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PREPARATION METHODS OF HYDROGEL FOR WOUND HEALING: A REVIEW

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ABSTRACT

This review article analyzes five primary preparation techniques for hydrogel-based wound dressings: suspension polymerization, grafting, irradiation, chemical crosslinking, and physical crosslinking, as well as the natural and synthetic biomaterials utilized in their production. Each method consists of different outcomes and limitations that determine the suitability of the hydrogel for wound healing applications. Suspension polymerization, especially the inverse water-in-oil technique, produced homogenous, superabsorbent hydrogels having high swelling capacity, but the use of toxic organic solvents gives biocompatibility concerns. Mechanical qualities were enhanced by grafting onto starch backbones using ceric ammonium nitrate or redox initiator systems, but toxic initiator by products require more purification before clinical use. Irradiation with cobalt-60 gamma sources accomplished concurrent crosslinking and sterilizing without chemical additions, resulting in pure yield, initiator-free wound dressings. Chemical crosslinking created mechanically robust, stable networks appropriate for harsh wound environment While physical crosslinking via ionic interactions and freeze-thaw cycling provided biocompatibility without the use of chemical agents, it had inferior mechanical strength. The reviewed biomaterials included natural polymers including chitosan, sodium alginate, and hyaluronic acid, which demonstrated bioactivity and compatibility with the extracellular matrix, whereas synthetic polymers such as polyvinyl alcohol (PVA), polyethylene glycol (PEG), polyvinylpyrrolidone (PVP) and PLGA (Poly(lactidecoglycolide)) provided reproducibility and mechanical strength. Future research must emphasize scalable,

economical preparation methods that incorporate mechanical durability, biocompatibility, and regulated medication administration to enhance hydrogel-based wound care.

KEYWORDS: Hydrogel, Wound healing, Preparation, Natural Biomaterial, Synthetic Biomaterial.

INTRODUCTION

Hydrogels are a class of three-dimensional crosslinked polymeric network that have the unique capability to absorb and retain large quantities of water. Hydrogels consist of three components which are monomer, initiator, and crosslinker, which together determine the structural integrity and functional properties of the hydrogel.[1] These polymeric matrix broadens in liquid due to swelling and forms crosslinking structure by using many monomers. It consists of physically or chemically crosslinked bonds which are hydrophilic in nature (such as hydrogen bonding, ionic interaction, or chain enlargement).[2] The hydrophilic functional groups attached to the polymeric backbone such as hydroxyl (–OH), carboxyl (–COOH), and amide ($–NH_2$) groups are responsible for water absorption, while the crosslinked network prevents dissolution of the hydrogel.[3]

In general, wounds are categorized as either acute or chronic. Acute wounds, such as lacerations and surgical incisions, usually heal on their own in 8 to 12 weeks through a systematic and prompt healing process.[4] On the other hand, chronic wounds often recur, fail to heal within 12 weeks, and are associated with untreated trauma or systemic conditions such immunosuppression, diabetes mellitus, and venous insufficiency. Wound healing is a complex process that involves multiple phases including hemostasis, inflammation, proliferation.[5]

Conventional wound dressings, such as dry gauze pads, cotton wool, and bandages, provide only passive protection to the wound and thus not promote wound healing. Wound healing and tissue regeneration requires optimal moist environment and cooling effects. Thus, hydrogel-based dressings medicaments have emerged as advanced wound care materials due to their ability to maintain a moist environment, absorb wound exudate, and provide a cooling effect that can reduce pain and inflammation of the tissue.[6,7] Multifunctional hydrogel systems have been developed with advanced bioactivity, aiming to support and accelerate wound healing.[8]

Recent years have witnessed substantial progress in the design and production of hydrogel-

based wound dressings, encompassing the development and investigation of smart, stimuli-responsive, bioactive, and self-healing hydrogels.[8] These systems are capable of responding dynamically to changes in the wound microenvironment such as pH, temperature, or enzymatic activity and of delivering therapeutic agents in a regulated and sustained manner, hence enhancing the wound healing process.[9] Therefore, the logical design and development of efficient wound care system requires a deep understanding of the various hydrogel preparation methods and material compositions. This review aims to provide a comprehensive overview of the classification, biomaterials, and preparation methods of hydrogels used in wound healing applications.

BIOMATERIAL FOR HYDROGEL PREPARATION

Natural Polymers

Since the polymer matrix directly influences the physicochemical characteristics, biocompatibility, biodegradability, and therapeutic efficacy of the final hydrogel, choosing the right biomaterials is essential to the design and functionality of hydrogel wound dressings. Because of their structural resemblance to the extracellular matrix (ECM) of native tissues, natural polymers such as chitosan, collagen, cellulose, sodium alginate, and hyaluronic acid are often used in hydrogel wound dressings.[10]

Additionally, a lot of natural polymers have inherent biological activity that promotes wound healing. For instance, hyaluronic acid enhances cell migration and speeds up wound healing through angiogenesis, whereas chitosan has antibacterial qualities and supports hemostasis. Despite these benefits, natural hydrogels have intrinsic drawbacks, such as comparatively poor mechanical strength, enzymatic degradation, and variation in structural stability.[11]

Table 1: Natural Biomaterials with their key properties, role in wound healing, advantages, limitations.

