscosity or modulus all affect how well polymers adhere to tissues. The development of bioartificial organs that combine various cell kinds, growth hormones, stem cells, and neuronal and vascular networks with anti-stress and anti-suture characteristics has been greatly aided by a variety of polymers. Polyurea's, a class of polymers, are widely used in coatings, sealants, and adhesive applications due to their viscoelastic properties. Hydrogels are increasingly being recognized as promising and advanced materials for wound healing applications.

They are gel forming polymers that imbibe large amounts of water or biological fluids while maintaining their structures and properties. The hydrated three-dimensional network allows cell migration and proliferation while maintaining moisture in the wound area, making it favorable for wound healing. Moreover, their adaptive abilities to swell, degrade, stick, and release drugs enable localized sustained drug delivery. These characteristics make smart hydrogels highly suitable for creating multifunctional wound dressings that respond to the micro-environment.

2. Types of Biomaterials

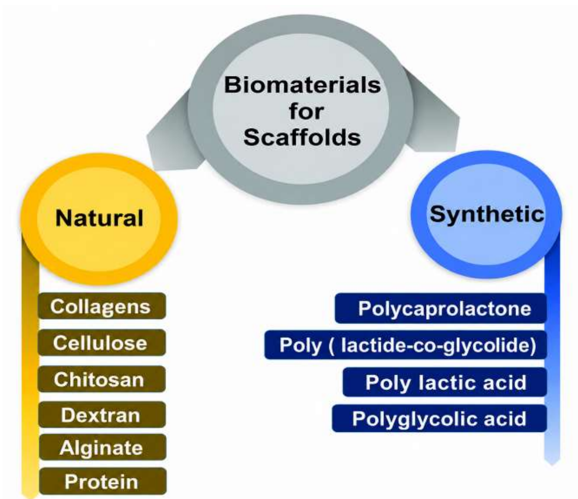

Figure.3 Represents the various types of biomaterial available for wound healing.

2.1. Natural Biomaterials

Gelatin and collagen, fibrinogen, silk, and keratin are the example of natural types of biomaterials which shown to improve healing process of wound because they resemble to the native ECM.[19] Collagen, in particular, is extensively utilized in biomedical applications likely because of its abundance in the skin and the body. Additionally, substances originating from animals, like keratin Have been demonstrated to release the various types of growth-promoting elements and aid in the process of healing of wound. Detail description of types of biomaterial is give in figure.3. Due to their many benefits, which include biodegradability, biocompatibility, ease of manufacturing process, strong adherence, increased absorption as well as permeability, as well as large capacity for tissue renewal and repair process, natural biomaterials drawn a abundant attention within the tissue fields skin wound healing and engineering process. These also include collagen, chitosan, silk, keratin, and soybean-derived coatings, offer unique benefits for skin reconstruction and wound healing applications.[20] For instance, collagen and silk sericin-based biomaterials enriched with flavonoids have demonstrated potential for the process of the healing purpose of the wound because they are biocompatible and biodegradability factor. These biomaterials have special advantages for skin reconstruction and wound healing applications. They include collagen, chitosan, keratin, silk, and coatings generated from soybeans. For example, because of their biocompatibility and biodegradability, collagen and silk sericin-based biomaterials enhanced with flavonoids have demonstrated potential for wound healing. Additionally, keratin biomaterials have been found to possess properties like biocompatibility, biodegradability, resistance to inflammation, and involvement in skin regeneration processes Composite biomaterials, which combine different materials to achieve specific properties, have been developed for biomedical applications.[22] For instance, a composite biomaterial containing cellulose, chitosan nanoparticles, and cellulose poly (methyl methacrylate) fibers has shown efficacy against Staphylococcus aureus and serves as an effective anti-infective bandage.

2.1.1. Alginate

Biomaterials, synthetic polymers, and biopolymers are used to produce wound dressings. Biopolymers, which include hyaluronic acid, fucoidan, chitosan, and alginate, are easily obtainable, biodegradable, immunogenic-free, and non-toxic. Because of its special qualities—which include non-toxicity, biocompatibility parameters, non-immunogenicity, easily available with high capacity of absorption —alginate is used in wound dressings.[22] However, the poor mechanical characteristics of biopolymers usually provide a limitation. To improve their mechanical qualities, they are mixed with synthetic polymers and specifically designed to alter their deterioration pattern. Because of its unique properties, alginate is a promising biopolymer that could improve exudate absorption and address problems with currently recommended wound dressings, lowering the risk of bacterial infections, lowering allergic reactions, promoting wound healing due to its biocompatibility, etc. Additionally, it has hemostatic qualities that are beneficial for wounds that are bleeding.[23] The capacity of wound dressings to decrease infections, decrease bleeding, tendency to absorb exudates, promote the process of healing and wound debridement, be easily sterilized, biodegrade, be non-toxic, have good permeability and gas permeability, and be easy to use are all crucial considerations in their design . Because of its unique properties, alginate is a promising biopolymer that could improve exudate absorption and address problems with currently recommended wound dressings. Detailed description of alginate biomaterial is given in Table.1.

