Review

polymers advanced technologies

Received: 11 July 2009, Revised: 28 October 2009, Accepted: 30 October 2009, Published online in Wiley InterScience: 7 December 2009

(www.interscience.wiley.com) DOI: 10.1002/pat.1625

A review on wound dressings with an emphasis on electrospun nanofibrous polymeric bandages

Payam Zahedi[a,b], Iraj Rezaeian[a]*, Seyed-Omid Ranaei-Siadat[b], Seyed-Hassan Jafari[a] and Pitt Supaphol[c]**

Wound dressings have experienced continuous and significant changes since the ancient times. The development starts with the use of natural materials to simply cover the wounds to the materials of the present time that could be specially made to exhibit various extraordinary functions. The modern bandage materials made of electrospun biopolymers contain various active compounds that are beneficial to the healing of wounds. These materials are fibrous in nature, with the size of fibers segments ranging from tens of nanometers to micrometers. With the right choices of biopolymers used for these fibrous materials, they could enhance the healing of wounds significantly compared with the conventional fibrous dressing materials, such as gauze. These bandages could be made such that they contain bioactive ingredients, such as antimicrobial, antibacterial, and anti-inflammatory agents, which could be released to the wounds enhancing their healing. In an active wound dressing (AWD), the main purpose is to control the biochemical states of a wound in order to aid its healing process. This review provides an overview of different types of wounds, effective parameters in wound healing and different types of wound dressing materials with a special emphasis paid to those prepared by electrospinning. Copyright © 2009 John Wiley & Sons, Ltd.

Keywords: wound healing; wound dressings; electrospinning; fibrous mats

INTRODUCTION

From the ancient times, for effective healing of a wound, a suitable material had to be used to cover the wound in order to prevent any infection. Historically, honey pastes, plant fibers, and animal fats were used as wound dressing materials.[1] Nowadays, with new biopolymers and fabrication techniques, a wound dressing material is expected to have extraordinary properties which enhance the healing process of a wound. For an effective design of a functional wound bandage, characteristics of the wound type, wound healing time, physical, mechanical, and chemical properties of the bandage must be taken into consideration. Ultimately, the main purpose is to achieve the highest rate of healing and the best aesthetic repair of the wound.[2]

Electrospinning is a simple and effective method for producing fibers from tens of nanometers to micrometers.[3] In this process, a polymer solution from a reservoir is ejected to a small opening of a capillary by means of Coulombic repulsion of charges that are accumulated at the tip of a pendant droplet as soon as an electrical potential applied between the capillary and a collecting device increases beyond a critical value.[4] As the charged jet travels to the collector, it readily dries out, forming nonwoven fibrous mats depositing on the collector. Due to the ability of fibrous mats and their porous nature, electrospun fibrous webs could be excellent functional wound dressing materials.[5] The porous nature of these mats is highly suitable for the drainage of the wound exudates and, allows appropriate permeation of atmospheric oxygen to the wound. They can be specially made to prevent the attack of microbes, thus refraining the wound from possible infections, which would ultimately result in delayed healing.[5]

The aim of this review paper is to discuss and summarize the basic principles pertinent to the healing of a wound and to give an overview of recent developments in different wound dressing materials with an emphasis on electrospun polymeric membranes used for this purpose. Standard tests for characterizing

* *Correspondence to: I. Rezaeian, School of Chemical Engineering, College of Engineering, University of Tehran, P.O. Box 11155-4563, Tehran, Iran. E-mail: rezaeian@ut.ac.ir*

** *Correspondence to: S.-O. Ranaei-Siadat, NanoBioTechnology Engineering Lab., Department of Biotechnology, Faculty of New Technologies & Energy Engineering, Shahid Beheshti University, Tehran, Iran. E-mail: o_ranaei@sbu.ac.ir*

a *P. Zahedi, I. Rezaeian, S.-H. Jafari*
School of Chemical Engineering, College of Engineering, University of Tehran, P.O. Box 11155-4563, Tehran, Iran

b *P. Zahedi, S.-O. Ranaei-Siadat*
NanoBioTechnology Engineering Lab., Department of Biotechnology, Faculty of New Technologies & Energy Engineering, Shahid Beheshti University, Tehran, Iran

c *P. Supaphol*
The Petroleum and Petrochemical College and the Center for Petroleum, Petrochemicals and Advanced Materials, Chulalongkorn University, Bangkok, 10330, Thailand

parameters which influence the final properties of a wound dressing material relevant to the physiological environment of a wound are also addressed.

WOUNDS AND WOUND HEALING PROCESS

Definition and types of wounds

A wound is defined as an injury or tear on the skin surface by physical, chemical, mechanical, and/or thermal damages. A more scientific definition of a wound is a disruption of normal anatomic structure and function of the skin.[6] On the basis of wound healing processes, there are two types of wounds: acute and chronic wounds. Acute wounds are caused by traumas, but the wounds are usually healable within 8 to 12 weeks.[7] These wounds can be caused by mechanical damage induced by sheer, blunting, and/or stabbing action of hard objects. Acute wounds can also be formed by exposure to extreme heat, irradiation, electrical shock, and/or irritated with corrosive chemicals. Cares for these wounds depend on the severity of the wounds.

Chronic wounds are those injuries which are produced as a result of specific diseases such as diabetes, tumors, and severe physiological contaminations.[8] Healing of these wounds could take more than 12 weeks[9] and recurrence of the wounds is not uncommon.[10] In addition to the above wound types, one can classify wounds according to their appearance. Figure 1(a–d) shows epithelializing (clean, medium to high exudates), granulating (clean, exudating), slough-covered and necrotic (dry) wounds, respectively.[11]

Principles of wound healing

Wound healing is a special biological process which is related to physiological parameters. Selection of a suitable wound dressing material for a specific type of wound requires comprehensive knowledge of the wound healing process. There are numerous published reports in the open literature describing the various biological and physiological stages of the healing process of a wound.[12–16] These can be summarized into five consecutive cascades of events of hemostasis, inflammation, migration, proliferation, and maturation. These phases of wound healing are shown in Fig. 2 (a–d), respectively.

The first stage includes hemostasis and inflammation which occurs soon after there is damage to the skin. Fibrinogen, which is one of the major components of the skin's connective tissues (Table 1), leads to the coagulation of exudates (blood without cells and platelets), and together with the formation of a fibrin network, produces a clot in the wound which stops.[17] Therefore, both hemostasis and inflammatory stages play an important role

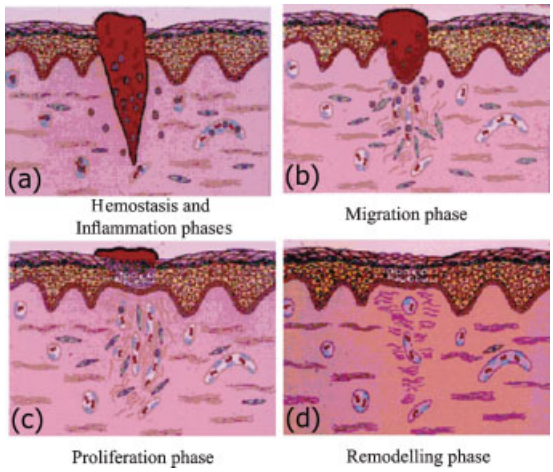


Figure 2. Schematic representation of different phases of wound healing (a) infiltration of neutrophils into the wound area (b) invasion of wound area by epithelial cells (c) epithelium completely covers the wound (d) many of the capillaries and fibroblasts, formed at early stages have all disappeared. (Reprinted from Reference [16], Copyright (2008) Wiley-Liss, Inc. and the American Pharmacists Association).

