Recent Trends in Polysaccharide-Based Hydrogel for Treatment of Wound Healing

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1. Abstract

Hydrogels have been shown to be useful in dressings due to their better biochemical and also and mechanical properties. However, as the performance of the hydrogel in wound healing has not yet been clearly defined. This article reviews the advanced capabilities of hydrogel dressings, including antimicrobial properties, adhesion, hemostasis, anti-inflammatory and antimicrobial properties, transport properties, self-healing, stimulus response, electrical conductivity, and the main recently developed wound care system, and provides insight into cutaneous tissue wounds. and provides insight into cutaneous tissue wounds. The methods used to complete these tasks are also separated and discussed. In addition, details are provided on the use of hydrogel wound dressings in the treatment of various conditions, including excisional and incisional wounds. Infections, burns, and diabetes are the main topics discussed. Finally, suggestions for the future directions of hydrogel wound healing are provided in detail. However, the performance of Hydrogels as wound dressings has not yet been that so deep clearly defined. This article reviews the advanced capabilities of hydrogel dressings, including some anti-microbial properties, adhesion, hemostasis, anti-inflammatory, and anti-microbial properties.

Keywords:

Polysaccharide-based hydrogel, Nanocomposite hydrogel, Scaffold material, Wound healing, Biopolymer, Tissue regeneration, Regenerative medicine, Drug delivery,

1. Introduction

The skin is the largest organ in the body and its primary function is to protect the body from the elements the elements. Wounds are defined as damage or disruption of the skin and can be cause d by Many of factors, including pressure, venous stasis, thermal injury, and chronic pain from diabetes [1]. The skin forms the outer layer and is the body's first line of natural defence, dehydration and chemical or electrical damage, and microbial invasion. Any injury that changes the structure and function of the skin is called a wound. The healing process begins as soon as pain occurs [2]. A disruption in the skin layer exposes the underlying dermis to air, causing injury. Blood vessels of the bone are the tissues exposed to air, depending on the skin damage and the location of the injury. Therefore, wounds are often divided into three groups [3]. The Diseases that affect only the epidermal skin are considered external wounds. Some cortical lesions affect those layers of the dermis, such as blood vessels, sweat glands, and roots. This occurs when deep tissue or subcutaneous fat breaks down in deep tissue. Depending on the temperature of the eye and whether the wound is partial or full-thickness, burns can be divided into first-degree, second-degree, and third-degree burns. Fourth-degree burns can damage subcutaneous tissue, tendons, ligaments, and bones [4].

2.1. Skin.

The outer layer of our body, the skin, is constantly under attack from the outside world [1]. As it is multifaceted and complex, with several specialized cells that are assigned to also perform different main functions [2]. The three layers of the skin (epidermis, dermis, and subcutaneous tissue to tissue) are arranged from the outer layer to the inner layer [3]. The skin has many functions. It acts as several anti–bacterial and anti-humidity agent and protects the skin from various damages such as UV, chemical and thermal explosion [4]. The outer layer of the skin called the epidermis effects the skin and acts as a barrier against water. Under the dermis epidermis, which is mainly connected to sweats glands, blood vessels, lymphatic vessels connected to sweat glands, blood vessels, lymphatic vessels root tissues Connective tissue and fat form the hypodermis, which is the deep subcutaneous layer [5].

2.1.1. Functions of skin

- Protects against pathogens, dehydration, UV light, and mechanical injury.
- Regulation of Temperature by absorbing or releasing heat.
- Sensation of pain as the skin is the first organ to sense pain, warmth, touch, and deep pressure.
- Mobility of the skin causes the body to move smoothly and gently.
- Immunity development of immunity against pathogens [4] [5].

2.1.2. Skin structure

The skin covers an area of about 1.8 square m and that mainly weighs about 6% of the total body weight, or 1/6 of the of the body weight (292). The main function of the epidermis is to keep the internal organs safe and waterproof [1]. It covers almost the entire body surface, and along with the main the thickness of 5 to 50 µm on the eyelid and 600 to 900 um on the feet. The skin does actually have the three layers. As the hypodermis is the third layers and the deepest layer, and the dermis is the layer beneath the epidermis; the epidermis is the outer layer of the skin [2].The Keratinocytes, or epithelial cells that synthesize keratin make up to 95% of the epidermis, while about the non-keratinocytes, or the cells that do not synthesize keratin, make up 5% or cells that do not synthesize keratin, that make up to 5%.And As the keratinocytes rise to the surface, their cellular content changes the surface allowing different cells to be compared [3].Thick skin, such as that of the palms and the toes, which consists of five layer of the epidermis mainly : stratum corneum, stratum lucidum, stratum spinosum, and Stratum granulosum, and the stratum corneum, basal layer. And also in other areas the epidermis has only only four layers, thus excluding the lamina lucidum. The dermis mainly consists of two layers: the papillary dermis (the uppermost layer) and the reticular dermis (the layer beneath) [4] .The tissue, subcutaneous tissue can be defined by the number of fat cells associated with the loose tissue [5].