Table.1. *Summarizes the key physiochemical characteristics of alginate and its important properties relevant to wound healing.*

S.No.	Characteristic	Description
1.	Molecular formula	$C_6H_{10}O_7$
2.	Molecular weight	396 g/mol
3.	Solubility	Alginate is inherently highly hydratable and has good water solubility
4.	Color	white to yellowish-brown
5.	Properties exhibit in wound healing	The process of swelling and diffusion inside the alginate gel facilitates the absorption of wound exudates, hence expediting the healing process. Absorbency: Because alginate dressings can gel when it come in touch with the exudate of wound, they are extremely absorbent. This aids in preserving the moist conditions that promote healing at the location of the wound. Exudate Management: Alginate dressings aid in preventing fluid pooling, which might otherwise impede healing and raise the risk of infection, by absorbing excess exudate from the wound. Conformability: Alginate dressings suit the wound comfortably and securely because they conform well to its shape. By encouraging the formation of connection between wound bed and wound dressing, this improves the healing process' efficacy. Gel Formation: Alginate and wound exudate combine to generate a gel that keeps the surrounding area wet. Additionally, this gel aids in the preservation of a physiologically moist wound environment, which is known increase the process of the migration of the cell, proliferation of the cell, and differentiation of the cell as well as other stages of wound healing. Hemostatic capabilities: Alginate dressings can help stop small amounts of bleeding from the wound bed because they have mild hemostatic capabilities. This is very helpful for wounds that exude from moderate to substantial levels. Biocompatibility: Alginate can be used in a variety of wound types, including those with delicate or sensitive surrounding skin,

		because it is typically well-tolerated by the body. Facilitation of Autolytic Debridement: The moist environment that alginate dressings provide facilitates autolysis of debridement, which include the segmentation of natural and non-living tissue through the action of body's enzymes. This process helps to eliminate necrotic material and encourages the formation of healthy tissue. [24]

2.1.2. Chitosan

Chitosan is a non-harmful in nature and composed of biodegradable polymer having characteristics that facilitate absorption, good biocompatibility, low immunological responses, and mucoadhesive properties. Wound healing can be improved by chitosan because of its exceptional biological qualities, which include promoting blood coagulation, fibroblast proliferation, and collagen deposition.[25] Research and development on chitosan-based biomaterials is still ongoing, and it has the potential to provide solutions for a number of medical and healthcare issues. They are important components in the field of biomaterials because of their antibacterial, biodegradable, and biocompatibility characteristics. Chitosan is a useful option for a biomaterial because it is adaptable and simple to modify in terms of structure or characteristics. Due to its inherent antibacterial qualities and capacity to efficiently transfer extrinsic antimicrobial substances into the affected area, chitosan, which is an example of cationic polymer and used investigated in great detail as an antimicrobial agent for the prevention and control of infections. According to one theory, the connection between the negatively charged microbial cell membranes and the positively charged chitosan molecules causes the microbiological membrane to burst, allowing internal components like protein to flow out. It is also suggested that chitosan modifies cell permeability via interacting with the cell membrane.[26] Detailed description of chitosan biomaterial is given in Table.2.

Table.2. *summarizes the key physiochemical characteristics of chitosan and its important properties relevant to wound healing.*

S. No.	Characteristic	Description
1.	Molecular formula	$C_{12}H_{24}N_2O_9$
2.	Molecular weight	396 g/mol
3.	Solubility	Because it is a weak base, chitosan is insoluble in both organic solvents and water. It does, however, dissolve in a weak acidic aqueous solution.
4.	Colour	clear and colourless
5.	Properties exhibit in wound healing	In Hemostasis phase because of its amino group, chitosan has a significant positive charge that enables it to connect and attract negatively charged materials like red blood cells at the wound site. When paired with a procoagulant, chitosan also forms a blood clot that rapidly stops bleeding [20]. Inflammation is a crucial phase in the healing of wounds, manifesting as redness, heat, swelling, and pain at the injury site. It involves drawing immune cells such neutrophils and primary

		macrophages toward the site of the lesion. Neutrophils help remove germs and foreign particles from the body, whereas macrophages are required to clear away debris and initiate tissue healing. Chitosan and its byproducts enhance the proliferative capacities of the various types of inflammatory cells including macrophages, polymorphonuclear leukocytes (PMN), osteoblasts, and fibroblasts, which expedites the healing process of wounds. Chitosan in proliferative phase PDGF (Platelets derived growth factors) and TGF (transforming growth factor) secretion can be stimulated by chitosan. Chitosan encourages macrophages to carry out tumor-curing tasks and provides a non-protein substrate for the growth of three-dimensional tissues. Chitosan in skin remodeling phase helps by creating a network that links cells and promotes the formation of collagen while maintaining sufficient oxygen penetration, chitosan precipitation across the dermis may aid in the healing of damaged cells.[27]