Biomaterial	Key properties	Role in wound healing	Advantages	Limitation

Cellulose[12]	Biocompatible with high structural stability. High mechanical integrity and water retention capacity. Ability to form nanofibrous scaffolds.	Provides structural support, maintains moist wound environment, promotes tissue regeneration.	Non-toxic, stable, good film-forming ability, high tensile strength.	Poor solubility in water; requires chemical modification to improve biodegradability.
Chitosan[13]	Derived from chitin; exhibits antimicrobial activity. Promotes hemostasis and bioadhesion. Cationic polysaccharide with reactive amino groups.	Enhances tissue regeneration, prevents microbial infection, supports cell proliferation and wound closure.	Biocompatible, biodegradable, antimicrobial, promotes hemostasis.	Poor mechanical strength in hydrated state; requires chemical modification or blending to improve stability.
Sodium Alginate[14]	Linear polysaccharide composed of D-mannuronate and L-guluronate units. Forms gels via ionic crosslinking with divalent cations (Ca^{2+}). High fluid absorption capacity.	Maintains moist wound environment, absorbs wound exudate, supports easy and non-traumatic dressing removal.	Excellent gel-forming ability, soothing effect on wound surface, non-toxic.	Low mechanical strength; poor long-term structural stability at physiological ionic strength.
Hyaluronic Acid (HA)[15]	Modifiable functional groups enable crosslinking. Promotes cell migration, angiogenesis, and tissue hydration.	Provides structural support, maintains moist wound environment, promotes tissue regeneration.	Non-toxic, stable, good film-forming ability, high tensile strength.	Poor solubility in water; requires chemical modification (e.g., carboxy-methylation) to improve biodegradability.

Synthetic Polymers

Synthetic polymers are frequently used in hydrogel wound dressings due to their reliable mechanical performance, chemical reproducibility, and capacity for large-scale manufacture with precisely tunable properties. Polymers with predictable degradation rates, changeable crosslink density, and repeatable physicochemical properties include PEG, PVA, PVP, and PLGA. However, synthetic hydrogels have a low level of biological activity and may occasionally produce residual crosslinking agents or breakdown products that cause inflammatory reactions in surrounding tissues, which restricts their use in stand-alone clinical settings.[16,17]

Table 2: Synthetic biomaterials with their key properties, role in wound healing, advantages, limitations.

Biomaterial	Key properties	Role in wound healing	Advantages	Limitation
PEG (Polyethylene Glycol)[18]	Highly hydrophilic ether-based polymer. Resistant to protein adsorption. Excellent biocompatibility and flexibility. Tunable molecular weight.	Used for drug delivery and treatment of chronic wounds including diabetic ulcers. Provides moist, protective wound environment.	Highly biocompatible, flexible, protein-resistant, low immunogeni-city.	Low inherent mechanical strength; lacks bioactivity; requires functionalization or blending for therapeutic effect.
PLGA (Poly(lactide-co-glycolide))[19]	Copolymer of PLA and PGA. Biodegradable with controlled degradation into lactic acid and glycolic acid. Good mechanical strength. FDA-approved.	Promotes controlled release of therapeutic agents. Supports tissue regeneration and wound repair.	FDA-approved, biodegradable, versatile, reproducible degradation rate.	Degradation produces acidic by-products (lactic and glycolic acid) that may cause localized inflammation at the wound site.
PVA (Polyvinyl Alcohol)[20]	Semi-crystalline hydrophilic synthetic polymer. Forms stable hydrogels via chemical crosslinking or physical freeze–thaw cycling. Biocompatible and non-toxic.	Provides protective barrier and structural support in wound dressings. Protects wound from external mechanical forces.	Strong mechanical properties, dimensional stability, cost-effective, non-toxic.	Requires crosslinking agents for hydrogel formation; limited biodegradability and bioactivity without modification.
PVP (Polyvinyl pyrrolidone)[21]	Water-soluble synthetic polymer. Excellent film-forming ability. High water absorption capacity. Good adhesion	Maintains moist wound environment, supports controlled drug delivery, provides protective film	Non-toxic, highly hydrophilic, good adhesion, transparent, easy to process.	Low mechanical strength, requires blending with other polymers or crosslinking for adequate structural integrity.

