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A Review on Promising Drug Delivery Hydrogel Formulation by Different Natural and Synthetic Polymers Treated in Wound Healing.

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KEYWORDS

Cellulose, chitosan, hydrogel, wound dressing, sodium alginate.

ABSTRACT:

Wound care is still a problem everywhere, despite the development of several dressing materials for the treatment of both acute and chronic wounds. Nowadays, one of the main causes of mortality globally is injury. The human body's biggest organ, the skin shields the body from the outside world. Serious skin defects need skin replacements to cover them since they do not heal on their own, despite their considerable potential for self-healing. Hydrogels, films, wafers, nanofibers, foams, topical formulations, transdermal patches, sponges, and dressings are amongthe wound treatments now in use. With their high-water content or ability to create a barrier against bacterial infection, hydrogels have special qualities that make them ideal for use as wound dressings. These attributes include the ability to promote wound healing in wet environments, improve wound management and leakage resistance, and facilitate the development of wound granulation. Products made of hydrogel are three-dimensional networks made up of polymeric material clusters that, because of their hydrophilic nature, can store a lot of water.

Introduction

Skin injuries are called wounds [1]. An essential area of study for biomedical materials has been wound dressing [2]. The most frequent wounds in real life are abrasions from falls and surgical incisions on the skin [3]. The four intricately linked stages of wound healing are hemostasis, inflammation, proliferation, and remodelling [12]. By 2026, chronic skin wounds are predicted to afflict 20–60 million people globally, making them a serious issue that is on the verge of becoming an epidemic [10]. Acute and chronic wounds are the two groups into which they fall. An acute wound is a sudden injury to the skin. It may take two to three months to heal, depending on its size and depth in the skin's layers of dermis or epidermis [8]. In this brief review, the materials of interest are mostly hydrogels, which are networks of polymers that have been heavily inflated with water. Often known as hydrogels, networks of polymer chains known as hydrophilic gels are often seen as colloidal gels with water serving as the dispersion medium [9]. Numerous descriptions of hydrogels have been offered by researchers throughout the years. Hydrogel, a cross-linked polymeric network created by the straightforward reaction of one or more monomers that swells with water, is the most widely used of them. It may also be thought of as a polymeric substance that, while expanding and retaining a significant quantity of water inside its structure, will not dissolve in water. In the last fifty years, hydrogels have attracted a lot of attention due to their extraordinary potential in a variety of applications [4-6]. Because of their high-water content,they also have a degree of flexibility that is extremely close to that of natural tissue. Three-

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dimensional cross-linked polymer networks known as hydrogels are intelligent enough to adapt to changes in their surroundings, including ionic strength, pH, temperature, the presence of enzymes, and electric fields, by expanding or contracting correspondingly. They are springy and squishy when swollen, similar to real tissue and displaying good biocompatibility [7]. Synthetic and biopolymers are the most often used polymers in the production of wound dressings. Naturally occurring polymers that are often employed include gelatin, hyaluronic acid, collagen, chitosan, cellulose, fibrin, elastin, and alginate [11].

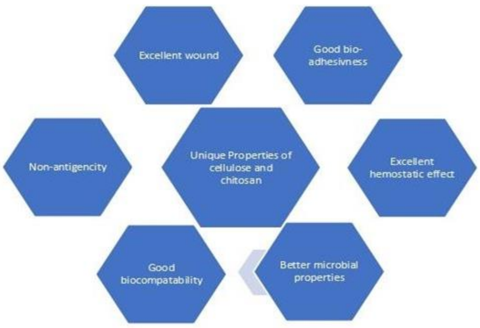

Fig. 1: Ideal Properties of Cellulose and Chitosan in wound healing

Phases of Wound Healing: The intricate method of wound healing results in the restoration of damaged skin tissue. The type of wound dressing that should be used for effective wound management depends on the stages of wound healing. The four stages of the wound healing process include haemostasis, inflammation, proliferation, and remodelling phase, which might overlap [12]. The surface, base, cavity, and wound margin are all parts of the wound, which is also referred to as the wound bed [13].