2.1.3. Silk

The naturally occurring protein fibers most closely linked to silkworms (Bombyx mori) are called silk fibers. In addition, flies, mites, spiders, and scorpions create them. At the moment, only silkworm silk is widely used. Silk fibers are vital to the textile industry and are used commercially in many other sectors of the economy. Nevertheless, they are also employed in medical settings for things like skin wound dressings and sutures.[28] The two types of proteins that make up silkworm silk are fibroin proteins, which make up roughly 70% of the cocoon and are the primary structural component, and sericin proteins, which form the bonds between the fibroin filaments and make up the remaining 30%. Silkworm silk is insoluble in water. Silk is an important biomaterial with a range of pharmacological and medicinal uses. Furthermore, due to its tunable properties and ability to be blended with additional substances like Ceramics, polymers, and proteins and peptides for better qualities and functionalities, silk has enormous potential for a variety of clinical treatments as well as many biomedical applications. It is renowned as function as a suture material notwithstanding, extensive this possibility has been shown by research investigation and in vivo and in vitro tests on silk. Additionally, the FDA has cleared this material for use in a few biological applications.[29] Detailed description of silk biomaterial is given in Table.3.

Table.3. *Summarizes the key physiochemical characteristics of silk and its important properties relevant to wound healing.*

S.No.	Characteristic	Description
1.	Molecular formula	$C_{15}H_{25}N_5O_8$
2.	Molecular weight	396 g/mol
3.	Solubility	It requires a highly concentrated aqueous solution containing particular acids, which include phosphoric, formic, sulfuric, or hydrochloric acid, as it is insoluble in a number of organic solvents and even water.
4.	Color	Light or Dark Brown, White, Yellow, Light Green, Grey, Red, Ruby, Emerald, Pale Green, Pale Pink, and Pale Blue
5.	Properties exhibit in wound healing	SF protein plays a physiological and molecular role during the complete wound healing phase. Silk sericin possesses the ability to promote collagen synthesis, cell migration, and proliferation. This is particularly crucial for the healing of wounds. Additionally, sericin possesses antibacterial and antioxidant properties. SF has been studied as a regenerative therapeutic Because silk is biocompatible, sticky, and non-toxic, it promotes wound healing. Moreover, silk resembles the extracellular matrix (ECM) helps with cell migration, angiogenesis, and re-epithelialization. Silk has been employed in the creation of various types of dressing material because of its desirable tunable qualities, especially

		for diabetic wounds.[30]

2.1.4. Gelatin

Gelatin is a transparent, colorless, flavorless, and fragile solid material that is made from the collagen found in the skin and bones of animals. It is frequently utilized as an agent for gelling Cosmetics, food and medicine, and photography. [31] Collagen is a fiber-like insoluble protein that is abundantly present in nature and serves as the main component of skin, bones, and connective tissue. Gelatin is a protein that is extracted from collagen by a controlled hydrolysis process. There are the various types of properties of gelatin like gelatin has the tendency to act as a gelling agent when mix with water. It is also hydrophilic in nature as it absorbs water and swell. Natural polymers share a number of intriguing characteristics, including low cost, non-toxicity, non-immunogenicity, and strong biocompatibility and biodegradation. Furthermore, several naturally occurring polymers demonstrate robust adhesion to damaged tissues, promoting hemostasis, expediting the wound healing process, and eliciting regeneration of dermal tissue. Gelatin has tendency for its potential to modulate inflammation in wounds. By reducing inflammatory cytokines and promoting anti-inflammatory responses, gelatin may contribute to a more controlled and efficient healing process. [32] The FDA has classified gelatin as generally acknowledged as safe (GRAS), meaning that it is a safe food or ingredient. The FDA revoked its permission for the use of any gelatin-containing intravenous medication products. Gelatin is still authorized for use in more ways. Detailed description of gelatin biomaterial is given in Table.4.

Table.4. *Summarizes the key physiochemical characteristics of gelatin and its important properties relevant to wound healing.*

S.No.	Characteristic	Description
1.	Molecular formula	$C_{31}H_{27}NO_4$
2.	Molecular weight	Type A gelatin has an average molecular weight of approximately 90–100 kDa and is more likely to preserve the integrity of α chain than type B gelatin, which typically possesses a molecular weight range of 40–90 kDa.
3.	Solubility	Water will totally dissolve gelatin, but only at temperatures exceeding than 35 to

		40 °C. Gelatin tends to expand at lower temperatures and quickly absorb 5–10 times its weight in water. The swollen gelatin will readily dissolve into a dense solution when heated.
4.	Colour	Colorless or slightly yellow appearance.
5.	Properties exhibit in wound healing	Gelatin-based biomaterials have the potential to stimulate vascular and epithelial cell regeneration, improve peri-wound antibacterial and anti-inflammatory characteristics, and aid in wound hemostasis. Collagen undergoes denaturation to produce gelatin. It has been discovered that gelatin is non-immunogenic, biocompatible, and biodegradable. Collagen undergoes denaturation to produce gelatin. It has been discovered that Gelatin is biocompatible, biodegradable, and non-immunogenic. Additionally, gelatin accelerates the process of tissue synthesis by transporting matrix metalloproteinase enzymes II and IX (MMP) to the lesion site. Gelatin is resistant to the proteolysis process that the enzyme proteases use to break down epidermal growth factor. Using gelatin film speeds up the healing process for wounds, and gelatin as a biomaterial protects skin from oxidative damage.[33]