Bioresorbable and Hybrid Polymer Systems

Bioresorbable polymers are of particular interest in wound care because they safely break down in the physiological environment at a rate that is compatible with tissue remodeling and reduces chronic inflammatory responses and support progressive regeneration.[22] Hybrid hydrogels that include both kinds of polymers have been created to get around the shortcomings of both synthetic and natural systems. These composite materials greatly enhance performance for advanced wound healing applications by combining the mechanical strength, chemical stability, and tunability of synthetic equivalents with the intrinsic bioactivity of natural polymers.[23,24]

PREPARATION OF HYDROGELS FOR WOUND HEALING

A hydrogel's crosslink density, swelling behavior, mechanical strength, and suitability for biomedical applications are all significantly influenced by the preparation technique employed to produce it. Depending on the polymer system and intended clinical usage, a variety of methods have been devised and refined for the creation of hydrogels meant for wound healing, each with unique benefits.[25] The five main preparation techniques—suspension polymerization, grafting, irradiation, chemical crosslinking, and physical crosslinking—are described in the sections that follow, along with sample preparation procedures for each technique.[26]

Preparation of hydrogel by suspension polymerization

Suspension polymerization is a heterogeneous polymerization technique in which water-insoluble monomers are dispersed as liquid droplets within an aqueous continuous phase using a suspending agent and mechanical agitation.[27] The monomers undergo polymerization within the individual droplets, forming solid polymer particles as a dispersed solid phase. During polymerization, the growing polymer chains preferentially migrate toward the droplet interface, leading to phase separation between the polymer and the internal solvent. This process results in the formation of core-shell microspheres with a solvent-filled core and a polymeric shell; removal of the solvent produces hollow polymeric microspheres. The principal advantages of suspension polymerization include ease of process control, efficient heat dissipation, and the production of hydrogel particles with relatively uniform particle size.[28]

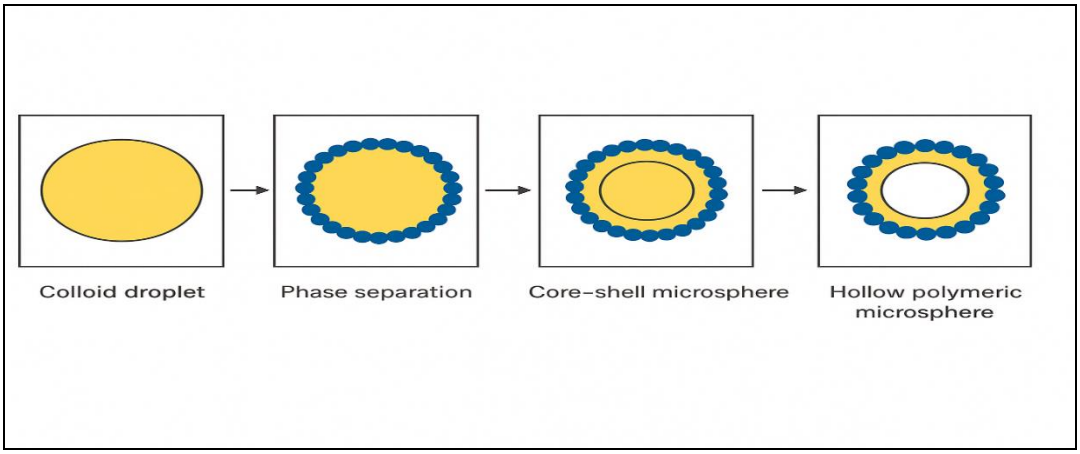

Fig. 1: Diagram of preparation of hydrogel by suspension polymerization.

Inverse (water-in-oil) suspension polymerization, in which the aqueous monomer phase is distributed within an organic continuous phase, is a particularly successful variation.[29,30] This method works particularly well for creating superabsorbent hydrogels with high water retention capacity and quick absorption kinetics—qualities that are ideal for wound dressing applications. Hydrogels with regulated network density and swelling behavior can be produced by using crosslinkers like N,N'-methylenebisacrylamide and surfactants like SPAN 80.[31]

Table 3. Preparation method of wound healing hydrogels by suspension polymerization with its outcomes and limitations.

Technique	Material used	Process	Outcome	Limitations
Inverse Suspension Polymeriz-ation[32]	Cyclohexane, Sorbitan monostearate (0.15 g), Sodium acrylate (SA) monomer, TMMAI monomer, N,N'-methylenebis-acrylamide (NMBA, crosslinker), ACVA initiator, Nitrogen gas, Cold	A four-necked flask fitted with a reflux condenser, thermometer, and stirrer was charged with 60 mL cyclohexane containing 0.15 g sorbitan monostearate to form the continuous organic phase. The aqueous dispersed phase, consisting of SA monomer, TMMAI monomer, and crosslinker NMBA, was added under continuous stirring.. The mixture was degassed under nitrogen and polymerized using ACVA initiator at 70 °C, 250 rpm for 4 hours. After cooling, the suspension was precipitated with cold	Uniform particle size; efficient polymerizati on; tight crosslinked network; high recovery (>95%).	Use of toxic organic solvent (cyclohexan e), residual surfactant may affect biocompatib ility, sensitive to agitation speed and temperature, requires extensive post-synthesis purification.