A. Epidermis

The epidermis is the outer layer of the skin that expresses many proteins and other substance and acts as protection and barrier [1].The outer layer of epithelial tissue that protects the body from external factors is called as epidermis [2].The basal cell layer is a columnar cell layer that proliferates to form a tightly packed layer of a cells including the multilayered and the squamous

specific epithelium, the and which is exactly found in the lowest layer of epidermis. In to addition to the stratum to the corneum (SC), so the nucleated epidermis that also provides other important physical barriers, particularly the cell – cell junctions and also their associated cytoskeleton proteins [3].

B. Dermis

The dermis is the middle layer of the skin between the epidermis and the subcutaneous tissue just below the dermis. The dermis is a strong layer with a specialized structure that protects the body from damage. Mainly its thickness varies greatly, from less than 1 mm in the eyelid to more than 5 mm in the dorsum [1].

As Collagen and elastin fibers are the main components of the dermis [2]. The dermis has two layers: that are the deeper, thicker reticular dermis and the thinner, superficial papillary dermis. The papillary; the papillary dermis lies beneath the dermal epidermal junction and consists mostly of loosely arranged collagen fibres. A network of thicker collagen bundles parallel to the skin surface forms the dermis [3].

2.2. Rational design and latest advancement of polysaccharide – based hydrogel

The most widely studied natural hydrogel which are composed of peptides and polysaccharides. Polysaccharides are particularly well liked since they are readily available and renewable, which means that they may be obtained without depleting resources. They are derived from plants and marine animals, such as seaweed. The method for producing polysaccharides is basically so easy and practical, affordable, and affordable for large-scale manufacturing. Polysaccharides have recently emerged as promising candidates for a number of biological uses, including wound dressing, gene delivery, and medication delivery. Excellent therapeutic effects are demonstrated by the modified polysaccharides (animated, PEGylated or zwitterionic dextran), supramolecular which contains heparin, of betacyclodextrin /adamamantane) for application such as wound healing or cancer therapy.

2.2.1. Design concerns and necessary characteristics of hydrogel based on polysaccharides for wound healing.

Monosaccharide’s and their by products, Homopolysaccharides are polysaccharides like starch, cellulose, and glycogen that are made up of a single monosaccharide. Polysaccharides like

hyaluronic acid and alginate are example of hetero-polysaccharides, which are made up of many mono-saccharine. Molecular chains vary in length and degree of branching depending on the kind of polysaccharide. According to claims, hydrogel based on polysaccharides are an efficient way to treat wounds with high water retention, non toxicity, biodegradability, capacity, renewability, and biocompatibility. Hydrogels based on polysaccharides are said to be a highly successful approach to treat wounds because of their high water-retaining capacity, renewability, biodegradability, biocompatibility, and no toxicity.

Design considerations

A. Biocompatibility

As long as the materials are designed for biomedical purposes, biocompatibility is typically the first factor taken into account. The hydrogel aim to have few or no adverse effects, poisonous, immunological, or foreign body reactions since the gels directly contact cells and the tissues to promote wound healing. If this condition is not met, the wound may become infected, difficult to heal, or scarred.

B. Degradation.

The degrading characteristics of hydrogel must frequently be taken into account. Degradability is not always required for wound dressings applied to the skin's surface. However, biodegradability is essential for deep wounds, chronic wounds, and internal bleeding. As degradation improves, the degradable hydrogel would gradually lose its ability to function and be replaced by new tissue.

C. Strength, stretch ability, and adhesion.

The mechanical characteristics of hydrogel must be addressed depending on the kind and location of the wound. Traditional dressing materials have holes around the arms and legs to treat wounds from skin injuries, especially at joints like the ankle, knee, and wrist. This causes discomfort and inconvenience for the patients. Plus, stable adherence between dressing materials and the wound site would improve their availability and dependability given the continuous motion and bending of extremities. The cross linking index or cross linking techniques can be changed to modify the mechanical properties of Hydrogels. In order to attain mechanical qualities that were balanced between toughness and stiffness, double-network (DN) Hydrogels were developed.