2.1.5. Starch

Anhydrous glucose units, which come together to form the polymers amylose and amylopectin, are the building blocks of starch. Starch granules consist of 20% to 30% amylose, a linear polymer.[34] It is made up of long chains that are connected by (1,4) units of D-glucose that have undergone some polymerization. Starch is an ideal polymer to utilize in wound healing applications because of its low cost, biocompatibility and ability to heal wounds biodegradability. The process of gelation occurs via cooking of starch in the residence of water. The drug delivery sytem in field of tissue engineering, starch serves as a scaffold and a substrate for cell seeding. Numerous processes, including gelatinization, cross-linking, phosphorylation, and hydroxypropylation, are used to modify starch. Cadaxomer iodine, hydroxyethyl starch, and oxidized starch are three types of modified starch that are used as wound dressings. [35] Detailed description of starch biomaterial is given in Table.5.

Table.5. *summarizes the key physiochemical characteristics of starch and its important properties relevant to wound healing.*

S.No.	Characteristic	Description
1.	Molecular formula	$C_6H_{12}O_6$
2.	Molecular weight	342.297gm/mol
3.	Solubility	Insoluble in cold water or alcohol.
4.	Colour	Pure starch is a white
5.	Properties exhibit in wound healing process	Due to its widespread availability, inexpensive cost, biodegradability, biocompatibility and wound-healing ability, starch is a desirable polymer for use in wound healing applications. The propensity of starch to gel when heated, which gives it a fluid which have non-Newtonian in nature and is another significant characteristic.[36]

2.2. Synthetic biomaterial for healing of wound

The applications for synthetic biomaterials involve drug delivery, wound healing, and hard and soft tissue engineering. They have minimal toxicity, regulated production and alterations, biodegradability, biocompatibility, and compatibility with intended use, among other qualities. Polyethylene oxide (PEO), polyvinyl pyrrolidone (PVP), polyglycolic acid (PGA), polyvinyl alcohol (PVA), and polyethylene glycol (PEG) are examples of frequently encountered synthetic biomaterials used in wound healing. Synthetic polymer dressings come in two varieties: interactive and passive.[37] Wounds are covered with passive, synthetic polymer dressings that are non-occlusive and help restore function below the polymer layer. Velvet and gauze are two varieties of these passive synthetic polymers. Interactive synthetic polymer dressings serve as a barrier to stop bacteria from entering the wound. They are available in occlusive and semi-occlusive varieties. They can take the form of hydrogel, films, foams, or hydrocolloids.

2.2.1. Polyglycolic acid (PGA)

Polyglycolide or polyglycolic acid is the most essential form of linear aliphatic polyester. PGA possesses a high crystallinity and is firm; it is not soluble in most organic solvents. This biodegradable polymer's fibers are durable and have an excellent modulus. PGA can be processed using injection, compression, or extrusion, just as other polyesters. By polymerizing of the glycolic acid through ring-opening and polycondensation, polyglycolic acid is generated. It serves in the neocartilage rejuvenation process. It is discovered that the glass transition temperature is 36°C and the melting point is 225°C. In general, solubility is low in organic solvents; however, hexafluoro-isopropanol is an exception. A biodegradable and biocompatible copolymer, polylactic co-glycolic acid was created by combining two distinct monomers, lactic acid and glycolic acid. PLGA is a polymer that degrades and which holds FDA authorization to be used in European medicine. PLGA functions as a carrier for anti-inflammatory medications, proteins, peptides, and antibiotics. [38] It also targets nucleic acids. According to a study by Proporato et al., PLGA has been used in wound healing because it can deliver lactate and encourage angiogenesis greater than PLA can. A number of reviews of the scientific literature confirm the use of PLGA as a drug delivery method for both fragile and powerful drugs. PLGA nanofibres increase the thermal stability and reduce the rate at which medicines degrade in vivo. In vivo experiments using PLGA hydrogel demonstrated a biphasic release pattern and increased wound contraction. PLGA nanoparticles are utilized to encapsulate hydrophobic or penurious soluble medications. In the event that a wound heals, it releases the medication gradually and deliberately. Additionally, it promotes the transport of basic fibroblast growth factor and vascular endothelial growth factor to the wound site. Utilizing PLGA provides the added advantage of insulating the medication from the degradation process.

[39] Detailed description of polyglycolic acid (PGA) biomaterial is given in Table.6.