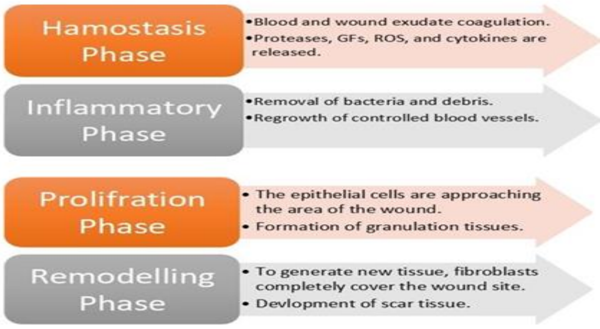

Fig. 2 Graphical representation of the steps during wound healing process.

- **Phase 1: Hemostasis:** Stopping the bleeding is the main goal of the hemostasis stage of wound healing. Your body triggers its blood clotting system to do this. The process of your wound healing begins when your blood clots at the site of the wound, keeping you from losing too much blood.[14]
- **Phase 2: Inflammation in wound healing:** In this stage, waste materials and germs are eliminated by using white blood cells and other blood cells. Inflammation keeps your woundclean and primes it for the synthesis of new tissue.[14]
- **Phase 3: Proliferation in wound healing**: As soon as the wound is clean, your body will begin the proliferation phase of the wound healing process. During this stage, you must bandage your wound.[14].
- **Phase 4: Remodelling in wound healing:** Sometimes it takes more than a year to finish the longest stage of the repair. But after your skin has fully healed, it should mirror its strength before the damage.[14]

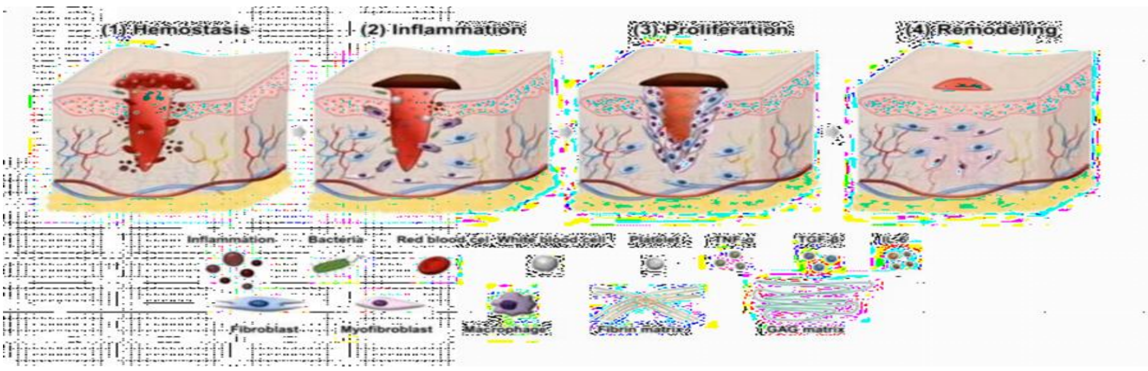

Fig. 3: Diagrammatic representation of different Phases of wound healing

Factors affecting wound healing:

Numerous factors could hinder the process of wound healing, including.

- **Diabetes:** Foot ulcers caused by peripheral neuropathy are a frequent consequence of diabetes. Peripheral ischemia brought on by peripheral vascular disease is another consequence. Both issues have an impact on the proliferative stage of healing and cause the healing process to slow down overall.[15]
- **Obesity:** Obesity raises the risk of ischemia and insufficient tissue oxygenation, both of which can cause necrosis or delayed wound healing.[15]
- **Necrosis:** Another condition that might prevent a wound from healing is unplanned tissue death, which necessitates surgical debridement to remove the damaged tissue before healing can continue.[15]
- **Poor nutrition:** Malnutrition, which is frequent in the elderly, may slow down the healing process of wounds by reducing the development of new blood vessels, collagen synthesis, and fibroblast proliferation. Inadequate ingestion of protein is one such indicator of malnutrition.[15]
- **Smoking:** Smoking cigarettes, especially when nicotine is used, causes vasoconstriction, which alters blood flow. Additionally, nicotine suppresses the immune system, which raises the possibility of a wound infection.[15]