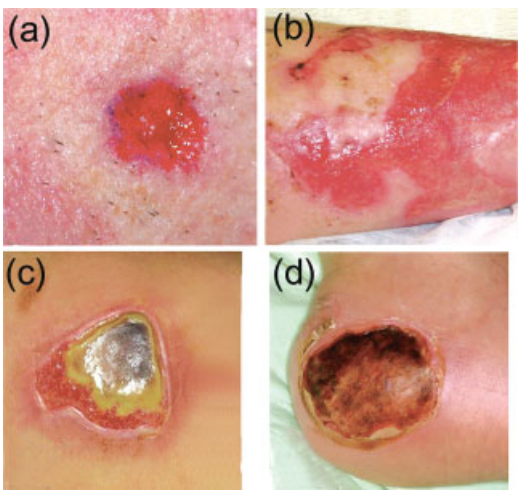


Figure 1. Types of wounds based on their appearances: (a) epithelializing (clean, medium to high exudates), (b) granulating (clean, exudating), (c) slough-covered, and (d) necrotic (dry).

Table 1. Cells and components of vascularized connective tissue

Intravascular (blood) cells	Neutrophils Monocytes Eosinophils Lymphocytes Basophils Platelets
Connective tissue cells	Mast cells Fibroblasts Macrophages Lymphocytes
Extracellular matrix components (ECM)	Collagens Elastin Proteoglycans Fibronectin Laminin

in the healing process of a wound.[18] The inflammatory phase occurring simultaneously with the hemostasis phase usually takes more than 24 h. At this stage, blood neutrophils followed by phagocytes enter the wound medium and penetrate inside the dead cells, (Fig. 2 (a)). In the migratory phase, the new and live cells called epithelial move towards skin injury to replace dead cells, (Fig. 2 (b)). The proliferation stage consists of the complete coverage of wound by epithelium. At this stage, new stromas usually known as granulating tissues are formed after about 4 days. Microphages, fibroblasts, and blood vessels move toward the wound environment and form a single unit.[19] The completion of this stage takes about 2 weeks. According to Figure 2 (c) during the growth of migration phase, a reduction in the inflammatory phase of the wound is gradually observed. The final stage in the healing process of a wound is tissue remodeling. At this stage fibroblasts completely cover the surface of the wound as a new layer of the skin and there is no evidence of the wound. This stage is also known as maturation phase in the healing process of wounds (Fig. 2 (d)).

WOUND DRESSINGS AND THEIR PROPERTIES

For years, man has used different materials such as linen, honey, animal fats, and vegetables fibers[20,21] for wound dressing. Continuous developments have led to extensive use of new bandages with improved performance. Today's wound dressing materials are usually based on synthetic polymers.

Classification of wound dressings

Wound dressings can be classified from different aspects.[22–24] The main classifications are as follows:

Passive products which are ordinary dressings, such as gauze and tulle, merely act as a common cover on a wound so that the wound can rehabilitate underneath. The second types of wound dressings are interactive materials containing polymeric films, and/or foams which are transparent and permeable to water vapor and atmospheric oxygen. These materials, such as hyaluronic acid (HA), hydrogels and foamed covers, are good barriers against permeation of bacteria to the wound environment. The last types of wound dressings are bioactive materials or in other words active wound dressing materials (AWD) such as hydrocolloids, alginates, collagens and chitosan (CS).[25–28] Table 2 and Fig. 3 show different types, appearances, and properties of the passive, interactive, and bioactive wound dressing materials.

The conventional wound dressing materials are not suitable for acute and chronic wounds as far as rapid healing of a wound is concerned. For this purpose functionalized biological and biochemical bandages were developed. One of the main advantages of using bioactive wound dressing materials is the modified chemical environment facing the physiological conditions of wound for more rapid healing. Additionally, longer periods are needed for their change. They are also more successful in clinical results as compared to the conventional wound dressing materials. The bioactive wound dressing materials are produced from a variety of biopolymers such as collagen, HA, CS, alginate, and elastin, etc. Recently, biopolymers containing active ingredients, such as antimicrobials and antibiotics, were used in wound dressing materials against contaminations and infections. A vast range of antibiotics, such as gentamicin in collagen foams,[47] ofloxacin in silicone gel sheets[48,49] and minocycline in CS, have been used which can be released from such wound dressing materials.[50] Also, new antimicrobial wound bandages with dry and cold fibrins for the release of tetracycline are used.[51] Other ingredients are also used for accelerating the inflammation stage of a wound in new wound dressing materials. These ingredients have a direct influence on the proliferation stage and activation of fibroblasts.[52] Different growth parameters in a wound healing process are as follows:

Epithelia growth factor (EGF), platelet derived growth factor (PDGF), fibroblasts growth factor (FGF), transforming growth factor (TGF), insulin-like growth factor (IGF), and human growth hormone and granulocyte-macrophage colony-stimulating factor (GM-CSF).[53,54] The other important active compounds in the healing of a wound are vitamins A, C, E; zinc, and copper minerals.[55]

Vitamin A in collagen synthesis is helpful for epithelial cell differentiation. Vitamin C is an essential compound for the intercellular matrix of tissues such as skin and other connective tissues.[56] Vitamin E and C have been reported to be helpful for acceleration of a wound healing process.[57] In addition, vitamin E is reported to have antioxidant and anti-inflammatory activity[58] which reduces scaring.[59]

The other ingredients of high importance in a wound dressing materials are nanosilver particles (nanoAg) used as antimicrobial in hydrocolloids, alginates and a hydrofibrous materials produced by electrospinning process.[46] On the other hand, besides nanoAg, iodines have also found increasing uses in electrospun nanofibrous bandages for wound dressing.[60] Table 3 shows commercial antibacterial wound dressing materials containing these bioactive materials.[61] Recent developments in wound dressing materials and their production methods as well as the ingredients used have been reviewed.[62–75]

Desirable properties of a wound dressing material

Depending on a wound type and its healing, the most suitable wound dressing system must be used. Usually for a rapid wound healing, different types of wound dressing materials can be used. Because of unique properties of nanofibrous bandages such as high surface area to volume ratio of the nanofibers, the applications of these materials on various types of wounds are abundant with respect to other modern wound dressing materials, such as hydrocolloids, hydrogels, and so forth. The following properties are generally considered for all modern wound dressing materials:

Maintain the most suitable environment at the wound/dressing interface, absorb excess exudates without leakage to the surface of a dressing, provide thermal insulation, mechanical and bacterial protections, allow gaseous and fluid exchanges, absorb wound odor, be nonadherent to the wound and easily removable without trauma, provide some debridement action (remove dead tissue and foreign particles) and be nontoxic, nonallergic, nonsensitizing (to both patient and medical staff), sterile and nonscaring.