	methanol, Distilled water(DW).	methanol, vacuum dried, and re-washed with methanol–water to yield a powdered hydrogel (>95% recovery) with uniform particle size and tight crosslinked networks.		
Water-in-Oil (W/O) Inverse Suspension Polymerization[33]	Acrylic acid, Aqueous NaOH solution, Toluene, W/O surfactant, N,N'-methylenebis-acrylamide (NMBA, crosslinker), Nitrogen gas, DW.	Acrylic acid was dissolved in aqueous NaOH while cooling, to obtain the aqueous dispersed phase. Toluene containing a water-in-oil surfactant was stirred under nitrogen to form the continuous organic phase. NMBA crosslinker was added to the aqueous phase under nitrogen. In a four-necked reactor fitted with a heating mantle and reflux condenser, the organic phase was added first; the monomer–crosslinker mixture was then added dropwise. Polymerization continued until full monomer conversion. The resulting superabsorbent hydrogel was isolated, washed, and dried.	Superabsorbent hydrogel with high swelling capacity and absorption rate; maintains moist wound environment; high purity.	Residual surfactant reduces biocompatibility, incomplete monomer conversion possible if conditions vary, toluene is highly toxic and flammable.

Preparation of hydrogel based on grafted starch

Grafting is a technique in which hydrogel-forming monomers are covalently bonded onto a strong polymer backbone to enhance the mechanical strength, structural integrity, and functional properties of the resulting hydrogel. Free radicals generated on the backbone polymer by chemical initiators or redox systems initiate in situ polymerization of the graft monomers, producing copolymer side chains anchored to the support structure. Starch gives good biodegradability, biocompatibility, low cost and owns natural abundance thus it is one of the most extensively studied backbone polymer for grafting.[34,35]

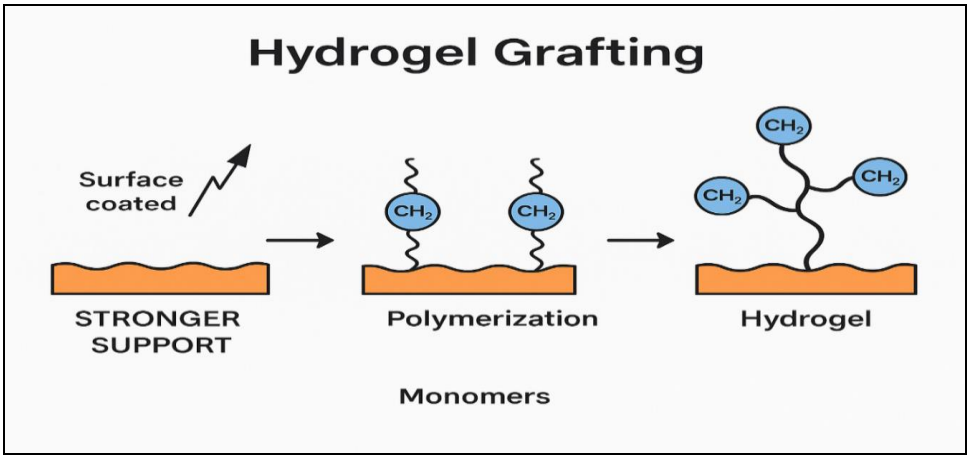

Fig. 2: Diagram of preparation of hydrogel based on grafted starch.

Depending on the extent of substitution on the starch backbone, starch-based grafted hydrogels are broadly classified as conventional or chemically modified. Initiator systems such as ceric ammonium nitrate (CAN), which is commonly employed that generates radicals selectively at the hydroxyl groups of the starch backbone, and redox systems such as hydrogen peroxide–ferrous sulfate (H_2O_2–$FeSO_4$), which are effective at ambient temperatures.[36] Crosslinkers such as N,N'-methylenebisacrylamide are incorporated to build the three-dimensional network. While grafting markedly improves mechanical properties, chemical initiators may produce toxic byproducts, causing purification before clinical use.[37]

Table 4. Preparation method of wound healing hydrogels by grafted starch with its outcomes and limitations.

Technique	Material used	Process	Outcome	Limitations
Free Radical Graft Copolymerization (CAN-initiated)[38]	Starch powder, Deionized water, CAN (initiator), Acrylamide (AM), Borax (crosslinker), Acetone, Nitrogen gas.	By dissolving starch powder in deionized water at 80 °C for 30 minutes in a nitrogen atmosphere, the powder was gelatinized. To create free radicals on the starch backbone, 5 mL of freshly made CAN solution was added and heated to 60 °C for 10 minutes. Acrylamide monomer and borax crosslinker solution were then added at 60 °C, and graft	Stable crosslinked hydrogel matrix; successful CAN-initiated graft copolymerization; controlled swelling behavior.	Residual borax and monomers need extensive purification, limited mechanical strength without further modification, requires strict nitrogen atmosphere.