Hydrogel

A hydrogel is a fascinating material composed of two main components: porous, permeable solids and interstitial fluid. The porous solid network forms a three-dimensional structure made of natural or synthetic polymers. Meanwhile, the interstitial fluid, which constitutes at least 10% by weight or volume, consists mainly of water or biological fluids. These properties make hydrogels highly versatile and find applications in various fields, especially in biomedicine. While many hydrogels are synthetic, some are derived from nature. The term “hydrogel” was coined in 1894.

Advantages of hydrogel:

- They have an approximately equal degree of flexibility as genuine tissue because of their high-water content.
- Timely release of nutrition or medications.
- They may be injected and are both biocompatible and biodegradable.
- Hydrogels may sense variations in temperature, pH, or metabolite concentration and adjust their load accordingly.
- Hydrogels are also easily modifiable and have strong transport qualities.

Disadvantages of Hydrogel:

- Expensive.
- Might be challenging to manage.
- Limited mechanical potency.
- Due to their non-adherent nature, they may require supplementary dressings to keep them in place. The movement of the maggots can also provide discomfort.
- Challenging to load with nutrition and/or medications.

Wound healing:

Because of their cross-linked nature, hydrogels can contain both drugs and water. Wound exudates may be held and retained by them because of their capacity to hold water. [91,92] When

applied, hydrogels based on gelatin and sodium alginate have the capacity to cover and shield the wound from bacterial infection. The ideal hydrogel material would have the functional properties listed below[94].

- Maximal equilibrium swelling, or absorption capacity, in saline.
- Ideal particle size and porosity, or the desired rate of absorption, based on the needs of the application.
- Absorbency under load (AUL) maximum
- The lowest possible soluble content and residual monomer quantity.
- The lowest price.
- Maximum durability and stability in a growing environment as well as during storage.
- The maximum degree of biodegradability without the production of harmful species during degradation.
- pH neutrality following water swelling

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- Completely non-toxic, colourless, and odourless.
- Photo stability.
- The hydrogel's rewetting capability is contingent upon the application requirement, such as in sanitary or agricultural settings. It must be able to either retain or return the ingested fluid.

Hydrogel Classification

1. Classification based on cross-linking:

Hydrogels fall into a variety of categories. However, because cross-linking networks are essentially used to create hydrogels, they can be divided into two groups according to cross- linking: Hydrogels that are (a) physically cross-linked or self-assembling and (b) chemically cross-linking. [16,17]

2. Physicallycross-linked hydrogels:

The use of reversible gels, also known as physically cross-linked hydrogels, has become more significant because of their simplicity of synthesis and the benefit of not requiring cross-linking chemicals. Physical relationships between distinct polymer chains prevent physically cross-linked gels from dissolving.[16]

Ionic Interaction:

Ion Interaction Dynamic interactions between oppositely charged groups or metal-ligand contact are two efficient ways to carry out ionic interactions.[18] Hydrogels with strong ionic conductivity, fatigue resistance, environmental reactivity, and self-healing qualities are the outcome of ionic interaction. However, the complex and insufficient mechanical characteristics. The preparation method continues to provide the major challenges for the potential future applications of hydrogels produced by ionic interactions.[19]

Hydrogen Bond:

Hydrogen bonds are often needed, and they may significantly increase the ability of hydrogels to heal and restore themselves.[20] The resultant hydrogels usually have poor utilisation rates because hydrogen bonds are often weak under water circumstances. Scientists are now developing DN hydrogels and IPN hydrogels in an effort to boost the impact of hydrogen bonding.[21]