Economical aspects of modern and conventional wound dressing materials

Payne *et al.* [76] carried out evaluation studies on the uses of wound dressing materials based on modern polymeric foams

Table 2. Wound dressing types and their descriptions

Dressing types	Products name	Descriptions	Reference
Passive	Gauze	Gauze is manufactured as bandages, sponges, tubular bandages, and stocking. These dressings can stick to the wounds and disrupt the wound bed when removed. Therefore, these are suitable for minor wound, e.g. Multisorb. (Fig. 3a)	[29,30]
	Tulle	Greasy gauzes consisting of Tulle gauze and petroleum jelly. This dressing does not stick to the wound surface and is suitable for a flat and shallow wound with minimal to moderate exudates, e.g. Jelonet. (Fig. 3b)	[31]
Interactive	Semi-permeable films	Semi-permeable, polyurethane membrane which has acrylic adhesive. These are transparent for allowing wound check and are also suitable for shallow wound with low exudates, e.g. Tegaderm. (Fig. 3c)	[25,26,32]
	Semi-permeable foams	Soft, open cell, hydrophobic, polyurethane foam sheet 6–8 mm thick. These dressing are designed to absorb large amounts of exudates. They are not used for low exudating wounds as they will cause dryness and scabbing, e.g. Allevyn. (Fig. 3d)	[33]
	Amorphous hydrogels	Amorphous gels are not cross-linked. They are used for necrotic or sloughy wound beds to rehydrate and remove dead tissue. They are not used for moderate to heavily exudating wounds, e.g. Intrasite. (Fig. 3e)	[34,35]
Bioactive	Hydrocolloids	These are semi-permeable polyurethane film in the form of solid wafers; contain hydroactive particles as sodium carboxymethyl cellulose that swells with exudates or forms a gel. Depending on the hydrocolloid dressing chosen they can be used in wounds with light to heavy exudate, sloughing, or granulating wounds. For example DouDERM. (Fig. 3f)	[36–39]
	Alginates	Calcium alginate which consists of an absorbent fibrous fleece with sodium and calcium salts of alginic acid (ratio 80:20). They are good for exudating wounds and helps in debridement of sloughing wounds. They are not used on low exudating wounds as this will cause dryness and scabbing. Dressing should be changed daily, e.g. Kaltostat. (Fig. 3g)	[40–43]
	Collagens	Collagens are dressings which come in pads, gels or particles and promote deposition of newly formed collagen in wound bed. They absorb exudates and provide a moist environment. (Fig. 3h)	[44,45]
	Hydrofibers	Hydrofibers are soft nonwoven pad or ribbon dressing made from sodium carboxymethyl cellulose fibers. They absorb exudates and provide a moist environment in a deep wound that needs packing, e.g. Aquacel. (Fig. 3i)	[46]

such as polyurethane (PU) and traditional materials like gauze. They also made a comparison between the relative costs of these two types of wound dressing materials for patients with a stage II pressure ulcer. The wound dressing materials were used for 4 weeks on 36 patients (men and women). It was concluded that, although the cost of foamed wound dressing materials is higher than that of the traditional gauzes, the foamed bandages have advantages such as time saving for nurses who change these wound dressing materials, a reduction in preparation and healing time process of the wound and their effectiveness. Their calculations showed that general preparatory costs for each patient, including materials and nurse's time consumption for the foamed PU and gauze wound dressing materials, are 5667 and 12,500 US dollars, respectively. Their studies also showed that the total costs during a period of 28 days for each patient bandaged by PU foam and gauze are 315 and 781 US dollars, respectively. This means that using a modern foamed wound dressing material makes a saving of about 466 US dollars.

ELECTROSPINNING OF NANOFIBERS AND THEIR USE IN PRODUCTION OF WOUND DRESSING MATERIALS

In 1934, Formhals patented his first invention about an instrument for production of synthetic fibers using electrical power.[4] Electrospinning is a unique approach using electrostatic forces to produce nanofibers. These fibers have very fine size pores and high surface area. Figure 4 shows schematic presentation of an electrospinning process. A high potential difference between the head of a syringe needle (with a flat end) and the collector including a foil sheet produces a jet from a

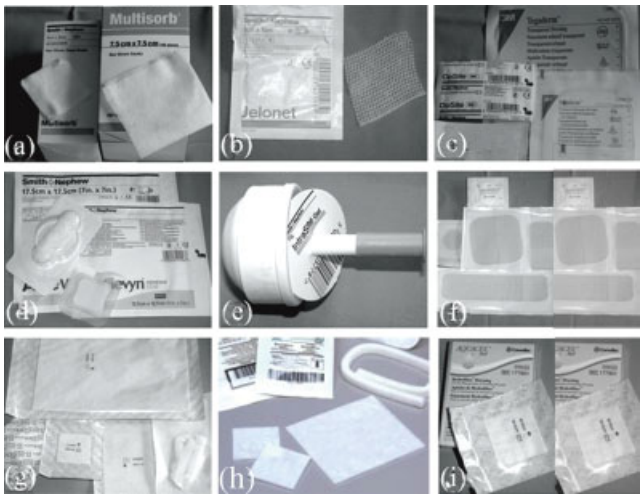


Figure 3. Different types and appearances of passive, interactive, and bioactive wound dressing materials: (a) gauze, (b) tulle, (c) polyurethane membrane, (d) polyurethane foam, (e) hydrogel, (f) hydrocolloid, (g) alginate, (h) collagen, and (i) hydrofiber. This figure is available in colour online at www.interscience.wiley.com/journal/pat

polymeric solution for the formation of nonwoven nanofibrous webs on the surface of the foil.[77,78] Table 4 shows a number of polymers which can be electrospun.[79] The wound dressing materials produced by electrospinning technology have special properties as compared to the dressings produced by conventional methods. These properties are as follows:[109]

Hemostasis: Nanofibrous wound dressings with their small holes and high effective surface area can promote hemostasis phase. The promotion of this phase is due to nanofibrous structure of the dressing material without using any hemostatic agent.

Absorbability: Due to the high surface area to volume ratio of the nanofibers, they exhibit water absorption of 17.9–213% whereas typical film dressings only show water absorption of 2.3%.[110] Thus, if hydrophilic polymers are employed, the nanofibrous dressings will be able to absorb wound exudates more efficiently than the typical film dressings.

Semi-permeability: The porous structure of a nanofiber dressing is excellent for the respiration of cells which does not lead the wound to dry up. This indicates an appropriate control of a moist environment for the wound. Also, the small pore size can effectively protect the wound from bacteria infection. Electrospun nanofibrous membrane wound dressings can also meet the

Table 3. Examples of antimicrobial dressings (from Reference [61])

Dressing name	Antimicrobial ingredient	Dressing format	Manufacture
Acticoat absorbent	Ionic silver	Calcium alginate	Smith & Nephew, Inc, Largo, FL, USA
Actisorb Silver 220	Ionic silver and activated charcoal	Silver impregnated activated charcoal cloth	Johnson and Johnson Wound Management, Somerville, NJ, USA
Arglaes	Ionic silver	Transparent film or powder	Medline Industries, Inc, Mundelein, IL, USA
Aquacel AG	Ionic silver	Hydrofiber	Convatec, Skillman, NJ, USA
Contreet H	Ionic silver	Hydrocolloid	Coloplast Corp, Marietta, GA, USA
Contreet F	Ionic silver	Foam	Coloplast Corp, Marietta, GA, USA
Iodosorb	Molecular iodine	Gel or paste	HealthPoint Ltd, Ft. Worth, TX, USA
Silvasorb Antimicrobial Silver Dressing	Ionic silver	Hydrogel sheet or amorphous gel	Medline Industries, Inc, Mundelein, IL, USA
Kerlix AMD Gauze	PHMB	Gauze	Tyco Healthcare/Kendall, Mansfield, MA, USA

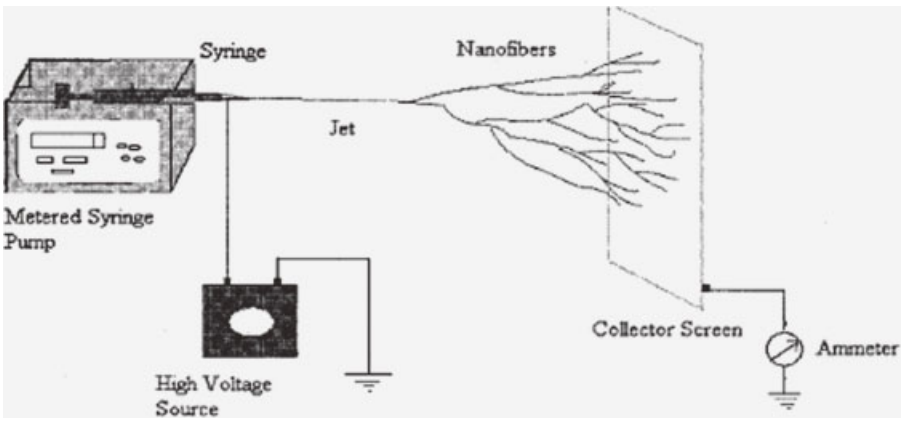


Figure 4. Schematic of electrospinning process. (Reprinted from Reference [79], Copyright (2005) Wiley Periodicals, Inc.). This figure is available in colour online at www.interscience.wiley.com/journal/pat