2.2.1.1. Chitosan-based hydrogel for wound healing

Chitosan is biodegradable, biocompatible, non-toxic, antimicrobial, biologically adhesive, biologically active, and homeostatic, and because it's amino and hydroxyl groups are easily reacted with and chemically modified, allowing for a high chemical diversity, it is regarded as the perfect material for hydrogel. The Materials based on chitosan often have strong wound tissue adhesion qualities, mild gel formation features, film-forming abilities, and a positive charge (at normal wound pH values). Also, the penetration-enhancing activity of this polymer is probably influenced by additional structural components.

Role of chitosan Based hydrogel

Chitosan-based hydrogel are beneficial during different phases of wound healing.

i) The wound undergoes coagulation and hemostasis, which start as soon as an injury occurs. Chitosan accelerates coagulation in vivo by inducing platelet activation and promoting surface-induced thrombosis and blood coagulation..

ii) As soon as an injury happens, the wound proceeds through coagulation and hemostasis. By stimulating platelet activation and encouraging surface-induced thrombosis and blood coagulation, chitosan speeds up coagulation. By restricting nerve terminals and promoting blood coagulation, chitosan, a naturally occurring blood clotting agent.

iii) Chitosan offers a non-protein matrix for 3D tissue growth and stimulates macrophages for tumoricidal effects. Proliferation, which begins 2–10 days after the damage and includes the main healing, processes actions. Hence, hydrogel based on chitosan may promote angiogenesis, fibroblast proliferation, regular collagen deposition.

iv) Remodelling: Important for the restoration of dermal tissue, N-acetyl glucosamine (NAG), which is found in chitin and chitosan, tissues of scarring. Particularly, low-deacetylation chitosan films have already shown promise in the treatment of superficial wounds.