Crystallization:

Crystallisation One of the most frequent methods of physical cross-linking is the freeze-thaw process. During the freezing phase of the cycle, the polymer chains are arranged around themselves by the produced ice crystals. The ice crystals then melt during the cycle's thawing process to form a microporous structure.[22]During the freeze-thaw process, the duration, temperature, number of cycles, and amount of polymer components may be changed to accommodate different pore sizes, mechanical strengths, morphology, or other properties.23],[24In order to recruit cells for wound healing, it is essential that stem cells placed on soft, flexible, and variable porosity hydrogels that can replicate extracellular matrix (ECM). These hydrogels also allow stem cells to respond and migrate in a directed manner in response to dynamic changes in ECM stiffness.[25]

Protein Interaction:

Protein Interaction An increasing number of proteins—gelatine, collagen, silk fibroin, matrix glue, and so forth—are used as the primary raw material in the production of hydrogels made from natural polymers[26, 27]. Temperature and phase transition are altered by non-covalent bond interactions between proteins or polypeptides to generate protein or polypeptide hydrogels. Spider silk self-assembles into -sheet-rich silk by exploiting sequence variations between eADF3-CTD and eADF4-CTD. The precise molecule abundance and composition enable the solution-geltransition process to be fine-tuned.[28].

Chemical Cross-Linking: Most hydrogel materials are currently manufactured using chemical cross-linking, and chemically cross-linked hydrogels frequently have good mechanical characteristics and higher stability[29]. They are dominated by the enzymatic, conjugation, and free radical polymerization reactions.

Conjugation Reaction:

The conjugation process has led to the cross-linking of hydrogels, which have gained significant attention. The conjugation process may be carried out under very moderate conditions, much as the Michael addition reaction, the Schiff's base reaction, and the Diels-Alder addition reaction.[30]An easy green method for the conjugate reaction is the Schiff's base reaction, which

involves the condensation of an amine and an active carbonyl group[31]. Numerous polysaccharide molecules, including cellulose, hyaluronic acid, starch, and alginate, contain nearby hydroxyl groups that periodate may oxidize to produce hydrogels via Schiff's base reactions[32, 33].

- **Free Radical Polymerization:**

Free radicals may be produced via heating, UV light, high energy radiation, electrolysis, and plasma initiation.[34]Under the influence of heat or light, unsaturated functional groups or photosensitive functional groups are used in thermally initiated polymerization and light-initiated polymerization to undergo free radical polymerization or cross-linking to form covalent bonds.[35],[36] Because of their stable and well-regulated structures, most hydrogels made using thermally induced cross-linking procedures are appropriate for deep wound healing.[35],[36]In the photoinitiated polymerization procedure, the precursor with the photosensitive functional group may polymerize under UV light directly, while the precursor with the double bond functional group can polymerize under UV light after adding a photo initiator[37, 38].

- **Enzymatic Reaction:**

Mild temperatures during enzymatic processes decrease biological activity loss, speed up gelation, and avoid the formation of hazardous chemicals. Right now, enzymatic rapid gelation seems to be a viable method for producing antibacterial hydrogels[39, 40]. In order to improve EC mobility, low molecular weight hyaluronic acid (LMWHA) derivatives were immobilized inside gelatin- based hydrogels using hydrogen peroxide and HRP. The results suggest that EC motility may be enhanced by enzymatic immobilization of LMWHA-Ph inside gelatin-based hydrogels, which might be further explored for vascular tissue engineering applications.[41]

Biomaterials for Preparing Hydrogels:

Biomaterials used in tissue engineering or regenerative medicine may be divided into two primary categories: Biomaterials that are both natural and synthetic [42]Regardless of the materials' origin, hydrogel dressings have to be highly biocompatible, have low toxicity, and encourage the growth of nearby cells. Additionally, among other characteristics, artificial hydrogel dressings need to be highly mechanical, moisture-retentive, biodegradable, antibacterial, antioxidant, non-adhesive, and have superior air permeability.[43]