Table.6. *summarizes the key physiochemical characteristics of PGA and its important properties relevant to wound healing.*

S.No.	Characteristic	Description
1.	Molecular formula	$(C_2H_2O_2)n$
2.	Molecular weight	76,05 g/mol
3.	Solubility	Additionally, polyglycolic acid (PGA) has a high degree of crystallinity (45–55%), which makes it insoluble in water.
4.	Colour	Violet & Undyed.
5.	Properties	In response to the limited inflammatory swelling associated to this substance, it may initially allow higher flow through relatively modest anastomoses.[40]

2.2.2 . Polycaprolactone

The significant cost of wound care on healthcare resources has lead to a rise in the creation of products for wound care. Because of their enormous potential as wound dressings, biodegradable polymeric materials are becoming more and more popular among scientists worldwide. These days, poly (E-caprolactone) (PCL), a synthetic, Biomaterial with great potential and versatility, is widely used in applications of wound healing. The polymeric material of choice in a variety of applications in biomedical field is PCL due to its adaptability, compatibility, availability, and affordability. Its remarkable mechanical strength and biological qualities have led to its widespread use in wound healing therapy. Among the most extensively used co-spinners among synthetic polymers is polycaprolactone (PCL), which is FDA-approved and biocompatible, biodegradable, and bioresorbable. [41] Detailed description of polycaprolactone biomaterial is given in Table.7.

Table.7. *Summarizes the key physiochemical characteristics of polycaprolactone and its important properties relevant to wound healing.*

S.No.	Characteristic	Description
1.	Molecular formula	$(C_6H_{10}O_2)n$
2.	Molecular weight	114.143 g/mol
3.	Solubility	Polycaprolactone (PCL) is soluble in many organic liquids, but has different solubility levels depending on the solvent: At room temperature, the following substances are soluble: chloroform, dichloromethane, carbon tetrachloride, benzene, toluene, cyclohexanone, and 2-nitropropane. Low solubility compounds include acetone, 2-butanone, ethyl acetate, dimethylformamide, and acetonitrile.
4.	Colour	white solid powder
5.	Properties	Promotes lipid synthesis, epidermal differentiation, and human skin fibroblast proliferation to improve epidermal regeneration while hydrating the skin.[42]

2.2.3. Polyurethanes

Any member of the family of synthetic resinous, fibrous, or elastomeric compounds produced by the reaction of diisocyanates is known as polyurethane. Soft and hard segments make up polyurethane materials, and the kind and ratio of the portions that are solid and soft and hard segments which can be changed to modify the material's performance. Great mechanical qualities, ease of processing, great biocompatibility, and minimal toxicity are all characteristics of polyurethane materials. Polyurethane is a type of polymer material that is synthesized via an addition reaction between diols and diisocyanate in polyester, polyether, or polycarbonate. The polymer chain is then expanded into a polymer using chain extenders. The primary polyurethane chain is made up of soft and challenging parts. The performance of polyurethane is influenced by the proportions of the soft and hard segments and their chemical structure due to the thermodynamic incompatibility between them. This also has an impact on the performance of polyurethane dressing materials.[43] Detailed description of polyglycolic acid (PGA) biomaterial is given in Table.8.

Table.8. *summarizes the key physiochemical characteristics of polyurethane and its important properties relevant to wound healing.*

S.No.	Characteristic	Description
1.	Molecular formula	$C_{27}H_{36}N_2O_{10}$
2.	Molecular weight	548.589 g/mol
3.	Solubility	Polyurethanes are generally hydrophobic and generally water insoluble, but can be dissolved in solvents that contain polar substances like dimethylformamide, dimethylsulphoxide, or N-methylpyrrolidone.
4.	Colour	Super Black. Ultra White.
5.	Properties	The interaction of this polyol, castor oil, and isophorone diisocyanate produced a polyurethane wound dressing. The dressing exhibited good cytocompatibility and antimicrobial action.[44]

2.2.4. Polyvinyl alcohol (PVA)

With the formula (C_2H_4O) x, Polyvinyl alcohol (PVA) is an artificial, colorless, odorless, and polymer soluble in water. It's melting and boiling points are 200°C and 340°C, respectively. PVA, or polyvinyl alcohol, is a vinyl polymer consisting only of carbon-carbon bonds. PVA is a well-liked option for coatings and packaging films because of its exceptional film-forming qualities. When polyvinyl acetate is partially hydrolyzed, a water-soluble synthetic polymer known as polyvinyl alcohol (PVA) is created. It is a colorless and odorless solid that is mostly utilized in a variety of field, including packaging, paper, textiles, adhesives, and coatings. The connection is the same as that of water-soluble polymers like polyacrylamide and common plastics like polyethylene, polypropylene, polystyrene and acid polyacrylic. 3,1-diol linkages are created in the structure of Hydrophilic polymer of synthetic origin, polyvinyl alcohol (PVA), following the breaking down polyvinyl acetate. Due to PVA's exceptional Because of its mechanical properties, high solubility, low toxicity, biodegradability, and biocompatibility, it has been recently applied to biomedical and wound healing applications. Polyvinyl alcohol (PVA), a hydrophilic synthetic polymer, is created by hydrolyzing poly (vinyl acetate), which is made by polymerizing vinyl acetate. [45] Detailed description of polyvinyl alcohol (PVA) biomaterial is given in Table.9.

