

# Concise Overview on Biomaterial Based Wound Dressing

Zahra Shahravi, Mahsa Mollapour Sisakht\*, Shiva Bahrami and Mohammad Amir Amirkhani\*

Stem Cell and Regenerative Medicine Center of Excellence, Tehran University of Medical Sciences, Iran

\*Corresponding author: Mahsa Mollapour Sisakht and Mohammad Amir Amirkhani, Stem Cell and Regenerative Medicine Center of Excellence, Tehran University of Medical Sciences, Iran



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## ABSTRACT

In recent years, patients with wounds and ulcers, especially non-healing wounds suffer from medical staff that they can't be more effective as a complete cure. Besides that, in most healthcare settings, these patients have to spend considerable amount of time to get treat at hospitals. Based on the different market studies wound care cause of waste huge amount of money regard to hospitality and human resources. Regenerative medicine as a new therapeutic option, try to combine different methods such as gene therapy, cell therapy, tissue engineering and using small molecules to cure different disease. Using various types of natural and synthetic polymers as a part of tissue engineering with/or without active ingredients introduced from 1980. Due to importance of using material in preparing scaffold, FDA give a definition of tissue engineering as a functional arm of regenerative medicine. The present review traces a brief list of most popular natural and synthetic polymers with introduce interesting commercial products made from each of those polymers.

**Abbreviations:** HA: Hyaluronic Acid; CMC: Carboxymethyl Cellulose; PCL: Poly Caprolactone; PVA: Polyvinyl Alcohol

## Introduction

The skin is the largest and most external organ that covers the whole body [1]. The primary function of the skin is preserved the primary layers of chemical, mechanical and physical factors [2]. The skin also has functions such as temperature regulation, immune barrier to prevent dehydration and production of vitamin D [3]. The skin consists of three layers of epidermis, dermis and hypodermis [4]. The epidermis is thick enough to continue the function as a critical barrier against pathogenic factors [5] and also has a high permeability that prevents bleeding and dehydration [6]. Keratinocyte is the most frequent cell in epidermis [7]. The dermis, located directly below the epidermis layer, forms the bulk of the skin [8]. The dermis is composed of extracellular matrix including collagen, elastin, and glycosaminoglycan, fibroblast and myofibroblast are the most cells in this layer with the role in wound healing [9]. Dermis play main role in flexibility and provides space for vessels, support angiogenesis, the lymphatic system and the nerves. The hypodermis is a layer underneath of the dermis and

contains huge amounts of adipose cells that contribute to the mechanical and thermal properties of the skin.

During past decade, different studies in the field of regenerative medicine trigger wound, especially non-healing wound as one of the major problems that can effect on quality of life [10]. Smart wound dressings should design based on the different condition and stage of wound and provide essential growth factor to push wound bed to complete cure like silver-containing products [11]. They have been used for many years as an antimicrobial agent [12] on burn wounds and unlike antibiotics, silver [13] disrupts bacterial cell wall, metabolism and damages intracellular activity [14]. According to different studies in this area, ideal wound dressing should be cost-effective, ease of use, convenient, accessible, consist of pain relief, wound protection against infection, accelerating healing, preventing body fluids lose, flexible, non-allergenic, optimal adhesion to the wound based on wound stage and finally proper mechanical properties [15]. Tissue engineering, cellular therapy

and gene therapy or in overall, regenerative medicine propose different method that accelerate time of healing significantly.

In compare with standard care (skin graft) for wound healing that have lots of limitation such as the complications of surgery and the lack of skin resources of the patient [3,15], genetic engineering used to manipulate keratinocyte and fibroblast cells to prepare modified skin substitute and prevent graft rejection in Epidermolysis bullosa Besides, tissue engineering using variety of natural and synthetic materials to produce suitable scaffold [16,17] and in combine with cells and/or without cells such as Biobrane® [18], Dermagraft® [19], Integra® [20], Apligraf® [21], Matriderm® [22], Orcel® [23], Hyalomatrix® [24] and Renoskin® [25]. In this study recent list of this kinds of products. But still there are challenges in the using tissue engineering for the treatment of injured organs, different research tried to design scaffolds in membranes or films physical shapes that can mimic the biological structure and function of an extracellular matrixes [26]. Nanofibers as a good option can provide a suitable scaffold for cell attachment, proliferation, migration, and cell growth [27]. In this review, we try to describe natural and synthetic materials that used recently for new generation of wound dressing. Besides that, this review provides data of different commercial products in the field of regenerative medicine.