Natural Biomaterials:

- **Sodium Alginate:**

One kind of linear anionic polysaccharide polymer is sodium alginate (SA).[44]Due to its high - COO content, SA exhibits clear pH sensitivity and gels fast under very mild settings, preventing the inactivation of active substances including enzymes, proteins, cells, and sensitive medications. Numerous wound care treatments capitalize on the structural similarities between ECM and alginate. [44,45,46]Nowadays, there is a lot of interest in green synthesis that draws inspiration from proteins. In addition to having strong antibacterial action, SA/SE-AgNPs semi-interpenetrating network hydrogels address SA's deficiency in cell adhesion capacity.[47]

- **Collagen:**

Animal ECM mostly consists of collagen (COL), which has strong biological activity, biocompatibility, and biodegradability. Its main function in wound dressings is to stimulate coagulation, encourage cell development and proliferation, and have mild antigenicity and prevents the production of scars, etc. [48]Col-HA hydrogels made using HRP covalent crosslinking shown excellent biocompatibility and biodegradability in addition to spontaneously stimulating angiogenesis and contributing to the development of collagen Fiber and epithelium.[49] When used as a wound dressing, hydrogels with self-healing properties might prolong the material's useful life, particularly in urgent circumstances, hence improving wound safety. Thus, the creation of premium collagen hydrogels with strong self-healing properties and injectable capabilities its, antibacterial, with hemostatic properties are highly useful in wound dressings. Potential [50]. The mechanical qualities of natural collagen are low, and its resistance to biodegradation is weak. Furthermore, in a humid environment, bacterial erosion can cause pure collagen to quickly degenerate.[51] To increase the performance of collagen-based hydrogels, scientists are now

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looking at a range of cross-linking techniques. EDC/NHS cross-linked collagen gel had a greater hemostasis impact than delayed hemostasis. [52]

- **Starch:**

A common ingredient in the creation of biodegradable hydrogels is starch.[53]Its benefits include low cost, broad source compatibility, renewable energy, biocompatibility, and non-toxicity. [54,55]Because of its drawbacks, including its poor mechanical strength and lack of hydrophilicity, starch is often not utilized exclusively for making hydrogels.[56]One of the significant modified starches is oxidized starch. Oxidized starch is a common ingredient in pharmaceutical products because of its low viscosity, high stability, transparency, film formation, and viscosity.[57]Unfortunately, the current state of research on starch hydrogel dressings is inadequate, and the primary factor preventing future development of this technology is starch's poor mechanical strength.

- **Cellulose:**

The most prevalent and plentiful polysaccharide in nature is natural cellulose, which comes from a highly rich source. It may be made by bacteria, fungus, algae, and plants. [58,59]Special emphasis has been paid to carboxymethyl cellulose (CMC) because of its inexpensive cost, superior transparency, and high absorbance dance.[60] Because CMC is very hydrophilic, wound exudate may be absorbed by CMC hydrogels more readily and the environment is kept moist the area to stop moisture loss from the tissue, which is crucial for burns and diabetic wounds.[61]Bacterial cellulose hydrogels high in thymol can be a useful material for treating third-degree burn wounds. Along with its outstanding antibacterial action, it also possessed amazing moisturizing qualities that made it an appropriate moist atmosphere to facilitate a seamless changeover between the stages of inflammation, proliferation, and remodelling [62]

- **Chitosan:**

The only naturally occurring cationic polymer with these qualities is chitosan (CS), which is also non-toxic, biodegradable, and possesses antibacterial, antifungal, and antitumor activities. It is a substance that is commonly utilized in biomedicine. Because CS increases tissue development and enhances hemostasis, it is also advantageous for wound healing. Hydrogels based on CS are crucial for wound healing. [63,64].Natural cationic copolymer chitosan has hydrophilic qualities and is highly biocompatible and biodegradable because human enzymes can break it down. [65,66]