Table 4. List of polymers and their solvents for electrospinning

Polymer	Solvent	Reference
Polystyrene (PS)	Dimethyl formamide (DMF) and diethyl formamide	[80–82]
Poly (3-hydroxyl butyrate-co- poly (3-hydroxyl valerate)	Chloroform	[83]
Polycaprolactone (PCL)	Dichloromethane/DMF	[84]
Polyethylene oxide (PEO) and polyethylene glycol (PEG)	Water/chloroform	[85,86]
Poly (methyl methacrylate) (PMMA)	Toluene/DMF	[87]
Cellulose acetate	Acetone	[88]
Nylon 6 (PA6)	DMF, m-cresol, formic acid	[89,90]
Polyvinyl chloride (PVC)	DMF, tetra hydro furan (THF)	[91]
Gelatin	Glacial acetic acid (AA), AA/2,2,2-triflouroethanol (TFE), AA/dimethyl sulfoxide (DMSO), AA/ethylene glycol (EG), AA/formamide (F)	[92]
PEO, polycarbonate (PC) and polyurethane (PU)	Isopropyl alcohol (IPA), DMF and THF	[93]
Polyacrylonitrile (PAN)	DMF	[94]
Poly (ethylene terephthalate) (PET)	Mixture of dichloromethane and triflouro acetic acid (TFA)	[77]
PET and poly (ethylene naphthalate) (PEN)	*O*- chlorophenol/o-chlorobenzene	[95]
Poly(ethylene-co-vinyl acetate) (PEVA), Polylactic acid (PLA) and PEVA/PLA.	Chloroform	[96]
Dextran (*Dex*)	Water	[97]
Poly-L-lactide (PLLA), (PC), Polyvinylcarbazole	Dichloromethane (DCM)	[98]
Silk and silk like polymer with Fibronectin functionality (SLPF)	Formic acid/hexafluoro isopropanol	[99,100]
Poly (vinyl alcohol) (PVA)	Water	[101,102]
Chitosan	(TFA)	[103–106]
Polybenzimidazole (PBI)	*N*,*N*-dimethyl acetamide (DMAc)	[107]
PLA/poly (glycolic acid) (PGA)	DCM	[108]

requirement of high gas permeation apart from providing effective protection of wound against infection and dehydration.

Conformability (3 D-dressing): Conformability or the ability to conform to the contour of wound is one of the parameters that needs to be clinically assessed for the flexibility and resiliency of the medical dressings. In the textile industry, it is widely recognized that the conformability of a fabric is closely related to the fiber fineness. Finer fiber fabrics are easier to fit to complicated 3-D contours. Therefore, dressing materials made of ultra fine fibers can provide excellent conformability and thus result in a better coverage and protection of the wounds from infection.

Functional ability: Multifunctional bioactive nanofibrous dressings are readily available because of the ease of incorporating therapeutic compounds into the nanofibers via a co-spinning process. Depending on the stage of treatment and the intended functionality of the drugs, active components including pharmaceutical compounds such as antiseptics, antifungal, vasodilators (e.g. minoxidil used to promote wound epithelialization and neovascularization), growth factors (e.g. FGF, EGF, and TGF), and even cells (e.g. keratinocytes) can be integrated into the same nanofibrous substrate. Another advantage of using electrospinning is that, unlike other commercial dressings, which use multilayer configuration to attain desired objectives and different functions such as medication, growth factors, and so forth, such functionalities can be achieved by electrospinning various functional materials into one blended layer to obtain an all-in-one wound dressing. This brings an extra benefit of reduced frequency in changing dressings which may disturb the regeneration of neotissue.

Scar-free: Ultimately, nanofibers also hold a promise of healing wounds without leaving scars. Although this is hard to achieve, nevertheless researchers and clinicians seek to heal a wound with as little scar as possible. For example, Coffee[111] used electrospinning technique to make fibrous dressings on a wound. He believed it would encourage normal skin to grow immediately instead of scarring because the biodegradable fibrous scaffolds would give the skin cells a better road map for self-repair. From a tissue-engineering point of view, biomimically adopting nanofibrous structure has good cell conductivity and can improve blood and other tissue fluid compatibility, which will facilitate wound healing and skin regeneration.

In the following sections the polymers used for production of wound dressing materials, which can be spun by electrospinning process, the preparation of nanofibrous membranes, their treatment and finally standard tests carried out on these wound dressing materials for evaluation of their compatibility with biological environment of a wound, the identification of their microscopic, thermal and mechanical properties are discussed.

Materials

Since, a wound dressing material has to be placed in the physiological and biological environment of a wound, the use of biopolymers capable of electrospinning process becomes inevitable. Table 5 shows some natural and synthetic biopolymers. Many of these biopolymers have an essential potential usage as an electrospun nanofibrous bandages for the wounds. Generally, biodegradable polymers can be used in *in*

vitro and *in vivo* systems. Table 5 gives the names and some information about these natural and synthetic biopolymers.[112] Only few polymers such as polycaprolactone (PCL), poly (L-lactic acid) (PLA), polyvinyl alcohol (PVA), CS, and gelatin have been studied in electrospinning process for wound dressing applications.[113]

Preparation of wound dressing mats

As mentioned before nanofiber mats are produced by the electrospinning process as a result of potential gradient between needle tip and collector. Most of the biopolymers used for the production of nanofibrous membranes are usually in solution for wound dressing applications. Therefore, the choice of an ideal solvent is highly essential. In order to obtain accurate control in producing nonwoven webs from nanofibers, the concentration of the solution must be kept in its threshold point. Usually, an Ostwald-type viscometer is used for the determination of the solution viscosity of biopolymers.[114] The next stage in producing an electrospun wound dressing material is stabilization of nanofibers structures against the aqueous environmental solubility and physiological medium of the wound with the appropriate methods such as heat,[115] and use of glutaraldehyde (GA) as a bifunctional crosslinker.[116]