Table.9. *summarizes the key physiochemical characteristics of polyvinyl alcohol and its important properties relevant to wound healing.*

S.No.	Characteristic	Description
1.	Molecular formula	$(C_2H_4O)x$
2.	Molecular weight	20,000 to 200,000 Da
3.	Solubility	It is insoluble in other organic solvents but soluble in water and just slightly soluble in ethanol.
4.	Colour	Usually colorless or white, but it can also be translucent, cream-

		colored, or have a mild odor.
5.	Properties	The three overlapping phases of wound healing are proliferation, remodeling, and an inflammatory reaction. The healing of wounds is a complicated and organized process. Vascular reactions during the inflammatory phase include exudation, blood coagulation, and hemostasis.[46]

2.3. Natural and Synthetic Composite

In tissue engineering in particular, synthetic biomaterials are essential for enhancing the mechanical characteristics and rate of degradation of collagen scaffolds. Polycaprolactone (PCL) is a synthetic biomaterial that is frequently used in conjunction with collagen to promote skin regeneration. Collagen-PCL scaffolds can be developed in a number of ways, involving electrospinning a collagen-PCL blend, encompassing collagen gel on collagen-PCL electrospun membranes in order to generate a secondary network of finer fibers, and impregnating freeze-dried collagen mats in PCL solution. These approaches aim to integrate mechanical strength and biological cues by combining extracellular matrix (ECM) derivatives with synthetic biomaterials.[47] Collagen-based scaffolds are of particular interest because of their mechanical qualities, biodegradability, biocompatibility, and capacity to sustain cell activity in bone tissue engineering. Collagen combined with artificial polymers such as poly (lactic-co-glycolic acid) (PLGA) is popular due to the acceptable mechanical strength and controlled degradation rate of PLGA. Moreover, the use of collagen in scaffolds for tissue engineering requires the incorporation of functional biomaterials to enhance collagen characteristics and scaffold structure. Collagen-based biomaterials are preferred for scaffold preparation due to their recognizable side groups that support cell adhesion and growth, while synthetic biomaterials offer precise control over physical and mechanical properties. Composite scaffolds, which combine natural and biomaterial of synthetic origin, are highly biocompatible and possess enhanced, tensile strength, making them effective for the regeneration process of the tissue. Additionally, in application of tissue engineering, the creation of hybrid scaffolds combining natural hydrogels and synthetic biomaterials has showed potential. In conclusion, PCL and collagen can be combined to create sophisticated scaffolds with improved mechanical qualities and rates of degradation, which rendering them beneficial instruments for regenerative medicine and tissue engineering.[48]

2.3.1. Classification of the Dressings by Physical Form

2.3.1.1. Hydrogel

The hydrogel works well for all kinds of wound repair. The hydrogel can be synthetic or natural in nature. The hydrogel is a three-dimensional material that is created by adding sheet dressing, glycerin, or polymer-based gel. Hydrogel has a cooling effect on the surface of the wound. It interacts with the wound and permits oxygen molecules to enter the hydrogel. Hydrogel is a three-dimensional structure made of hydrophilic polymer that expands to contain water. The concept behind wound healing gel is that it should be able endure heavy secretions and exudates in order to stop harmful microorganisms from accessing the site of wound. The hydrogel enables a more sophisticated kind of self-healing and is less hazardous and biocompatible. By donating water molecules to the dehydrated tissue, the hydrogel permits the interaction of water vapor and oxygen molecules with the wound surface.[49] This increases the phagocytic and enzymatic activity and eliminates the devitalized tissue during the wound's destructive phase. The idea behind wound healing gel is that it should be able to tolerate thick secretions and exudates in order to stop harmful microorganisms from entering the wound site. The hydrogel offers a more advanced kind of self-healing and is less hazardous and biocompatible. By donating water molecules to the dehydrated tissue, the hydrogel permits the interaction of water vapor and oxygen molecules with the wound surface. In the destructive phase of wound healing, this results in an increase in phagocytic and enzymatic activity and the removal of devitalized tissue. In addition, the hydrogel is employed as an electrode, a wound dressing material, a contact lens, and a vehicle delivery system. Hydrogel products include Nugel, Purilon, Granugel, Aquaform, and Sterigel. Hydrogel displayed the phenomena of swelling and shrinking as a result of connection and dissociation. Before reaching equilibrium, the hydrogel exhibits swelling properties. A stiff mesh size that shields the wound from different bacteria makes up the structure of hydrogel. The hydrogel dressing is tailored for several drug delivery applications, such as regulated and continuous medication release from the wound site, because of its unique physical characteristics.[50] Antibiotics and other medicinal compounds can be simply included into the hydrogel. There are several ways that release happens. Hydrogel can be produced using chemical processes, freeze-thawing, or high energy radiation techniques (such as X-rays, electron beams, and gamma rays). When hydrogel is created via the radiation approach, its mechanical strength is low. When the hydrogel is created using the freeze-thawed approach, excellent strength is seen. Hydrogel gains strength and stability through the process of cross-linking, but its flexibility and elasticity are reduced. Patil *et al.* (2016) created a hydrogel by combining chitosan with meth acrylamide, which has been shown to improve collagen synthesis and boost oxygen availability during wound healing.[51] The injectable polysaccharide hybrid hydrogel was created by Li *et al.* (2015) as a scaffold to aid in burn wound healing. The hydrogel produced in this manner, which contained a greater quantity of carboxymethyl chitosan, exhibited good cytocompatibility and cell attachment.[52] Injectable hydrogel was created by Zhao *et al.* (2017). It is electroactive and functions as a self-healing dressing for wounds with good adhesiveness for cutaneous wound healing.[53] The created hydrogel encourages the deposition of collagen and demonstrates good clotting capacity in vivo due to its ability to scavenge freely. To create the hydrogel, various types of polymers are utilized.