- **Hyaluronic Acid:**

One of the primary elements of the extracellular matrix (ECM) is hyaluronic acid (HA), which interacts with cells via CD44 and other receptors on the plasma membraneto encourage the development of capillaries.[67]HA accumulates in the wound region during the inflammatory phase of wound healing and controls the production of pro-inflammatory cytokines by controlling inflammatory cells to ingest invasive microbes and stimulate fibroblasts and keratinocytes. adenocytes to move and multiply when the process is remodelling and proliferating. As a result, HA is crucial for angiogenesis and tissue regeneration. Researchers have improved the hydrophilicity of hydrogel dressings and accelerated wound healing by combining these benefits of HA with other biological materials. [63,68,69] The lack of an antibacterial effect, poor mechanical qualities, and poor structural stability of HA-based hydrogels are some of its drawbacks, which may limit their specific effectiveness. The lack of an antibacterial effect, poor mechanical qualities, and poor structural stability of HA-based hydrogels are some of its drawbacks, which may limit their specific effectiveness.[70]

Synthetic Materials for Hydrogels:

- **Acrylamide:** Acrylamide (AM) and its derivatives have a number of advantageous properties, including excellent biocompatibility, non-carcinogenicity, non-toxicity, simplicity of processing, mechanical adjustability, precise and regulated elastic features, and strong swelling capacity.[71].The hydrophobic contact and ionic cross-linking that produced the SA/PAM-Fe DN hydrogels demonstrated excellent heat stability, puncture resistance, fatigue resistance, and pH sensitivity in addition to outstanding self-healing properties.[72].
- **Polyvinyl Alcohol:** Common polymers like polyvinyl alcohol (PVA) have strong mechanical

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qualities, are non-toxic and non-carcinogenic, are soluble, and are biocompatible [73,74]. Nevertheless, the pure PVA hydrogels lack flexibility and hydrophilicity and lack the effects of hemostasis and antibacterial, among other things. Researchers have been concentrating on using PVA in conjunction with other useful elements to accelerate wound healing in recent years. At Currently, PVA is combined with a wide range of substances (oxidized cellulose, gelatin, SA, CS, etc.) to produce hemostasis.[75] Blood coagulation is promoted and accelerated by hydrogels that stick to the wound surface, block damaged blood vessels, and encourage platelets to produce coagulation factors.[76]

- **Polyethylene Glycol:** One type of amphiphilic polymer with a broad molecular weight range is polyethylene glycol (PEG).[77] PEG has been a common ingredient in wound dressings in recent years due to its non-toxicity, excellent biocompatibility, biodegradability, ease of availability, steady action, and inexpensive preparation cost. [78,79]However, the generated hydrogel dressings are cytotoxic since cross-linking agents including formaldehyde, glutaraldehyde, and epichlorohydrin are used.[79] As a result, recent studies concentrate on lowering PEG-based hydrogels' toxicity. Nowadays, a lot of workers create hydrogels by cross-linking citric acid (CA).[80] According to a paper, CA was used to make CMC-PEG hydrogels, which demonstrated significant benefits for chronic wound healing when used as an environmental cross-linking agent.[81]
- **Polyurethane:**Synthetic polymer Polyurethane (PU) has urethane linkages on its main chain and is made up of soft segments made of polyester or polyether blocks and hard segments constructed of diisocyanates and chain extenders. [82,83] PU possesses favourable mechanical, chemical stability, low biotoxicity, blood compatibility, biodegradability, and biocompatibility qualities.[84] Due to their broad spectrum of action, drug-loaded hydrogels that are chemically covalently linked or physically combined frequently attract interest.[85]
- **Polyvinylpyrrolidone:** Reduced toxicity, excellent water solubility, biocompatibility, biodegradability, heat resistance, wettability, adhesion, and film-forming qualities are among the qualities of polyethylene pyrrolidone (PVP). For this reason, it's frequently utilized in food, cosmetics, medicine, and other industries.[86] Recent years have seen an increase in the usage of PVP-based hydrogel dressings due to PVP's resistance to microorganisms. PVP/PVA/Ag@ZnO NCs hydrogels were produced by Khan et al., and the antibacterial activity investigation shown that by reducing the elevated incidence of infection, the dressing might enhance the pace at which wounds healed.[87]. PVP has a strong water solubility, which helps it release the medicines loaded fast.