		copolymerization was carried out for 2 hours under nitrogen. The resulting hydrogel was rinsing with distilled water followed by soaking in acetone, then dried.		
Redox-Initiated Graft Polymerization (H_2O_2–$FeSO_4$ system)[39]	Starch, Ethyl alcohol, Acrylonitrile (AN), Non-ionic surfactant, Distilled water, Hydrogen peroxide (H_2O_2), Ferrous sulfate heptahydrate ($FeSO_4 \cdot 7H_2O$), Nitrogen gas.	In distilled water (liquor ratio 1:10), washed starch (100 g), acrylonitrile (140 g), and non-ionic surfactant (5 mL) were combined under nitrogen sparging with magnetic stirring. Grafting was started by injecting H_2O_2 and $FeSO_4 \cdot 7H_2O$ solutions at a weight ratio of 6:1. Stepwise, the reaction was conducted for 30 minutes at room temperature, 30 minutes at 30 °C, 15 minutes at 35 °C, and 15 minutes at 40 °C. After filtering, the product was cleaned with distilled water and allowed to dry at room temperature.	Successful graft copolymer of starch and acrylonitrile; stepwise temperature increase improves grafting efficiency.	Stepwise temperature control is difficult to reproduce, iron residues (Fe^{2+}) may cause discoloration of product, low grafting efficiency at room temperature stage.

Preparation of hydrogels by irradiation

For biomedical and wound care applications, radiation-based hydrogel production is often chosen because it allows simultaneous polymer crosslinking and sterilizing in a single step without the need for chemical initiators or crosslinking agents. The absence of chemical additives eliminates residual toxicity concerns and simplifies post-processing. Additional advantages include precise control over crosslink density through adjustment of radiation dose and dose rate, reduced processing cost, and generate no chemical waste.[40]

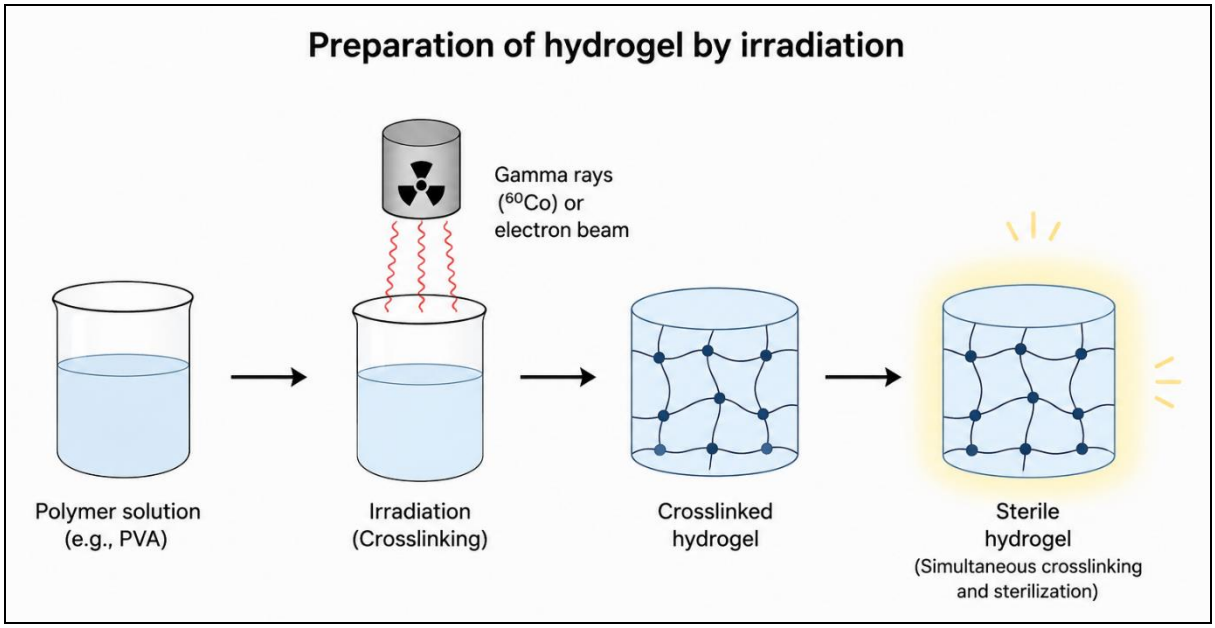

Fig. 3: Diagram of preparation of hydrogel by irradiation.

High-energy ionizing radiation such as gamma rays from cobalt-60 (^{60}Co) sources and accelerated electron beams initiates crosslinking by generating hydroxyl radicals through water radiolysis and macroradicals along polymer chains.[1] Recombination of these reactive species forms covalent crosslinks, which produces a three-dimensional network structure. The resultant hydrogels are extremely pure, initiator-free, and especially well-suited for sterile wound dressing applications.[41]

Table 5. Preparation method of wound healing hydrogels by irradiation with its outcomes and limitations.