2.3.1.2 Film dressing

An essential component of film dressing is polyurethane, which has a thin, transparent, sticky, and porous structure. The polyurethane's structure allowed water vapor, carbon dioxide, and oxygen to migrate out of the wound site. It also gives bacteria impermeability and shows signs of autolytic debridement. Dressing of film types: Originally, nylon was used to make the film, and from that nylon was produced a product made of supportive and adhesive polyethylene. Because of their limited absorption capacity, film dressings based on nylon-derived products are inappropriate for severely extruding wounds and can lead to wound maceration. Compared to other forms of film dressing, materials serve as superior in boosting compliance among patients, bioavailability, and patent extension for active medicinal components.[54] Alginate, collagen, and chitosan are examples of natural polymers that can be used to fabricate films. The films made from naturally occurring materials can be absorbed in bodily fluids and biodegraded without having an adverse effect on health. Products made from nylon have dressings that are elastic, flexible, and can take on any shape without the need for extra tapping. Because the transparent film has taken place, it is simple to detach the wound dressing and complete the examination of the wound closure. The locations of surgical incisions and superficial lesions are covered with transparent films. Eighty patients undergoing elective split-thickness skin grafting were enrolled in a randomized trial in which paraffin gauze and foam were employed. The results were evaluated after fourteen days and indicated that the addition of polyurethane film was more comfortable and offered easier removal access. In 2015 showed the establishment of a chitosan-based film-forming gel envelop of tyrothricin by Kim *et al.,* who also noted the high granulation formation and wound epithelization.[55] The film-forming gel is helpful in the healing of burns, abrasions, incisions, and excision wounds, among other types of wounds. Opposite TM, Tegaderm TM, and biocclusives TM are a few examples. The most effective option for quick epithelization is film dressing.

2.3.1.3. Dressing with foam

Foam dressings are made primarily of polyurethane and polyvinyl alcohol and are extremely absorbent and permeable sheets. The purpose is to deliver moisture to the region where the wound resides. The Foam dressings' fundamental function is to prevent wound extrusion. They are very adaptable because of their excellent absorbent qualities, which make them an excellent choice for both complete and partial thickness wounds and for slowing the flow of wound extrudates. Apply and remove with ease and without causing stress to the wound. Apply and remove with ease and without causing stress to the wound. At the wound site, foam dressing promotes thermal insulation. Foam dressing affords a channel for oxygen and vapor.[56] Water-loving wound surfaces and water-hating foundations are embraced by two to three sheets of foam made of polyurethane, which further enhances its very absorbent qualities. The water-hating surface permits gas exchange while providing liquid protection. Maceration is not generated by the dressing. Antibacterial substances such as manuka honey, silver, and antibiotics can be added to bioactive foam dressing for altering it. Additionally, foam dressing demonstrated its great enzyme compatibility. According to estimates, the polyurethane foam significantly decreased pain and delivered ibuprofen into the wound bed. The 3-degree burn is not appropriate for the foam dressing. Two liquid form foams are combined to create the foam generated by the silicone embrace of silicone elastomer polymer. They need to be changed after they become saturated with the extrudes, however they can deposit for up to 4–7 days. Foam dressing limitations necessitate repeated dressings; hence, they are not appropriate for dry wounds. As an illustration, consider Lyofoam™, Allevyn™, and Tielle™.