In order to produce an active wound dressing material, in addition to structural control of electrospun nanofibrous mats, loading suitable drugs is a significant parameter which must be considered. As previously mentioned, these drugs can be organic or inorganic. Materials such as vitamins, antibiotics, growth factors for increasing proliferation, anti-inflammatory agents and other materials have been used. One of the most applicable additives is the nanoAg particle which is incorporated to biopolymeric electrospun membranes. This will cause the wound environment to have an antibacterial property which prevents it from infections (Table 3). When nanoAg particles are added to polymeric solution, due to precipitation of Ag^+ ions on the needle tip of the syringe or the surface of metallic collector, the electrospinning process might stop by the closure of the syringe needle tip. Therefore, using usual methods such as aging, the Ag^+ ions are converted to Ag^0 species. In a research work reported by Hong[117] UV light was used for Ag^+ ions reduction in electrospun PVA webs loaded with nanoAg particles. Also, Rujitanaroj *et al.*[116] used the aging process for the preparation of antimicrobial gelatin nanofibers from $AgNO_3$ in polymer solution. In this work Ag^+ ion is reduced to Ag^0 element in several steps. The formation of elemental Ag (nAg) nucleus from interaction between Ag^+ ions with –COOH, $–NH_2$ or both on the main collagen chain is the reason for this conversion (Scheme 1). The simple binding between the lone electron pairs on O or N atoms in the $–NH_2$ and –COOH groups with Ag^+ ions is believed to be responsible for formation of nAg nucleus. The other treatment on the nanofibrous membranes for using in biological environment of a wound is the crosslinking of these materials to get a better drug release process and to reduce their solubility. Usually, the wound environment is aqueous and some biopolymers such as collagen, dextran and PVA are soluble in these media and gels are formed. In order to prevent this situation, these mats must be crosslinked. For this purpose heat or crosslinking agents such as GA, acetaldehyde (AA), formaldehyde (FA), glycidylmethacrylate (GMA), and other chemicals are used. Usually, these methods form chemical crosslinks which are not suitable for wound dressing. Yao *et al.*[118] have suggested that the post-spinning treatment with methanol has led to replacement of the residual water in the fibers thus allowing PVA-water hydrogen bonding to be replaced by hydrogen bonding between PVA chains. This is expressed as an increase of crystallinity. The strong hydrogen bonding in the crystallites serves as physical crosslinks. Figure 5 (a–c) shows scanning electron microscope (SEM) micrographs of spun PVA nanofibers with no treatment, treated with methanol and heat treated samples, respectively. It can be seen that the PVA nanofibers produced by the heat treatment method have a separate and fine structure and could preserve their web structure better than the nanofibers produced by the other methods.

Characterizations of wound dressing mats with some standard tests

For characterization of a wound dressing material usually standard test methods are used and the results need to be confirmed by official compendia such as British and US Pharmacopoeia; national test standards such as British Standards and American Standards for Testing and accredited laboratories such as the Surgical Materials Testing Laboratory (SMTL). These tests are carried out on different wound dressing materials such as hydrocolloids, alginates, PUs, and hydrogels. These tests are usually about antibacterial, cellular properties such as proliferation, culture, adhesion, healing of a wound and quantitative measurements such as histology, water vapor permeability (WVP). Various other tests, such as differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), X-ray diffraction (XRD), and mechanical properties, are also performed on modern wound bandages.

Antibacterial evaluations by releasing drug

The growth rate of bacteria in a wound is highly dependent on the rate of drug release from the nanofiber surface in a wound dressing material. Hong *et al.*[115] investigated the release rate of from Ag^+ ions nanofibers of PVA/$AgNO_3$. They found that when heat and UV radiation treatments are used for PVA nanofibers, the release rate Ag^+ ions is considerably reduced and some Ag^+ ions are converted to Ag^0. The release rate of Ag^+ ions under these two conditions are shown in Fig. 6 (a and b). It is seen that after 15 h, a steady state is reached for PVA/$AgNO_3$ nanofibers which are heat treated only. The nanofibers treated with heat and UV has about 40% release rate of the heat treated samples. The antibacterial activity of gelatin nanofibers containing $AgNO_3$ on aerobic bacteria which are produced on wounds from burning were investigated.[116] The rate of stoppage for bacterial growth for *E-coli* (ATCC-25922), *Pseudomonas aeroginosa* (*P. aeroginosa*) (ATCC-27853), *Staphylococcus aureus* (ATCC-2503), and *methicillin-resistant S. aureus (MRSA)* (ATCC-20627) by gelatin nanofibers filled with silver drug and without that and also the situation when these nanofibers were crosslinked for 1–3 h and then washed with glycine were investigated. These studies were based on standard disc penetration tests which are defined by US Clinical and Laboratory Standards Institute (CLSI). In these investigations, the antibacterial drug vancomycin was used for bacteria *MRSA* and *S. aureus* and antibacterial gentamicin was used for *E. coli* and *P. aeroginosa* bacteria. The obtained results are given in Table 6. These results show that *P. aeroginosa*, *S. aureus*, *E. coli*, and *MRSA* bacteria show the most highest

Table 5. Biopolymers classification and their properties

Natural biopolymers		
Group	Name	Description
Polysaccharides	Cellulose and derivatives	Cellulose is a polysaccharide based on glucose. Cellulosic compounds are primarily used as wound dressings. Hydroxyalkyl celluloses and carboxymethyl celluloses (CMC) are used as matrices for drug delivery
	Alginates	The family of alginates is composed of a great number of polysaccharide type polymer chains that are composed of glucuronic and mannuronic acids. Alginates are primarily used as absorbing wound dressings. Because they easily form hydrogels by complexation with calcium ions. Alginates have been proposed as suitable materials for drug delivery and for cell entrapping
	Dextran	The family of dextrans is composed of polysaccharides based also on glucose but the sugar building blocks are linked together via α-1–6 bonds with some other secondary linkages leading to branching. They are used as isotonic plasma substitutes in order to regenerate the volume of body fluids after great loss of blood
	Chitosan	The family of chitosan-type polymers is composed of macromolecules of the glycosaminoglycan-type derived from chitin, an alternating copolymer of acetylated glucosamine and glucose. Chitosan polymers have inherent antibacterial activity which are obtained by deacetylation of chitin. Their properties depend very much on the degree of deacetylation. However, some members have been found hemotoxic, probably because of the presence of protonated amino groups along the chains. Whether chitosan polymers are totally biodegraded in an animal body is still not known
	Hyaluronic acid	Hyaluronic acid is a glycosaminoglycan found in conjunctive tissues of any vertebrate. The macromolecule is composed of N-acetyl glucosamine and glucuronic acid. At concentrations higher than 0.2 g/l, a gel is formed. Hyaluronic acid can also be cross-linked. The resulting compounds are used as temporary prostheses for sinovial fluid to treat arthrosis. Hyaluronic acid is rapidly biodegraded in a human body where it is normally regenerated
Bacterial polyesters (polyhydroxy alkanoates)	Poly (β-hydroxy butyrate), (PHB). Poly (β-hydroxy valerates), (PHV).	Some micro-organisms, especially bacteria, can synthesize aliphatic polyesters of the poly (β-hydroxy acid)-type, namely poly (β-hydroxyalkanoates) (PHA). This compound is used by the micro-organisms to store carbon and face a starving situation. Of course, this biopolymer is biodegradable and bioassimilable by microorganisms to recover the use of the stored carbon. From the viewpoint of biomedical applications, PHAs are biocompatible
Proteins	Collagen	Collagen is probably the most common protein in the field of biomaterials. Actually, 19 different kinds of collagen have been identified. Collagen is used in soft tissue and plastic surgery to fill up tissue defects. Nowadays, collagen is regarded suspiciously because of the risk of protein-associated disease transmission. Collagen can be cross-linked by the glutaraldehyde (GA) method and by using other cross-linkers
	Fibrin	Fibrin is primarily used to make the so-called biological glue that is used in different surgical applications to control bleeding and provide air and fluid tightness. Fibrin glue is based on two components derived from plasma. The thrombin and the fibrinogen components are isolated from plasma pools of healthy donors

(*Continues*)

Table 5. (Continued)