Technique	Material used	Process	Outcome	Limitations
Radiation-Induced Copolymerization (^{60}Co Gamma Irradiation) [42]	Acrylamide (AAm, 1 g per sample), Itaconic acid (IA, 0–60 mg), Distilled water, PVC straw molds, ^{60}Co Gamma cell 220 (dose rate: 0.72 kGy h^{-1}), Fricke dosimeter.	AAm (1 g) was mixed with itaconic acid (IA) at concentrations of 0, 20, 30, 40, 50, and 60 mg in DW to a total volume of 1 mL per sample. Each solution was placed into PVC straw molds and irradiated using a ^{60}Co gamma cell at rate of 0.72 kGy h^{-1}; and dose was calibrated. The irradiated solutions formed crosslinked cylinders, which were sectioned, washed thoroughly with DW, and	Initiator-free crosslinked copolymer; clean production method; no chemical residues; suitable for biomedical applications,	Radiation dose must be precisely controlled, limited polymer compatibility, safety hazards from radioactive source handling.

		dried under air.		
Gamma Irradiation of PVA–Polysaccharide Blend (Wound Dressing) [43]	PVA (average MW 125,000), Agar-agar, Carrageenan, Double-distilled water, Gamma Chamber GC-5000, Polypropylene trays, Polyester film, Polyethylene bags.	Aqueous solutions of PVA, agar, and carrageenan in double-distilled water were prepared and sterilized at 121 °C, 15 PSI for 15 minutes in an autoclave. The hot solutions were poured into polypropylene trays, cooled to induce initial gelation, covered with polyester film, and sealed in polyethylene bags. Gamma irradiation was applied at a dose of 25–30 kGy using the GC-5000 chamber. Simultaneous crosslinking and sterilization produced hydrogel wound dressings.	Sterile, transparent, flexible, mechanically strong, and biocompatible hydrogel dressing; single-step sterilization and crosslinking.	Radiation may degrade natural polysaccharides (agar, carrageenan), limited control over final crosslink density, requires autoclave pre-sterilization adding processing steps.

Preparation of hydrogel by chemical crosslinking

Chemical crosslinking involves the formation of permanent covalent bonds between polymer chains by using chemical crosslinking agents or initiator systems, which results in stable three-dimensional network structure.[44] Unlike physical crosslinks, which are reversible and depend on non-covalent interactions, chemically crosslinked networks are irreversible and provide superior mechanical strength, dimensional stability, and resistance to swelling under physiological conditions.[45] Chemical crosslinking methods which are employed in hydrogel preparation include free radical polymerization, copolymerization, graft polymerization, interpenetrating polymer network (IPN) formation, and enzyme-mediated crosslinking.[46]

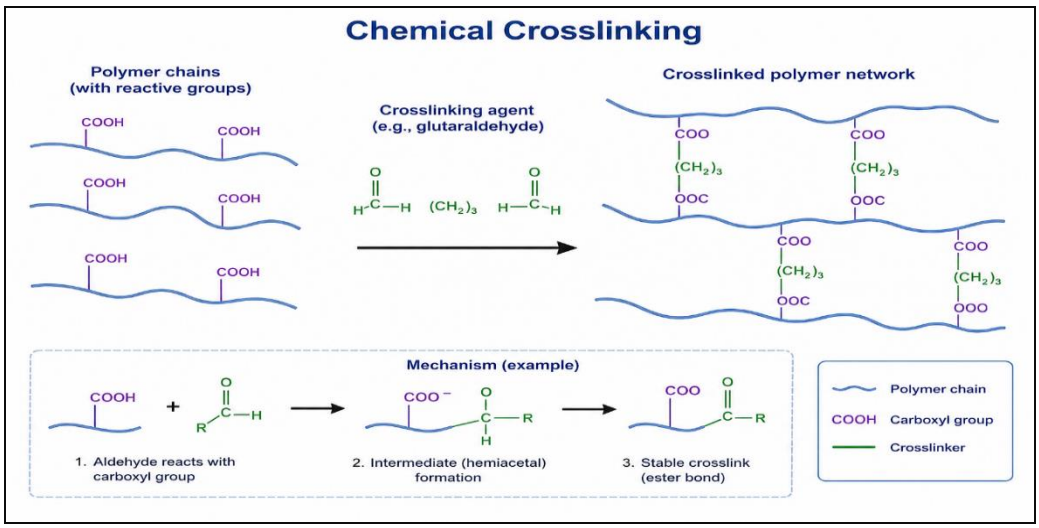

Fig. 4: Diagram of preparation of hydrogel by chemical crosslinking.

Hydrogels synthesized by chemical crosslinking using initiators such as potassium persulfate ($K_2S_2O_8$) or azobisisobutyronitrile (AIBN), and crosslinkers such as N,N'-methylenebisacrylamide, epichlorohydrin, or glutaraldehyde, exhibit excellent gel content, water vapor transmission rates, and mechanical properties suitable for wound dressing applications.[47,48] This approach is applicable to both natural and synthetic polymers, allowing broad versatility in material design.[17]

Table 6. Preparation method of wound healing hydrogels by chemical crosslinking with its outcomes and limitations.