Table 1: Hydrogel-based polymer applications in medicine

Applications	Polymers	Reference
Wound care	Agar, polyethylene glycol, polypropylene glycol, polyvinyl pyrrolidone, polyurethane, and polyethylene glycol	[88]
Drug-delivery, pharmaceutical	The three materials are poly (vinyl pyrrolidone), poly (acrylic acid), and poly (starch).	[88]
Dental Supplies	Hydrocolloids: gums (Kerensis, Karaya, andGhatti)	[89]

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Technical goods (pharmaceutical, cosmetic)	poly (acrylamide N-isopropyl ether), poly (vinyl methyl ether)	[90]
Implants and Tissue engineering	Hyaluronic acid	[90]
Polymeric system that can beinjected	Hairpin peptide	[90]

Characterization of Hydrogels: In general, the morphology, swelling characteristic, chemical structure, and elasticity of hydrogels are what define them. The following are crucial characteristics for hydrogel characterization as follows:

- **pH:** With a digital pH meter, the pH of hydrogels is determined. A pH metre has to be calibrated before use.
- **Scanning Electron Microscopy (SEM):** Surface topography, composition, and other characteristics of the sample, such electrical conductivity, may all be determined using SEM. When using SEM, magnification can be from around 10 to 500,000 times, regulated across a range of up to 6 orders of magnitude.
- **Fourier Transform Infrared Spectroscopy:** It is a helpful method for figuring out a substance's chemical structure. It is predicated on the idea that a substance's fundamental constituents, or chemical bonds, may be stimulated and absorb infrared light at typical chemical bond-based frequencies.
- **Swelling measurement:**There are now three approaches available for measuring swelling in hydrogels:

Method A: This approach involves using a roller mixer to submerge the dried hydrogel in deionized water for 48 hours at room temperature. Following swelling, a stainless-steel net filters the hydrogel.

Method B: The dry hydrogel (0.05–0.1g) was mixed with a large enough amount of water (25–30 ml) in a volumetric vial and let to stand at room temperature for 48 hours. After that, the mixture is centrifuged to separate the unabsorbed water from the layers of water-bound substances. After the free water has been evacuated, the swelling may be calculated using the previously mentioned Method A.

Method C: In procedure C, the dry gel is left at room temperature for 16 hours while submerged in deionized water. Following swelling, a 100-mesh (149 μm) stainless steel net was used to filter the hydrogel. The formula for swelling is as follows: -

Swelling= C×100/B

where B is the weight of the insoluble component following water extraction and C is the weight of the hydrogel that is formed after drying.[95]

- **In -Vitro drug release study:**Studies on release are conducted to comprehend the process of release since hydrogels are swollen polymeric networks with drug molecules inside of them. during the course of the application. In order to determine if the medication solutions are equivalent, the parameters are matched with the standard plot.[96]
- **Rheology:**Hydrogel viscosity is measured at 4ºC constant temperature using a cone plate type viscometer. When it comes to assessing viscosity, this viscometer is quite specific. Thestraightforward formula for the angle of repose, which also determines height and length, determines viscosity.
- **Spreadibility study:** The device consisted of two glass slides with a pan fixed to a pulley and a wooden block with a scale. 100 gram of excess formulation was sandwiched between two glass slides. To compare the formulation and achieve consistent thickness, weight was applied to the upper glass slide for a duration of five minutes. Weight may be added, and the duration needed to divide the two slides was calculated to account for spreadibility.