2.3.1.4. Dressing based on nanofiber

Materials which are soft with a high area to volume ratio are accepted by nanofibers. Filaments of polymeric type with a diameter of less than 1µm are employed in the fabrication process. The area of surface to volume ratio of the nanofibres has increased, and their linked porosity—which is further made up of pore size adjustment—has also increased. The majority of synthetic polymers, such as polyvinyl alcohol and poly-lactic acid, and natural polymers, such as collagen, silk fibroin, chitosan, and gelatin, are utilized for the manufacturing of nanofibers. A particular method used to create nanofibres involves electrospinning. These techniques are efficient in producing the two-dimensional and three-dimensional polymeric structures that serve as implanted scaffolds. By using the aid of a polymeric solution, electrospinning is a cheap, easy, and straightforward method for creating nanobots and nanofibres of consistent size.[57] Utilizing this technique, a variety of hydrophobic and hydrophilic enzymes and growth factors can be produced. By charging and releasing the melted biomaterials through a spinneret, providing a high voltage electric field of up to 30 kV, and subsequently solidifying the material to form filament, electrospinning can produce ultrafine fibers. Additionally, the hemostasis, ease of functionalization, and good mechanical strength were all improved by the nanofibre dressing. The electrospinning technique renders it feasible to deliver small molecules. The electrospinning technique is further divided into the Coaxial-electrospinning technique, which is based on core-shell electrospun nanofibres and utilizes two coaxial alignments with a nozzle. The drug is inserted into the inner jet of the nozzle, while the polymer is inserted into the outer tubing. This indicates extended drug delivery at the wound site. The structure of the electrospun nanofibres and the extracellular matrix, which promotes cell adhesion and proliferation, are identical. High medication loading and bacterial infection protection are made possible by electrospun nanofibres.

2.3.1.5. Three-dimensional printed dressing

The medical field is being transformed by the rapid growth of three-dimensional printing. Numerous healthcare organizations produced specialized medications and implants. 3D printing is utilized for the production of structure via the layer by layer procedure. Its incorporation of three phases First, information is transmitted layer by layer about the various tissues and organs that are used for model design and material selection; next, the information is transformed into an electrical signal that instructs the printer to print tissues; and last, a stable structure is created.[58]

Natural biomaterials including alginate, cellulose, chitin, and cellulose provide numerous advantages when used in 3D printing processes, including low toxicity, biodegradability, and mechanical stability as well as high moisture content. The utilization of appropriate biomaterials boosts the numerous positive aspects of 3D printing technologies. A study conducted in 2012 by Koch *et al.* revealed how 20 layers of keratinocytes and 20 layers of fibroblasts were embedded in collagen.[59] The three-dimensional skin, which resembles the structure of the dermis and epidermis, was printed on a Matriderm® sheet using a laser-assisted bioprinter . In the year 2019, Hafezi *et.al* created a three-dimensional printing chitosan as a dressing which has been crosslinked with genipin, a substance that may help with wound healing over time.[60] Drug solubility, cell viability, morphological characteristics, fluid handling, scanning electron microscopy, Fourier transform infrared spectroscopy, and X-ray diffraction have been utilized to characterize 3D printing. Increased swelling capacity and non-toxic behavior were demonstrated by the plasticized films, making them an appropriate agent for use in wound healing applications.

3. Future Work and Outlook. Wound healing is a multi-stage process that involves a lot of hemostasis and other things. When one of the above phases gets interrupted due to persistent inflammation, infection, oxidative stress or impaired angiogenesis, a chronic or non-healing wound may result. Biomaterials have established themselves as worthwhile candidates to develop a conducive microenvironment that stimulates tissue regeneration. Biomaterials that occur in nature as well as synthetic biomaterials may either be used for wound management because they offer certain advantages. Natural materials like collagen, chitosan, cellulose, dextran, alginate, and protein-based biomaterials possess biocompatibility, biodegradability, moisture retention, and biological factors that aid cell adhesion and proliferation. Synthetic materials, including PGA, PCL, polyurethane, PVA and hydroxyapatite, allow for more control over mechanical strength, degradation rate, porosity and structural properties. The combination of various materials can overcome the limitations of each individual material and provide multifunctional wound-healing platforms. Various dressing systems based on biomaterials such as hydrogels, films, foams, and nanofibers are developed to suit the wound. Hydrogels offer moist environment under the dressing and controlled drug release. Films provide a barrier function. Foams are good with exudates. Nanofibrous materials can resemble the extracellular matrix and improve cell interactions, whereas incorporating nanoparticles and nanocarriers can enhance the stability, retention, and controlled release of therapeutic agents. Thanks to recent advances in 3D printing and bioprinting technologies, patient-specific dressings can be designed that feature controlled architecture, porosity and distribution of bioactive components. Despite these advances, there are challenges with mechanical stability along with degradation, sterilization, toxicity, reproducibility, scalability, and regulatory requirements among others. As a result, future research efforts must now focus on multi-functional, smart, microenvironment-responsive biomaterials targeting infection, inflammation, oxidative stress, impaired angiogenesis, and tissue regeneration attacks. Integration with nanotechnology, controlled drug delivery, biosensors, artificial intelligence, and 3D bioprinting might enable personalized and adaptive wound care. Biomaterials have evolved from traditional dressings to cost-effective regenerative platforms that can modulate the wound microenvironment. Composites of natural and synthetic materials judiciously integrated with hydrogels, nanofibers, nanoparticles, and 3D printed systems offer the promise of faster and better healing of acute as well as chronic wounds. Further preclinical and clinical studies are necessary to bring these promising technologies to the clinic in a safe, reproducible, and clinically-effective manner.

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