Technique	Material used	Process	Outcome	Limitations
Thermal-Initiated Chemical Crosslinking Using Free Radical Initiator (PVA)[49]	PVA (10% w/v), $K_2S_2O_8$ (0.1–2.5% w/v), DW, Rotary evaporator, Teflon tray, Laminar airflow hood.	Heating under reflux in a rotary evaporator produced a 10% w/v PVA solution. $K_2S_2O_4$ (0.1–2.5% w/v) was used as a crosslinking agent and chemical initiator. Free-radical crosslinking was started by keeping the mixture at 80 °C for 95 minutes. Hydrogel films with a thickness of about 1 mm were created by casting the resultant solution onto a level Teflon tray and air-drying it under a laminar airflow hood.	Excellent mechanical properties; high water absorption capacity; optimal water vapor transmission rate; suitable as wound dressing film.	Residual persulfate initiator may cause cytotoxicity, high temperature (80°C) limits thermosensitive polymer use, requires controlled drying conditions.
Chemical Crosslinking of Chitosan–Sodium Alginate Hydrogel (DCC crosslinker) [50]	Chitosan (2 g), Sodium alginate (2 g), 0.5 M Acetic acid, Distilled water, Dicyclohexyl carbodiimide (DCC, 10 mg, crosslinker), Catalyst T-12 (2 drops), Teflon Petri dishes.	Chitosan stock solution: 2 g chitosan was dissolved in DW with vigorous stirring at 120 °C for 25 minutes, then 0.5 M acetic acid was added to a final volume of 100 mL. Sodium alginate stock: 2 g alginate was dissolved in distilled to 100 mL Crosslinked chitosan–alginate hydrogels were prepared at 1:1 and 1:2 ratios by adding alginate stock (25 or 50 mL) to chitosan stock under continuous stirring. Each mixture received 10 mg DCC crosslinker and 2 drops catalyst T-12, then was cast into Teflon Petri dishes and allowed to gel.	Porous 3D structure; improved mechanical properties (elasticity, tensile strength); biocompatible; supports cell growth.	High processing temperature (120°C) may degrade chitosan, requires precise 1:1 or 1:2 polymer ratio control, catalyst T-12 residues may affect biocompatibility.

Preparation of hydrogel by physical crosslinking

Physical crosslinking doesn't involve the formation of permanent covalent bonds but it includes the formation of polymer networks through non-covalent interactions, including hydrogen bonding, ionic interactions, hydrophobic associations, and chain entanglement.[51,52] Physically crosslinked hydrogels are generally biocompatible, non-toxic, and biodegradable, and are considered environmentally favorable compared to chemically crosslinked counterparts as no chemical crosslinking agents are employed in this process.[53]

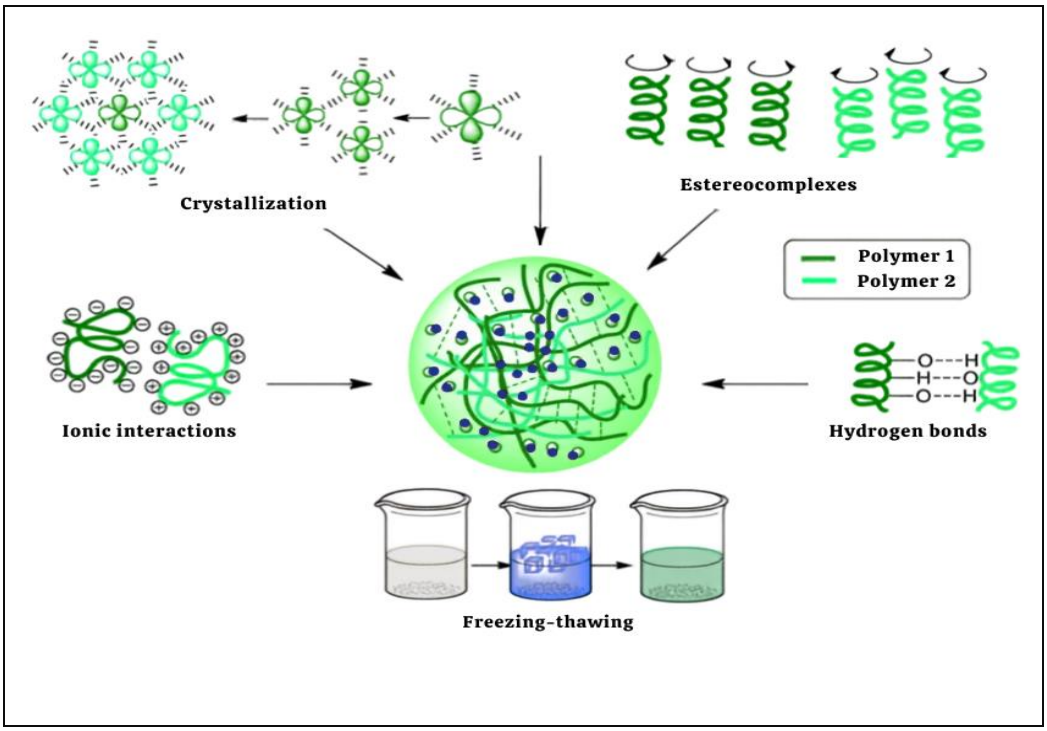

Fig. 5: Diagram of preparation of hydrogel by physical crosslinking.