S= (m × l) / t where t is the time taken in seconds, l is the length of the glass slide, m is the weight fastened to the upper slide, and S is spreadibility.

- **Skin irritancy test studies:**Tests for skin irritancy are performed on rabbits. Two rabbits were given

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the preparation, and the affected region was covered with bandages or gauze. Within a day, the mixture was eliminated, and the region was examined for erythema and edema.Average irritation scores= (erythema reaction + edema reaction scores) / time interval.

- **X-ray diffraction:**To determine if polymers deform or preserve their crystalline structure throughout the pressurization process, X-ray diffraction is utilized.

Table 2. Some examples of commercial hydrogel-based wound dressings [97]

Product	**Company**	**Main Component**	**Application**
Algisite	Smith and Nephew	Alginate	Minor burn wounds, abrasions, rips in the skin, and lacerations
Medihoney	Derma Sciences	Alginate	Partial to complete thickness burns and wounds
Kaltostat	Convatec	Alginate	Wounds with moderate to heavy exudation both acute and chronic wounds
NU-GEL	Systagenix	Alginate	Management of chronic wounds throughout all stages of healing
Condress	Smith and Nephew	Collagen	Chronic and acute wounds
Helix3-cm	AmerxHealth Care	Collagen	Chronic and acute wounds
Comfeel	Coloplast	Hydrocolloids	Designed for difficult-to-dress areas
Inadine	Systagenix	Polyethylene glycol	Open wounds that may become infected
CovaWound	Covalon	Hydrocolloids	Ulcerations on the legs and feet, pressure, and superficial, partially-thick burns
Cutimed	Bsn Medical	Dialkylcarbamoyl -chloride	Care for sloughy and necrotic tissues in long-term wounds
Sofargen	Sofar	Colloidal silica	For cuts, scrapes, burns of the first and second degrees, and other injuries
DermaFilm	DermaRite	Hydrocolloids	Skin grafts, superficial ulcers, closed surgical wounds,

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Table 2. Hydrogels in clinical trials/ marketed products.

Hydrogels	Clinical TrialOutcomes/Marketed Products	References
Nanofibrillar cellulose wound dressing	In an average of eighteen days, the wound dressing will come off the epithelialized skin transplant donor site.	[98]
Bacterial nanocellulose	The majority of the patched skins exhibited no signs of bullae, vesicles, or oedema. It was safe for the additional assessment and non-irritating.	[99]
Nanoderm™ Ag	It showed heightened pliability and enduring antibacterial qualities. efficient in the treatment of contaminated wounds.	[100]
Nanoskin®	It is biocompatible, non-allergenic, and entirely natural. It works well for treating burns and surgical wounds. Wounds from diabetic ulcers, skin grafting sites, and so on.	[101]
CelMat®	Beneficial in the management of chronic wounds, burns, and ulcers. It facilitates better gas exchange, pain alleviation, and absorption and fluid desorption.	[101]
EpiProtect®	Useful for treating burn injuries in children following enzymatic debridement.	[102]
ExcelArrest® XT	In order to stop skin bleeding, it quickens the coagulation process.	[103]

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Conclusion

In conclusion, the field of wound healing has seen significant advancements in the development of hydrogel-based wound dressings, with a particular focus on natural polymers such as cellulose, chitosan, and sodium alginate. These hydrogels have demonstrated remarkable potential for wound management, thanks to their high-water content, biocompatibility, and ability to create a moist environment conducive to healing. The use of cellulose and chitosan in hydrogel formulations has shown promising results in promoting wound healing and preventing bacterial infections. Additionally, the incorporation of sodium alginate in hydrogels has contributed to their ability to absorb wound exudates and maintain an optimal healing environment. Overall, the versatility and effectiveness of hydrogels as wound dressings highlight their significance in addressing the challenges associated with wound care, making them a valuable asset in the field ofmedical science.

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