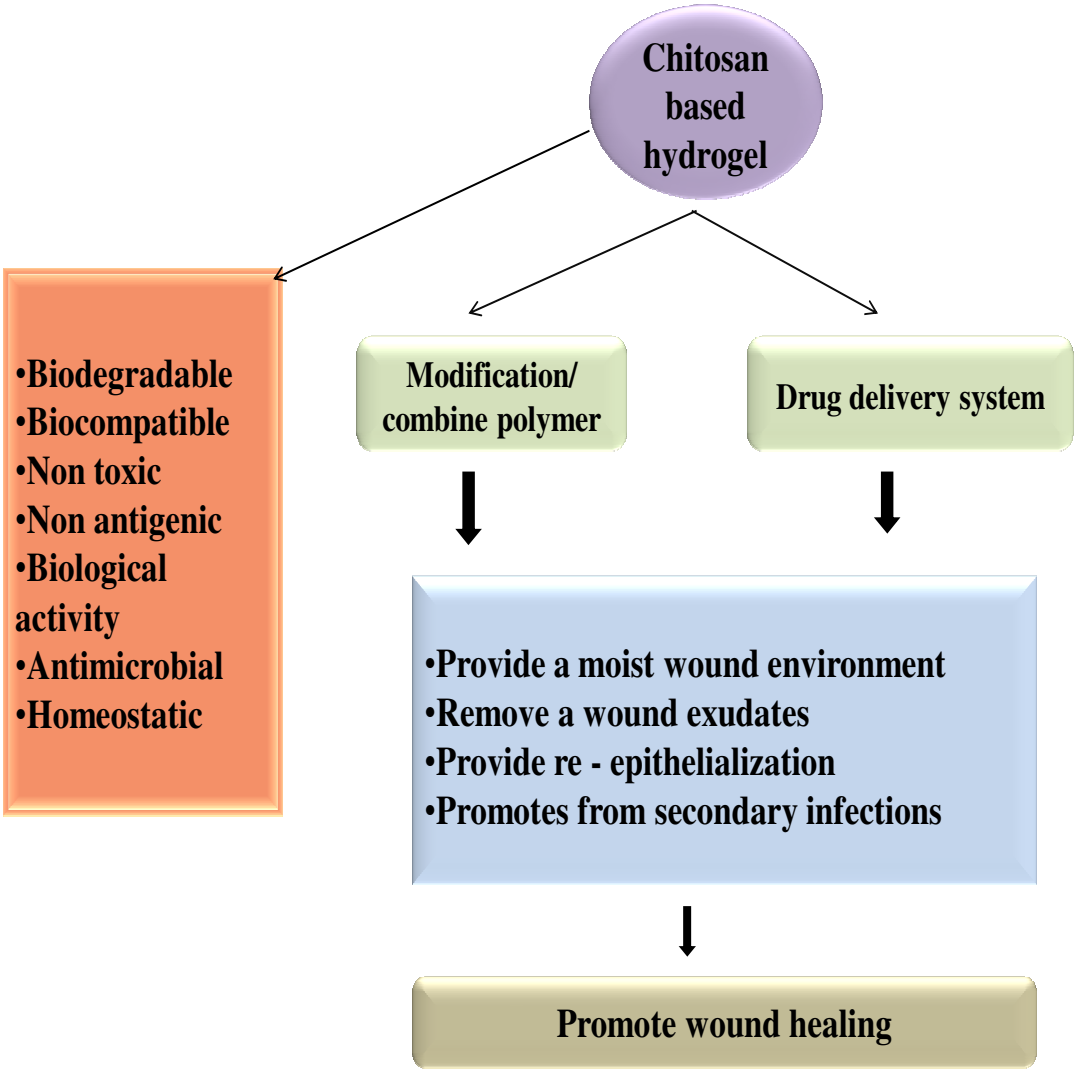

Fig1. Chitosan based hydrogel

2.2.1.2. Alginate based polysaccharide hydrogel

Alginate, a naturally occurring polymer derived from seaweed, has a number of advantageous properties. Chemically, these are made up of leftovers of L-guluronic acid (G block) and D-mannuronic acid (M block), organized as building units in the chain of polymers. M and G blocks, which are composed of alternating or random units, divide these homogenous blocks. The swelling, viscoe-lasticity, and absorption characteristics of alginates are defined by this M/G ratio.

Mechanism

Dry film dressings containing alginate are appropriate for superficial wounds that leak fluid. The alginate in the dressing product absorbs the fluid whenever a moderate to high exudates wound is covered with an alginate-based dressing, accelerating the healing process by preventing the surrounding tissues from macerating. Applying alginate films releases the mixed calcium ions from the dressing materials, which are then replaced by the mono-valent sodium ions found in the wound bed or exudates to produce hydrophilic gels Additionally, by keeping the environment wet, this process encourages cell migration, proliferation, and epithelialization while lowering bacterial infections.