Common strategies for physical crosslinking include ionic gelation, freeze-thaw cycling, hydrogen-bond-mediated gelation, and hydrophobic self-assembly.[54,55] In freeze-thaw cycling, larger pore sizes and higher swelling capacities hydrogels are produces than those prepared by thermal annealing methods.[56] Hydrophobic interactions play an important role in the gelation of polysaccharide-based hydrogels which are derived from sacran and carrageenan. Despite their favorable biocompatibility and ease of preparation, physically crosslinked hydrogels generally exhibit lower mechanical strength than chemically crosslinked networks, which may restrict their use in mechanically demanding wound sites.[57]

Table 7. Preparation method of wound healing hydrogels by physical crosslinking with its outcomes and limitations.

Technique	Material used	Process	Outcome	Limitations
Dual Ionic Crosslinking (Sodium Alginate / Hardystonite –Aspartic Acid System)[58]	Sodium alginate (low viscosity, 1.5% w/v), Hardystonite ($Ca_2ZnSi_2O_7$) (HS); 1%, 2%, 5% w/w of alginate), L-Aspartic acid (Asp; 0.25–1% w/w of alginate), $CaCl_2$ (0.1 M).	In a 1.5% w/v sodium alginate solution, HS particles at 1%, 2%, and 5% w/w of alginate were evenly distributed while being vigorously stirred. The same technique was then used to integrate L-aspartic acid (Asp) at 0.25%, 0.5%, 0.75%, and 1% w/w of alginate. Cylindrical molds were filled with the resultant mixes. Gelation was accomplished via dual ionic contact between alginate carboxylate groups and Ca2+ ions. Control samples (pure alginate, without HS or Asp) were created by ionic crosslinking with 0.1 M $CaCl_2$.	Rapid gelation; good biocompatibility; improved mechanical properties due to dual ionic crosslinking.	Precise concentration control of HS and Asp required, Low mechanical strength at higher alginate concentrations, Limited biodegradation rate in physiological conditions.
Solvent Casting of Physically Crosslinked Sacran Hydrogel Films[59]	Sacran (0.5% w/w), DW (50 mL), Polypropylene boxes	Sacran (0.5% w/w) was dissolved in 50 ml of distilled water while being stirred for eight hours. To guarantee total disintegration, the solution was kept at 80 °C for up to 24 hours. To create hydrogel films, the solution was then transferred into polypropylene boxes and dried for 48 hours at 60 °C. To improve network formation and mechanical integrity, the resultant films were heated to 110 °C for at least two hours.	Improved wound healing and anti-inflammatory properties attributed to sacran; good swelling ability; film format suitable for direct wound application.	Poor mechanical strength compared to chemically crosslinked hydrogels, Long drying time (48 hours) reduces production efficiency, Poor adhesion to wound surface.

CONCLUSION

Hydrogels' capacity to sustain a moist wound environment and promote tissue regeneration has made them useful materials for wound care. This review looked at five preparation techniques that produced hydrogels with different structural and functional characteristics:

suspension polymerization, grafting, irradiation, chemical crosslinking, and physical crosslinking.

Although suspension polymerization uses hazardous organic solvents, it offers good particle size homogeneity. Grafting onto starch backbones improves mechanical qualities, however before being used in clinical settings, hazardous initiator byproducts must be carefully purified. Irradiation is particularly advantageous as it simultaneously crosslinks and sterilizes the polymer without chemical additives, making it well-suited for sterile wound dressings. Chemical crosslinking produces durable, strong, networks but leftover crosslinking chemicals may cause biocompatibility issues. Physical crosslinking avoids chemical agents and is intrinsically biocompatible, though the resulting hydrogels tend to exhibit lower mechanical strength.

Natural biomaterials, including cellulose, chitosan, alginate, and hyaluronic acid, provide favorable bioactivity, whereas synthetic polymers such as PVA, PVP, PEG, and PLGA provide mechanical strength and consistency. Advanced wound care could benefit greatly from hybrid systems that combine both types of polymers. To meet the increasing clinical demands of wound care, future research should focus on scalable, economical preparation methods that combine mechanical durability, biocompatibility, and controlled drug delivery.

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CONFLICT OF INTEREST

The author declares no conflict of interest.

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