### Natural Biomaterials

Natural substances are compatible to human skin tissues in their properties. Also, surface modifications can be done to improve cellular interactions based on chemical structure, the natural polymers can be classified into three major classes:

- (1) Polysaccharides,
- (2) Proteins, and
- (3) Lipids [28].

It should be noted, natural polymers have better biological performance than synthetic polymers. Disadvantages of using natural-bio polymer are weak and uncontrollable mechanical properties [29].

### Collagen

Collagen is the most common protein in the extracellular context of skin tissue [30]. It is one of the important regulating factors for the physical and biological properties of the scaffolds [31] and is also an effective factor in cell adhesion. Collagen scaffolds were former kind of scaffold that used in wound dressing [32]. There are different types of commercial products that contain collagen as main component of scaffold like, Integra® [20] made from bovine tendon collagen and shark Glycosaminoglycans (GAGs). Fibracol® from Systagenix that composed of 90% collagen & 10% Calcium Alginate [33]. Helitene® from Integra life science is microfibrillar collagen absorbable hemostatic sponge [34], also Biobrane® from

Smith & Nephew is artificial skin substitute [18]. BIOstep® is collagen matrix from Smith & Nephew [35].

### Alginate

Alginates are composed of a numbers of polysaccharide chains containing guluronic acid and Mannuronic acid [28]. Alginate in compare with other biomaterials used more as wound dressing with drug release due to its homeostasis properties. Alginate is an anionic polysaccharide which is used for the preparation of hydrogels at room temperature under normal conditions. This natural polymer is biocompatible, biodegradable, sensible price and easy gelation process [36]. Different shape of Alginate is also used as biomaterial such as gelly like structure that produced by calcium ions as a binding agent. Elasticity properties, absorption of secretions, permeability and ability to create a humid environment in some cases of wound made alginate interesting option as scaffold for tissue engineering [28]. There are different types of commercial products that contain different combination of alginate such as Algivon® from Advancis [37] and Medihoney® [38] from Dermasciences that made from alginate fiber dressing pad impregnated with manuka honey [39]. Kaltostat® from ConvaTec as sodium alginate composite dressing have nonwoven calcium [40]. Carboflex® multi-component dressing consists of alginate and carboxymethylcellulose fibres, bonded to a plastic From ConvaTec [41], Another product is NobAlgin® (Calcium-Alginate-Dressing (contain soft calcium alginate fibers with very high absorption potential [42]. Comfeel® Plus transparent wound dressing contains alginate and hydrocolloid which forms a gel layer upon release of ions from alginate fibers [43].

### Honey

Honey can improve healing process through its antioxidant, anti-inflammatory properties. These effects are due to the antimicrobial and osmotic feature of honey. Wound dressing market also consist of variety of products with honey such as MANUKAtex® from ManukaMed as non-adherent gauze dressing impregnated with manuka honey, coated with a dry-touch absorbent hydrocolloid [44]. Medihoney® is Honeycolloid Sheet of gelled manuka honey [45]. MelMax® from Dermagenics as Non-adherent wound dressing impregnated with a mixture of polyhydrated ionogens ointment and buckwheat honey [46]. MelDra® from Dermagenics is Open-weave acetate fabric impregnated with buckwheat honey. HoneySoft® from Taureon is Polyvinylacetate dressing soak with Chilean multifloral honey. Ointment, gel, honey with alginate and Sterile gas entrapped in honey from Dermascience Company [38].

