Exploiting Various Natural Polymers for its Wound Healing

Janaki R1, Vijaya Gowri E2

1Vwr-Aventor, Coimbatore; 2Vanavarayar Institute of Agriculture, Manakkadavu, Pollachi

ABSTRACT

Wound healing is a multifaceted and intricate process which encompasses the rejuvenation of impaired cells and the reconstitution of tissue structure. The duration of this tailoring journey can range from immediate to long span of years. For futuristic healthcare system, the advancement of wound healing and tissue engineering holds paramount significance. Recently, there has been a surge in the adoption of biomaterial-assisted therapeutic approaches, exhibiting promising outcomes in expediting the wound healing and skin restoration processes. Being one of the easily available biomaterials, the natural polymers have gained importance due to their biocompatibility, biodegradability and tissue regeneration. These polymers are presently employed as natural scaffold for wound dressing formulations. The present review aims to elucidate the fundamental principles as well as the recent advancements in wound healing and tissue repair strategies, and additionally, it delves into the origins and applications of various natural polymers.

Keywords: Wound healing, Natural polymers, Chitosan, Alginate, Cellulose

INTRODUCTION

Skin serves as the largest organ of our body functioning as a barrier between the external environment and internal physiology. The major role of this organ is to safeguard us from the pathogens and various forms of thermal and mechanical damages.1 A wound represents a breach in the protective layer compromising its vital role resulting in disruption of cellular and anatomic continuity of cells and tissues.2 The damage may extend deeper into the dermis, muscle and finally reaches the bone.3 Wound healing process involves the interaction of cells and the receptors.4 Injuries like hematoma, laceration, contusions may intricate the wound. The wound healing cascade involves chemotaxis, cellular proliferation, neovascularisation, extracellular matrix formation and scar tissue regeneration.5 The healing process involves replacement of damaged or lost tissue with the newly generated tissue. The epidermis on the skin surface and the dermis, deeper connective tissue serves as a barricade against the external disturbances. When this impermeable layer is breached, a cascade of chemical reaction jumps into action of repairing process. The healing phases, advancement in the natural polymers based wound healing has been discussed.

Phases of wound healing

Wound healing involves four different interconnected and overlapping phases which include haemostasis, an inflammatory response, and a proliferatory stage which facilitates the regeneration of tissues followed by remodeling of tissue.6 Various internal and external factors may affect the wound healing process and there may be changes or oscillation in phases of healing.9 Improper healing or tissue regeneration may be due to various factors which include physical trauma, radiations, exposure to harmful chemicals.7 There exist a substantial energy demand during the wound healing process as there is a deprivation of protein and energy reserve of the body. The unhealable chronic wound may be due to the health condition of the patients with diabetics, arterial diseases and other ageing issues. Around 3-6 millions of elderly population of America suffer from the unhealing wound issues.8 Over past decades several advancement has
The use of nanomaterial-based approaches has numerous advantages over conventional wound care methods because they possess the fundamental comprehension of wound healing strategies to assimilate the novel techniques and procedures. Wound can be classified basically into two categories: one is chronic and the other being acute. The acute wound is a basically the injury that achieves a rapid healing and proper closure of wound in the anticipated time and rate. Minor injuries with smooth cut objects like knives, irregular jagged wounds, surgical wounds, scratches and insect bites are few examples of acute wound. Usually they occur suddenly and can occur in any part of the body which include minor scratches to severe injury damaging the blood vessels, muscle tissues nerves etc., swelling near the wound, tenderness and sometimes fever are the severe complications that the injured patient may face as a consequence of acute wound. A series of molecular events helps in restoring the structural integrity of the damaged area. If an acute wound is left untreated or found to be unhealed in an appropriate time it may grow into chronic wound. Persistent inflammation, necrosis are characteristics of chronic wound. Local wound management and its documentation becomes mandate for prevention of unhealed chronic wound. Symptoms of chronic wound include continuous pain, loss of normal functioning and mobility, increased stress, isolation, anxiety, depression, and an extended hospital stay. Appropriate treatment become mandate as the patient may suffer from emotional and physical stress due to the chronic wound. The wound healing process involves four high overlapping phases which include haemostasis, Inflammation, proliferative and remodeling phase.

**Haemostasis**, the first phase encompasses forty eight hours of wound healing. Upon the emergence of a wound on the body, the blood vessels within the wounded vicinity undergo constriction, thereby eliciting vasoconstriction as a means to diminish blood circulation. Concurrently, haemostatic agents are discharged at the wound site, culminating in the coagulation of fibrin with clotting factors, thus engendering a thrombus, more commonly referred to as a blood clot. This clot establishes a barrier between the disrupted blood vessels, effectively safeguarding against haemorrhage.