Synthetic biopolymers		
Group	Name	Description
Aliphatic polyesters	Poly (L-lactic acid) (PLLA) Poly (glycolic acid) (PGA) PLGA copolymers	Poly (glycolic acid) (PGA), poly (lactic acid) (PLA), and their copolymers are the most widely used synthetic degradable polymers in medicine. Alternative sutures composed of copolymers of glycolic and lactic acids are currently marketed under the trade names Vicryl and Polyglactin 910. Whereas PGA is highly crystalline, crystallinity is rapidly lost in PGA-PLA copolymers. Thus, copolymers tend to degrade more rapidly as compared to PGA and PLA
	Poly (β-malic acid)- copolymers (PMLA)	In order to make a water soluble polymer and to enlarge the bioresorbable polymer family on the basis of the same strategy, carboxylic acid-bearing polymers derived from malic acid, namely (poly(β-malic acid) or PMLA, were synthesized for the first time many years ago
	Polycaprolactone (PCL)	Poly (e-caprolactone) (PCL) is aliphatic polyester that has been intensively investigated as a biomaterial. The discovery that PCL can be degraded by microorganisms led to evaluation of PCL as a biodegradable packaging material. PCL has low glass transition temperature of -62°C, low melting temperature of $\sim 57^{\circ}$C and high thermal stability
Aliphatic polyamides	Poly(L-lysine citramide), (PLCA). Poly(L-lysine citramide- imide) (PLCAI)	Bioabsorbable water soluble polyamide-type polymers have been synthesized from citric acid and L-lysine. Various derivatives that are based on poly (L-lysine citramide), (PLCA), and poly (L-lysine citramide imide), (PLCAI) backbones have been synthesized. Drugs can be embedded within these carriers.
	Poly(amino serinate) (PAS)	This polyamine is a potential carrier for oligonucleotides and DNA fragments. It can make bioresorbable polyelectrolyte complexes where drugs could be easily entrapped for some time
Polydioxanone	Polydioxanone (PDS)	The poly (ether-ester) polydioxanone (PDS) is prepared by a ring-opening polymerization of p-dioxanone. PDS has gained increasing interest in the medical and pharmaceutical fields due to its degradation to low-toxicity monomers *in vivo*. PDS has a lower modulus than PLA or PGA, thus it became the first degradable polymer to be used to make a monofilament suture
Poly (ortho esters)	2,2-diethoxytetrahydrofuran 3,9-bis(ethylidene-2,4,8,10-tetraoxaspiro{5,5}-undecane) (DETOSU)	Poly (ortho esters) are a family of synthetic degradable polymers that have been under development for several years. Devices made of poly (ortho esters) can be formulated in such a way that the device undergoes "surface erosion". Because surface-eroding, slablike devices tend to release drugs embedded within the polymer at a constant rate, poly (ortho esters) appear to be particularly useful for controlled-release drug delivery
Polyanhydrides	Bis-(p-carboxyphenoxy propane) and sebacic acid derivaties (Trade name is Gliadel)	Polyanhydrides were first investigated in 1932 and considered in the 1950s for possible applications as textile fibers. A comprehensive evaluation of the toxicity of the polyanhydrides shows that, in general, the polyanhydrides have excellent *in vivo* biocompatibility. The most immediate applications of polyanhydrides are in the field of drug delivery
Polyphosphazenes	Aryloxyphosphazenes	Aryloxyphosphazenes and closely related derivatives have also been extensively studied. One such polymer can be cross-linked with dissolved cations such as calcium to form a hydrogel matrix because of its polyelectrolytic nature

activity in the cultivated environment while wound dressing materials without silver particles, before and after glycine washing, had no activity against bacteria. Samples containing Ag in absence of glycine are more effective against *S. aureus* and *MRSA* as compared to samples containing Ag and glycine. On the other hand, stoppage of the growth rate of *E. coli* and *P. aeroginosa* bacteria by Ag samples washed with glycine was better.

$$H_2N{-}COOH + AgNO_3 \leftrightarrow H_2N{-}COOAg + HNO_3, \quad (1)$$

$$H_2N{-}COOH + AgNO_3 \leftrightarrow AgHN{-}COOH + HNO_3, \quad (2)$$

Scheme 1. Ionic interactions between Ag ions and either $-NH_2$ or –COOH groups, or both, on gelatin chains. (Reprinted from Reference [116], Copyright (2008) Elsevier Ltd. All rights reserved.).

Proliferation, culture, and adhesion of cell assays

Duan *et al.*[119] carried out cell proliferation test on PCL nanofibers containing Ag loaded zirconium phosphate nanoparticles (nanoAgZ). They used primary human dermal fibroblasts (HDF) for seeding on the sterilized neat PCL and nanoAgZ loaded PCL nanofibers, placed in the 24-well tissue cultivating dishes. The nanofibers were remained in the cultivating environment for 1, 3, 5, and 7 days. Using methylthiazolydiphenyl-tetrazolium bromide (MTT) in order to stain the surface of these samples, colorimetric tests were carried out according to a procedure reported elsewhere.[120] In Fig. 7 proliferation information for the dermal fibroblast culturing *in vitro* environment is plotted. It is seen that by the addition of nanoAgZ particles to PCL electrospun nanofibers, the topography of the surface, which is one of the

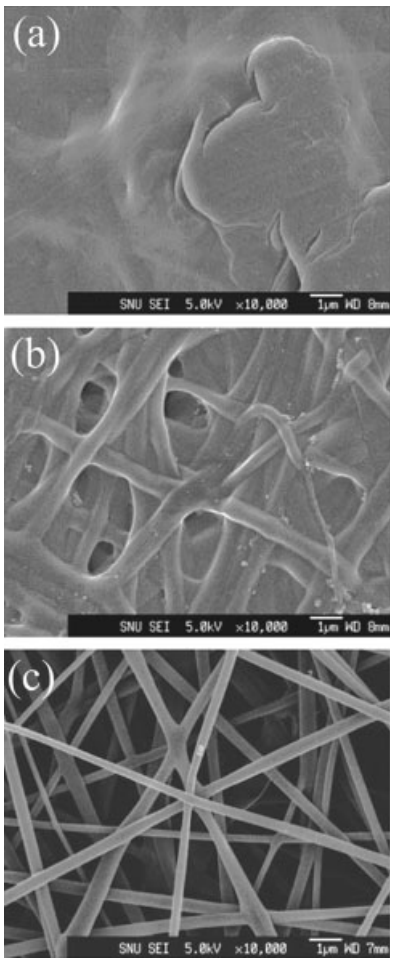


Figure 5. SEM images of (a) as-spun, (b) methanol treated, and (c) heat-treated PVA/$AgNO_3$ nanofibers after water immersion at 37.8°C for 5 hr. (Reprinted from Reference [115], Copyright (2006) Wiley Periodicals, Inc.). This figure is available in colour online at www.interscience.wiley.com/journal/pat

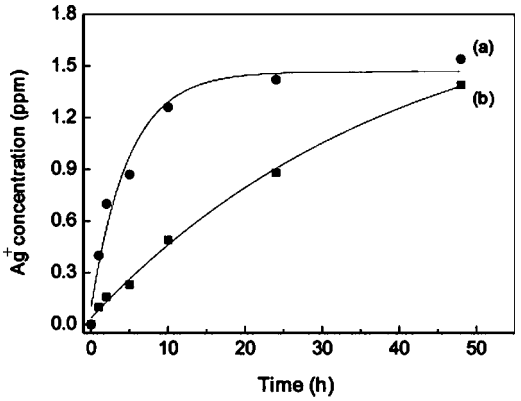


Figure 6. Release profiles of Ag ions from (a) the PVA/$AgNO_3$ nanofibers after heat treatment and (b) the PVA/$AgNO_3$ nanofibers after heat treatment and subsequent UV irradiation. (Reprinted from Reference [115], Copyright (2006) Wiley Periodicals, Inc.).

effective parameters in adhesion and propagation of the cells, changes as a result of proliferation phase in the cell tissues. Because of this change the PCL nanofibers containing nanoAgZ have higher rate of cell proliferation than the neat samples. Zhou *et al.*[121] studied the adhesion extent and growth of mouse fibroblasts (L929) on the blend of crosslinked nanofibers of carboxyethyl chitosan (CECS) and PVA (CECS/PVA). After sterilizing the nanofibers with phosphate-buffered saline (PBS), the CECS/PVA mats were placed in 24-well culture plates containing mouse fibroblasts with 1.5×10^4 cell/ml spreading. Fortyeight hours later the produced cell structure were studied by SEM. Prior to the microscopic studies, the samples were dehydrated with ethanol and dried in air. Figure 8 (a–d) shows the SEM micrographs of the crosslinked nanofibers made from CECS/PVA (50/50) blend. These images were used to study the adhesion behavior, rate of propagation and interaction of fibroblasts mouse cells (L929). Due to a high surface area to volume ratio of nanofibers, tendency of cells for adhesion to the surface of nanofibers, reproduction and growth along the nanofibers are very high leading to epithelialization in the cultivation environment.