### Hyaluronic Acid

Hyaluronic acid (HA) as one of the main components of the extracellular matrix is a type of glucose aminoglycan found in tissues and in combination with glucuronic acid and N-acetyl glucosamine. HA rapidly degraded in the human body. Hyaluronic acid is a

natural polysaccharide with appropriate physical and chemical properties to the skin texture that can be effective as a viscoelastic tool. Hyaluronic acid present in various weight and molecular formulation [47]. F Anica hyaluronic acid dressing Hyalofill® [48] F brand is an absorbent, critical wound coating, contains HYAFF (a component of hyaluronan). Release of hyaluronic acid into the environment is intended to cure and improve the healing process of wet and acute wounds [49]. After rubbing Hyalofill® on the wound, the product not only absorbs the wound secretions, it forms a gel layer due to release of hyaluronic acid on the wound bed. Besides, this company have combination of alginate powder with hyaluronic acid and transparent hyaluronic acid dressing [50].

### Aloe Vera

Aloe Vera contains vitamins, amino acids, minerals, enzymes and glycoproteins. It has been traditionally used for various type of treatment for skin damage such as sun burn and dermatitis [51]. Aloe Vera has anti-inflammatory and antibacterial properties and reduce the inflammation [52], irritation, itching and ulceration associated with radiation-induced dermatitis [53]. It also accelerates the healing of chronic leg ulcers by decreases the blood glucose, surgical wounds and frostbite [54,55].

### Chitosan

Chitin is one of the most widely approachable/accessible polymers due to having multiple functional groups and active structure [56] Although it is biocompatible, biodegradable polysaccharide, well coating for burn wounds and accelerates the healing process. Disadvantage of using chitosan are poor mechanical properties and low electrostatic potential either which is improved in combination with other materials to enhance it. Axiostat® is chitosan hemostatic dressing with US FDA Approval that applies to inhibit moderate to deep bleeding within minutes. This product has anti-inflammatory, pain management, Anti-microbial and hemostatic properties that proper for oral maxillofacial surgeries, dental surgeries and tooth extraction [57]. HemCon® and chitoflex® (HemCon Medical Technologies, Inc., Portland, OR) wound dressings contain chitosan with a special use in homeostasis [58].

### Sodium Carboxy Methyl Cellulose (CMC)

Carboxymethyl cellulose (CMC) or cellulose gum is a cellulose derivative with carboxymethyl groups bound to some of the hydroxyl groups. CMC as a natural polymer is an interesting choice for different companies, commercial products such as Hydroactive Hydrotul® from Hartman which is non-obstructive primary dressing impregnated with non-drug triglyceride ointment [59]. Purilon® gel [60] from Coloplast and Regranex® [61] gel from Smith and Nephew are the most famous example of available products in wound dressing market. AQUACEL® Ag plus, made of fiber and 100% pure carboxymethyl cellulose. This product produce by Convatec inc. has unique anti-microbial advantages for wounds that are infected or at risk of infection along with ionic silver. This dry dressing is soft,

non-woven, adaptable and highly absorbent. ease to use and does not cause scarring or sickness [62]. Another product in this field is ColActive® PLUS Collagen Matrix Dressing is an advanced dressing, after covering wound with this dressing, it make a soft gelatinous layer with optimal moisture content that accelerate granulation and promotes epithelialization, lead to complete wound healing. It consists of sodium alginate, EDTA and CMC [63]. Biatin® alginate from Coloplast contains 85% calcium alginate and 15% CMC [64]. Calcium alginate & CMC can absorb wound exudate, in addition, a gelly structure of these material can fill the cavity of deep wound as well. This gel provide moisture to accelerate wound healing time and pain relief result as a consequence of protection free nerve ending at wound site by this gel [65].

### Gelatin

Gelatin found in ligaments, tendons, and tissues. It can be used as an alternative to collagen due to its properties such as biodegradable and biocompatibility. The pros and cons of using gelatin contain low cost, anti-thrombogenic and anti-inflammatory but it needs chemical bonding and demonstrate less stability [66,67]. DouDerm® dressings is composed of a three-dimensional network comprising sodium carboxymethyl cellulose (CMC), pectin, and gelatin that have special arrangement of this triple grid with unique formulation of Convatec America company [68].