The commencement of the inflammatory phase endures for a period ranging from 24 to 48 hours, occasionally extending up to a fortnight in certain instances. This phase serves to rouse the haemostatic mechanisms that expeditiously forestall the exodus of blood from the wounded locale. Emanating from this stage is the discernible manifestation of cardinal indicators of inflammation, specifically rubor, calor, tumor, dolor, and functional impairment. Vasoconstriction and the aggregation of platelets constitute distinctive features of this phase, facilitating the promotion of blood coagulation, which is soon succeeded by vasodilation and the process of phagocytosis, thereby inciting an inflammatory response within the confines of the wound site.

The proliferative phase comprises of the synthesing the reparative substances and predominates in the context of most skeletal muscle injuries.

The remodeling phase involves a significant facet of tissue repair and the phase is overlooked. Through a culmination of these integrated processes, the ultimate outcome will be the restoration of the damaged tissue accompanied by scar formation.

**Advances in Wound healing**

Numerous new treatments for patients with acute and chronic wounds have been developed over the past decade. The field of wound care seems to have however many different treatment choices and modalities as the quantity of wound care experts. Skin substitute, epidermal graft, and dermal replacement are among the most cutting-edge wound healing procedures. An intriguing and novel idea is the application of organically produced compounds and phytochemicals to chronic wound healing. CAM is a suitable strategy for further developing clinical and clinical difficulties related with ongoing injuries that don’t mend. Exogenous development variables can adjust the mending system, and with recombinant DNA innovation, development elements can now be delivered in enormous enough amounts to be utilized restoratively. In clinical trials, a number of growth factors have shown promise, particularly in cases of impaired healing like chronic ulcers. Preclinical exploration proposes that extra development elements might have restorative likely in various injury mending applications. The use of growth-factor inhibitors, sequential and combinatorial dosing regimens, and specifically designed and modified growth factors can all contribute to improved wound healing. Tissue engineering methods for wound healing and skin regeneration have been developed over the past few decades. The nanomaterial-based approach has numerous advantages over conventional wound care methods because of its multifunctionality.

Tissue designing, development factors, creature fetal cell research, undifferentiated organism research, quality treatment, human skin substitutes, and dressings have all brought about progressive advances in injury recuperating information and treatment. These progressions in treatment have given patients experiencing convoluted injuries new expectation, yet there is as yet areas of strength for a for further developed strategies for treatment that consolidate the rule of limiting mischief and supplement the essential standards of wound care. Electrical currents that have been shown to increase the rate at which chronic wounds heal and heal completely. The essential ES advances that have been
accounted for to further develop wound recuperating are business ES gadgets that produce direct current (DC) and mono and biphasic beat current waveforms. \(^{18}\)

Polymers, being macromolecules comprised of repetitive structural units, are interconnected by covalent chemical bonds. Both synthetic and natural polymers exist, but the latter are more desirable for pharmaceutical applications due to their cost-effectiveness, abundance, and non-toxic nature. They can be chemically modified, potentially biodegradable, and, with few exceptions, bio compatible. \(^{19}\) Natural polymers, specifically polysaccharides, such as collagen, elastin, and fibrinogen, constitute a significant portion of the body’s extracellular matrix (ECM). The ECM provides structural support and mechanical integrity to tissues while facilitating communication with cellular components to regulate daily cellular processes and promote wound healing. \(^ {20}\) Many natural polymers possess antibacterial properties, making them suitable for wound dressings. Aloe Vera, chitosan, curcumin, honey, keratin, pectin, and propolis are few of the natural polymers that have been recently investigated for their antibacterial efficacy. \(^{21}\) Natural compounds have been utilized in the treatment of wounds for their therapeutic nature and these compounds were found to possess anti-inflammatory, antimicrobial, and cell-stimulating properties. Notably, chitin and chitosan have demonstrated promising applications in wound healing. \(^{22}\) Recent advancements in use of chitosan and chitin nanofibrils in wound healing, was found to yield varying degrees of success. \(^{23}\) Talymed®, a commercially available product developed utilizes chitosan nanofibril technology and has shown higher efficacy in the treatment of venous leg ulcers compared to standard treatments. \(^ {24}\)

Different natural polymers have been employed in wound healing, each demonstrating varying levels of effectiveness. Natural polymers possess the highest biocompatibility, excellent biodegradability, and non-toxicity among all polymers. \(^{25}\) Carbohydrate polymers, in particular, exhibit properties that make them valuable in wound healing applications. Cellulose, a renewable and abundant biopolymer and is composed of glucose units linked by glycosidic bonds, cellulose possesses functional groups that make carboxymethyl cellulose (CMC) valuable in controlling reactive oxygen species during antibiotic synthesis. CMC maintains moisture in the wound area, facilitating extracellular matrix production, rapid epithelialization, and wound recovery. \(^ {26}\)