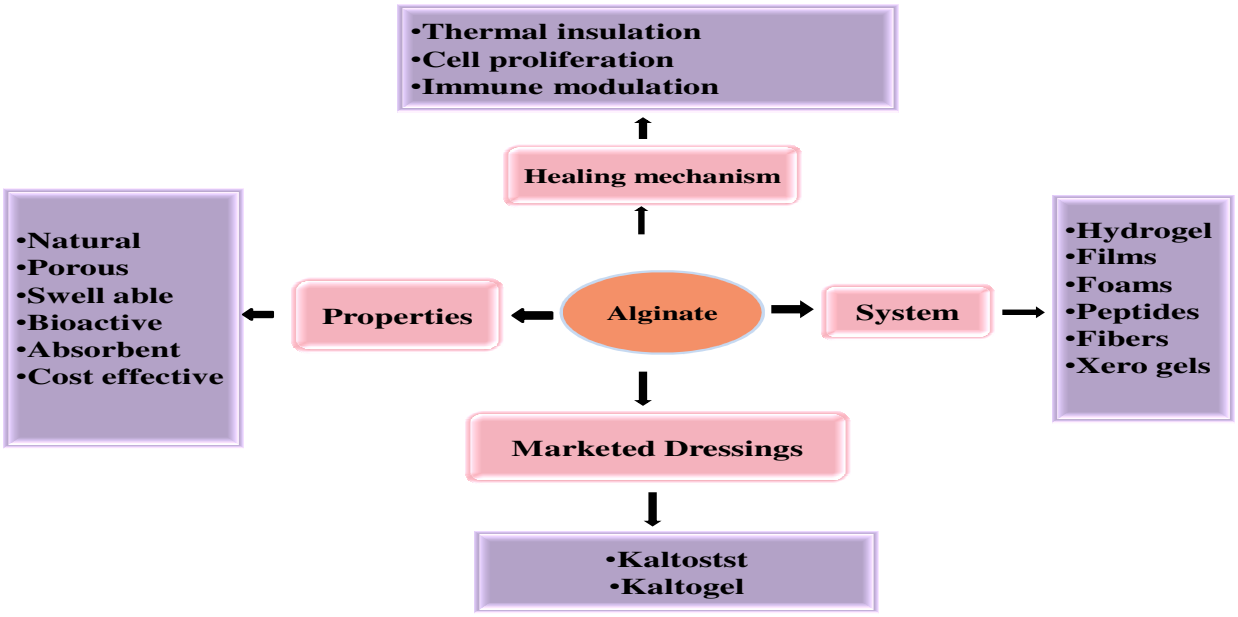

Fig2. Alginate based hydrogel

2.2.1.3. Hyaluronic acid-based hydrogel

N-acetyl-D-glucosamine and D-guluronic acid units alternately form hyaluronic acid, which is connected by β-1,4- and β-1,3-glucosidic linkages. The primary constituent of connective tissues including the extracellular matrix and synovial fluid, hyaluronic acid serves a variety of physiological purposes, including lubrication, water retention, extracellular space maintenance, and osmotic pressure adjustment. Since hyaluronic acid contains a lot of carboxyl and hydroxyl groups, it is prepared to generate both intermolecular and intermolecular hydrogen bonds in aqueous solution. The biodegradability, biocompatibility, no toxicity, non-immunogenicity, and

non-inflammatory characteristics of hydrogel based on hyaluronic acid make them an excellent foundation for wound healing. For example, Cho and colleagues created a hydrogel patch based on hyaluronic acid that may be used as a ready-to-use tissue tape for a variety of biomedical applications.

The first step involved modifying hyaluronic acid using pendant bis phosphonate (BP) ligands. The hydrogel formed instantly after the addition of silver (Ag+) ions to the modified hyaluronic acid solution because of the coordination cross linking between Ag+ ions and BP groups that were attached to the hyaluronic acid backbone. Both Gram-positive and Gram-negative bacterial strains were shown to be extremely susceptible to the Hydrogels antimicrobial qualities, which allowed for the prevention of infections in wound care.

2.2.1.4. Cellulose-based hydrogel

The β-1, 4 glycoside link polymerizes D-glucopyranose to form cellulose, the most prevalent renewable polymer on the planet. Cellulose and its byproducts have been extensively utilized as medicinal materials for both clinical and laboratory research because of their low toxicity, biodegradability, biocompatibility, and affordability. Hydrogels based on cellulose are also excellent carriers. For the purpose of treating burn wounds, human dermal fibroblasts and epidermal keratinocytes were added to a bacterial cellulose/acrylic acid (BC/AA) hydrogel. Nanocellulose also plays a significant role in the creation of hydrogel.

3. Conclusion

The process of repairing tissue layers and cellular structure is complex and dynamic. Many studies have been conducted to develop new technologies for wound healing. In recent years, smart dressings have gained widespread attention as a way to improve wound healing. Hydrogels are considered one of the most unusual materials due to their high water content; moisturizing properties; biocompability, and controlled drug release. Hydrogels have been proposed as a potential dressings materials for acute and wounds due to their superior properties such as maintaining a mist surface, chronic absorbing secretions and necrotic materials, and providing sufficient strengths to cover lesions with various morphological. Hydrogels can be of various morphological related conditions. Hydrogels can be made using natural or synthetic polymers.

4. Future perspective and challenges

Furthermore, we provided an overview of the dressing materials and therapeutic uses of the hydrogel products based on polysaccharides that are now on the market and undergoing clinical trials. The most widely used substances; sodium alginate and hyaluronic acid, will eventually take up a larger portion of the market. However, wound healing is a dynamic and complex process, making it challenging to have an optimal dressing at all times (Brumberg et al., 2021; Zhou et al., 2021).As an alternative to conventional hydrogel wound dressings, there is a growing effort to incorporate electronic components into hydrogel to record minute alterations in the wound site, enabling more thorough and precise healing process monitoring. Hydrogels that resemble micro needles or have a more value topological surface profile are also the subject of recent study aimed at improving their ability to suit the needs of different kinds of wounds. Lastly, we believe that increasingly sophisticated and portable techniques will be used in the creation of hydrogel wound dressings based on polysaccharides.

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