Wound healing and histology

Along with *in vitro* situations, the *in vivo* environment is considered to be very important as far as wound dressing properties on healing and qualitative observations are concerned. Usually, wound healing tests are carried out on an animal model, such as Sprague-Dawley (SD) rats.[122] In this test, a wound with sufficient thickness and 2 cm × 2 cm surface area is cut from the back of the SD rat and then the wound dressing material under investigation is placed on the wound to cover it completely. After the necessary predetermined time, the reduction of wound surface is recorded. Chen *et al.*[123] used nanofibrous membranes of collagen/CS for these investigations. For two other types of wound dressing materials, namely gauze and commercial collagen sponge, were also used. The performance of all these three wound dressing materials was investigated after they were placed for 3, 7, 10, 14, and 17 days on the wound. Figure 9 shows the healing rates of these three wound dressing materials which were placed on similar wounds produced on the back of SD rats. The rate of wound healing, i.e. the increase in the

Table 6. Antibacterial activity of the gelatin electrospun nanofibrous mats in presence and absence of $AgNO_3$, after having been crosslinked with GA for 1–3 h with or without washing with glycine, against some usual bacteria on burned wounds (from Reference [116])

	Antibacterial activity in terms of disc diffusion method reported as inhibition zone diameter (cm)/sample diameter (cm)			
Sample types	*P. aeroginosa* 27853	*S. aureus* 25023	*E. coli* 25922	*MRSA* 20627
Neat gelatin nanofibrous mats				
1 h-crosslinking without glycine washing	1.60/1.60	1.50/1.50	1.50/1.50	1.50/1.50
1 h-crosslinking with glycine washing	1.60/1.60	1.50/1.50	1.50/1.50	1.50/1.50
3 h-crosslinking without glycine washing	1.65/1.65	1.50/1.50	1.50/1.50	1.50/1.50
3 h-crosslinking with glycine washing	1.50/1.50	1.50/1.50	1.50/1.50	1.60/1.60
$AgNO_3$ containing gelatin nanofibrous mats				
1 h-crosslinking without glycine washing	2.00/1.50	2.20/1.60	2.40/1.50	1.87/1.50
1 h-crosslinking with glycine washing	2.07/1.60	2.43/1.60	2.43/1.50	2.03/1.60
3 h-crosslinking without glycine washing	1.77/1.50	2.37/1.60	2.43/1.60	2.17/1.60
3 h-crosslinking with glycine washing	2.20/1.60	2.47/1.50	2.27/1.60	1.93/1.60

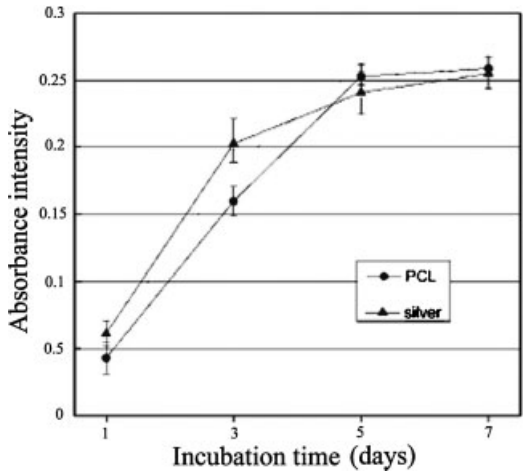


Figure 7. HDFs proliferation on neat PCL nanofibers, and nanoAgZ-containing composite fibers. (Reprinted from Reference [119], Copyright (2007) Wiley Periodicals, Inc.).

rate of reduction in the wound surface with respect to time, is much higher for nanofibrous collagen/CS than those of the gauze and commercial collagen sponge.

Use of histological methods for qualitative observations of wound tissues and their heating rate from inflammatory to granulating phases are very important.[124] Khil *et al.*[125] used histology test for the investigation of different phases of wound healing. Two different wound dressing materials were used; one was electrospun PU nanofibers and the other was commercial Tegaderm™. 1 cm × 1 cm wounds were cut on the back of male adult guinea pigs. Then the wounds were completely covered with these wound dressing materials. The wound dressings were changed every 3 days. The process of wound healing after 3, 6, and 15 days was recorded for histology test. For sample preparation, at predetermined time intervals, sections of the wound tissues were dissected and immersed in a 10% phosphate-buffered formalin (PBF) solution and then embedded in paraplast. About 5–6 μm of these embedded samples were cut by a rotary microtome and stained with hematoxylin and eosin (HE). Microscopic studies were carried out on the prepared samples using a Leica DMRBE microscope. Figure 10 (a–f) shows histological images of these wounds after 3, 6, and 15 days. Figure 10 (a and b) shows the wound status after the third day post operative for two groups of wounds covered by Tegaderm™ and PU nanofibers membrane, respectively. As can be seen from Fig. 10 (a), the wounds have severe percolations of inflammatory phase cells with a thick scab. In Fig. 10 (b) these percolations of inflammatory phase cells are more moderate with a thin scab. However, as can be seen in the images there are no signs of epithelialization. Again after 6 days post wounding, the wounds were carefully inspected. Figure 10 (c and d) shows the wounds covered by the PU nanofibers membranes. It is observed that the wounds have granulation tissues along with cells rich from inflammation phase and neovascularization. Some cells rich from collagen were also seen. Finally after 15 days inspections were made from Tegaderm™ (Fig. 10 (e)) and PU membranes (Fig. 10 (f)) wound dressing materials. The epithelialization process is seen in both images, but still some traces of inflammation phase cells for the Tegaderm™ group can be observed. For PU nanofibers membranes, the rate of epithelialization process is higher and dermis is formed.

Wettability, water-uptake capacity, and water vapor permeability (WVP)

Wettability or fluid affinity is a very important parameter for the studies on the rate of fluid absorption of a wound dressing material especially for exudates wounds. As a result of fluid absorption, rehydration of necrotic tissues of a wound is facilitated, and hence autolytic debridement of the wound is promoted.[126]

Water-uptake or fluid retention is a gravimetric test for the determination of the maximum amount of fluid absorption and fluid retention on the wound for a wound dressing material. The fluid retention of a wound determines the performance of a wound bandage under very severe conditions in an *in vivo* environment. Especially, the weight increase of a wound