Chitosan, derived from deacetylation of chitin, has glucosamine and N-acetyl glucosamine units linked by glycosidic bonds. \(^ {27}\) It has been extensively studied for its wound healing properties, although its mechanical strength remains a limitation. To overcome this, chitosan has been combined with various inorganic nanomaterials to create effective wound care solutions. Chitosan can be utilized in various forms, including gels, nanocomposites, scaffolds, sponges, beads, powders, and films, making it versatile in applications such as tissue engineering, drug delivery, pharmaceutics, agriculture, wound repair, and bone healing. \(^ {28}\)

Alginate, a derivative of brown seaweeds and modified bacteria, is a marine polysaccharide. Comprising d-mannuronic acid and glucuronic acid, alginate wound dressings offer non-toxicity, biocompatibility, oxygen permeability, reduction of wound odors and discomfort, biodegradability, and haemostatic properties. \(^ {29}\) These dressings create a moist environment at the wound site, facilitating the healing process and production of granulation tissue. Alginate solutions undergo ionic cross-linking with calcium ions to form gels, which are then processed into fibrous nonwoven dressings or freeze-dried porous foams. Dry alginate dressings absorb wound exudates and re-gel, providing moisture to dry wounds, thus reducing the risk of pathogenic infections. \(^ {30}\)

Natural polymers such as starch, chitosan, and gelatin have found widespread utilization across diverse industries, spanning from food and textiles to cosmetics, plastics, adhesives, paper, and pharmaceuticals. \(^ {31}\) Their versatile applications include acting as effective thickening agents in snacks, meat products, and fruit juices, as well as serving as the building blocks for disposable items like fast food utensils and containers. In the pharmaceutical sector, these polymers have garnered significant usage as binders, diluents, disintegrants, and matrixing agents in solid oral dosage forms. Natural polymers, which encompass proteins and polysaccharides, play multifaceted roles in various industrial processes, encompassing functions such as gel formation, viscosity enhancement in aqueous solutions, stabilization of foams, emulsions, and dispersions, prevention of ice and sugar crystal formation, and control of flavour release. \(^ {32}\)

Notably, natural polymers such as chitosan have exhibited efficacy in oral and nasal delivery systems owing to their mucoadhesive properties. Collagen, on the other hand, finds extensive applications as gene-activated matrices capable of localized, targeted delivery of significant amounts of DNA. The presence of reactive sites within most natural polymers allows for facile modifications, including ligand conjugation, cross-linking, and other functionalization approaches, enabling customization of the polymer for a broad range of clinical applications. \(^ {33}\)

Furthermore, natural polymers have emerged as promising agents for the removal of toxic dyes from wastewater generated by the dye industry. While modified polymers are often preferred for their enhanced efficacy in dye removal, the biodegradability and non-toxic nature of natural polymers necessitate larger quantities for optimal results, leading to higher associated costs. \(^ {34}\)
DISCUSSION

Wound healing is a multi-staged complex process which involves a series of phases from cell growth, restoration of epithelial cells followed by regeneration of the tissue. The advancement in wound healing process was successfully enhanced by use of various kinds of dressings among which natural polymers were found to play a profound role and the importance of various natural polymers in the healing process had been discussed. They were found to be cost effective, abundant and non-toxic compared to the synthetic polymers. Their versatility to be used in various forms and diversified uses of these natural polymers other than wound healing property which include their use in various industries.

CONCLUSION

The natural polymers have been found to the promising materials for wound healing with their unique characteristics which include biodegradability and biocompatibility. They were found to possess antibacterial, anti-inflammatory, tissue regeneration potential and speeding the process by providing moist environment for the healing. The chitosan, cellulose, alginate, starch were found to be extensively studied for their wound healing potency. Their uniqueness in biological functionalities make them the suitable candidates to be employed in wound dressings, scaffolds, and drug delivery systems. The abundance, cost-effectiveness, and sustainability of natural polymers make them attractive alternatives to synthetic counterparts. However, further research and clinical studies becomes mandate to optimize, formulate and evaluate their long-term efficacy, and also to explore their potential combination with other therapies for enhanced wound healing. Overall, natural polymers serves as an important stakeholder in advancing the field of wound care and have the potential to revolutionize the wound healing process.

ACKNOWLEDGEMENT

Authors acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript. The authors are also grateful to authors / editors / publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

Source of Funding: No funding is involved.

Conflict of Interest

The authors declare that they there is no conflict of interest.

Authors’ Contribution:

First author collected the data and the corresponding author drafted the manuscript. Both the authors had reviewed the final version of the manuscript.

REFERENCES