### Synthetic Polymers

#### Poly Caprolactone

Poly Caprolactone (PCL) is an aliphatic polyester that has been extensively has been studied. This semi-crystalline polyester has high processability and is soluble in a wide range of organic solvents [69]. The limitation of PCL based scaffolds has a hydrophobic property that may affect cell adhesion and degradation rate. Improvement of hydrophilic properties for this polymer is to combine it with hydrophilic polymers [70]. PCL shows biodegradable properties for a long time [71].

#### Polyvinyl Alcohol

Polyvinyl alcohol (PVA) is a semi-crystalline hydrophilic polymer; and this polymer consist of a large number of medical products including contact lenses, ophthalmic materials, tendon repair and wound dressing with drug release [72,73] around the world. Proper chemical resistance, biocompatibility, physical properties, high degree of degradation in water or carbon oxide and biodegradability of PVA led to the develop numerous commercial products based on this polymer. PVA has neutral physiology, safe and easy to process, it can crosslink with various agents [10]. Different studies showed that concentration of PVA related to the diameter of the fibers after polymerization.

#### Poly Lactic Acid/Lactic-Co-Glycolide

Dextrose from corn or sugar beet is used as the raw material used for to produce poly-lactic acid (PLGA). PLGA belongs to the

family of aliphatic polyesters, which are usually made of hydroxide acids and this is considered as degradable and combinable materials. PLA is degraded by ester bond through simple hydrolysis and the presence of enzymes is required for the catalytic formation of this hydrolysis [74]. L-Mesitran<sup>®</sup> from Triticum is soft mixture of honey (not manuka) with lanolin, polyethylene glycol, vitamins C and E [75].

### Polyurethane

Polyurethane has a unique property, has been of interest in wound healing fields. Biatain from coloplast company with PU foam / PU film [65] and ALLEVYN<sup>®</sup> Ag non-Adhesive from Smith and Nephew consists of polyurethane and silver [76] are famous products in this field. FarmActive<sup>®</sup> foam dressing (polyurethane) as a sterile dressing with three different layers; the upper layer (breathable semi-permeable polyurethane), the middle layer (polyurethane absorbent foam) and the inner layer that can be on the wound bed [77]. Hydrosorb<sup>®</sup> is a transparent hydrogel dressing from Hartman Company contain hybrid polymers, adsorbent polyurethane and propylene glycol. The back of this dressing is made of polyurethane tape. These types of dressing are not stick to the scar. Transparent wound cover cause to examine the wound even without removing the dressing. The Hydrosorb<sup>®</sup> coating has a hypoallergenic strip (suitable for people with allergies and allergies) and does not need to use other materials for greater safety [78].

### Silicone

Wound dressing contain silicone provide gentle adhesion, minimizes size of wound and surrounding skin trauma [79]. There is variety of products in world market that contain silicon such as MediClear<sup>®</sup> Scar from Covalon Company. This dressing is a thin, transparent and self-adhesive silicone consist of a polyurethane film coated with a soft silicone adhesive gel. It can adhere to the areas around the scar and accelerate time of healing or prevent colloidal and hypertrophic scars [80]. Renosigel<sup>®</sup> from T & L Company is also another silicone scar removal dressing. Renosigel is a soft, flexible, self-adhesive sheet to improve red and dark scars [81]. Optifoam<sup>®</sup> as an antibacterial silicone silver foam dressing provides mild adhesion and use after optical surgery, this dressing can be removed from the wound and return to the wound again. The moisture evaporation rate (MVTR) is adjusted according to the amount of discharge [50].

### Conclusion

More than thousand types of dressings are available in the worldwide market that categorized based on the different feature of wounds. Totally, Ideal wound dressing should capable to maintain humidity at the wound bed while removing exudate, free of toxic particle, non-allergic, easy remove from wound, transparent to see process of healing and check time of changing and cost effective. The new generation of wound dressing in the field of regenerative medicine contain live cells that capable complete healing in short

time. Actually, nowadays there is variety of products with live cells but still needs more studies to generate different kind of dressing with internal vessels network. This network helps cells to be alive for long time and settle in wound bed till complete healing. Biomaterial that we reviewed in this article after years and years of application still interesting option for physician due to cost effective and ease of use, so, we think more different studies, especially, systematic review needs to show efficacy of using biomaterial in wound healing process.

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