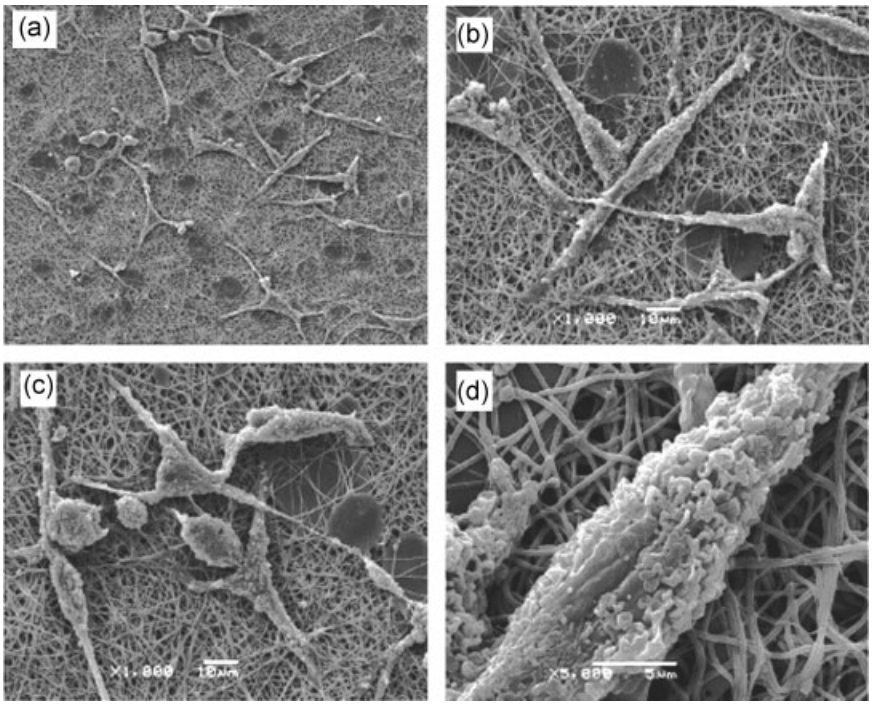


Figure 8. SEM images of L929 cell seeded on nanofibrous membrane of CECS/PVA (50:50) after 48 h culture. (Reprinted from Reference [121], Copyright (2008) American Chemical Society). This figure is available in colour online at www.interscience.wiley.com/journal/pat

dressing material after fluid absorption and swelling during a defined time is taken as an indication of water-uptake and retention. Though the above tests represent a meaningful means of characterizing different wound dressing materials, they are mainly based on the structure of the base polymer (hydrocolloid, alginate, or hydrogel) rather than the performance of the wound dressing materials. As a result, these tests have some limitations in predicting a dressing's performance in *in vivo* environments.

In WVP or moisture penetration tests, usually wound dressing materials such as hydrocolloids in a sheet or film form are

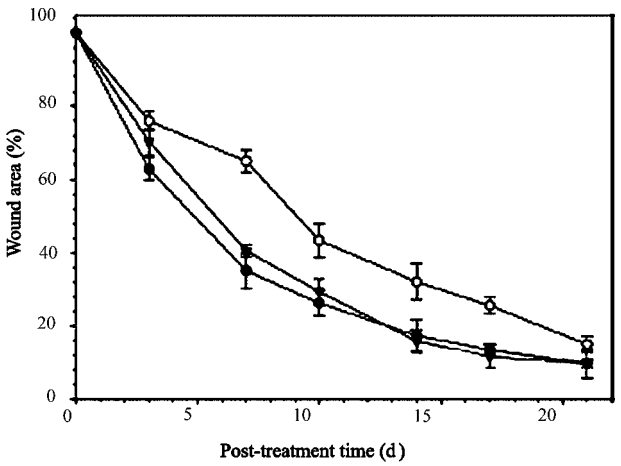


Figure 9. Wound healing tests of (○) gauze, (▼) commercial collagen sponge, and (●) collagen/chitosan electrospun membranes. (Reprinted from Reference [123], Copyright (2007) Elsevier B.V. All rights reserved.).

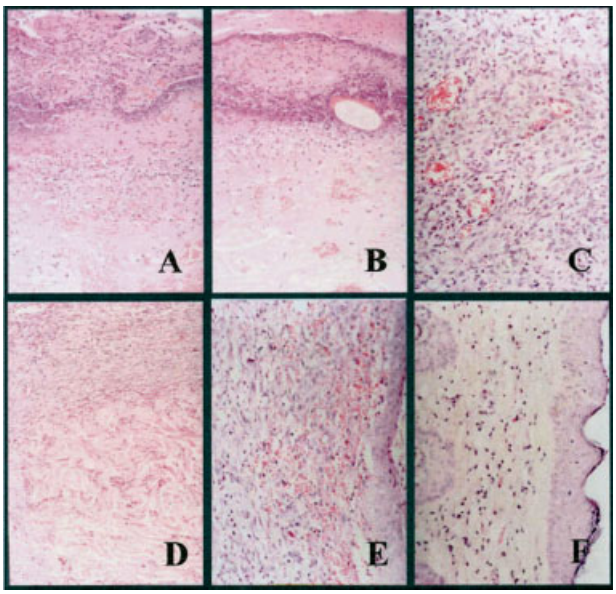


Figure 10. Histological findings of wound (a) at 3rd day post wounding of the control group; (b) at 3rd day post wounding, polyurethane-membrane group; (c), (d) at 6th day post wounding of the polyurethane-membrane-treated group; (e) at 15th day post wounding of the control group; (f) at 15th day post wounding of the polyurethane-membrane-treated group. (Reprinted from Reference[125], Copyright (2003) Wiley Periodicals, Inc.).

used.[127] The WVP is officially referred to as the Moisture Vapor Transmission Rate (MVTR) of permeable film dressing in the British Pharmacopoeia[128] and it is a measure of the amount of water vapor lost through a dressing to the atmosphere from the wound bed over defined time periods.

Xu *et al.*[67] prepared wound dressing materials using CS/HA and studied the effect of HA concentration on the wettability, water-uptake, and WVP. In wettability test, the static contact angles of the film samples are determined by contact angle measurements. For determination of water-uptake capacity, the hybrid CS/HA films were immersed in distilled water at room temperature and the weight of wet films after 24 h were measured (W). The water-uptake of these samples was calculated as a ratio of weight increase ($W-W_0$) to the initial value (W_0). They also carried out WVP test for the hybrid CS/HA films by a modified ASTM standard test.[129,130] Briefly, the films were fixed at the circular opening of a permeation bottle (3 cm diameter and 5 cm height), which were stored in desiccators at a relative humidity of 40%. Then the weight of the bottle with water was measured at different time intervals. The WVP of a hybrid film is defined as

$$\mathrm{WVP} = \frac{-\Delta W}{A \times \Delta t} \quad (1)$$

where, ΔW is the change in the amount of the water weight, A is the exposure area of the film and Δt is the exposure time.

Because of the great importance of water loss control for an open and wet wound, controlling of this factor is a very critical property for a wound dressing material. To determine this factor the water-uptake and WVP tests during the wound-healing period in an environment containing PBS and an *in vitro* environment were carried out. After placing neat CS and CS/HA films under the above conditions, it was found that by adding HA the water-uptake of the films increases and the highest values were obtained for CS/HA films in the ratio of 50:50 (Fig. 11). As a result, it can be concluded that the rate of water-uptake has a direct relation with the hydrophilic properties of the films. This is confirmed by wettability test and contact angle measurements (Table 7). Usually, for normal skin, WVP is about 0.85 mg cm^{-2} h^{-1} and for an injured skin it is 1.16–21.41 mg cm^{-2} h^{-1}. A wound dressing material must have a suitable WVP in order to prevent additional dehydration reaction and also exudates build up. Therefore, a wound bandage with WVP in the range of 8.33–10.42 mg cm^{-2} h^{-1} is suggested.[131] Figure 12 shows weight variations of permeation bottle as a function of time in 40% relative humidity (RH) and 24 ± 1°C conditions. The corresponding WVP values of different kinds of films are calculated and summarized in Table 8. As compared to the blank control sample (without film), all the films show reduced WVP values. Because of the high water absorption potential and HA retention, HA incorporation can be very effective in the reduction of WVP of a film.

Differential scanning calorimetry (DSC)

Zhou *et al.*[121] studied thermal analysis of electrospun carboxyethyl chitosan (CECS)/PVA fibers using a DSC technique. Figure 13 shows the DSC thermograms for CECS, PVA and CECS/PVA nanofibers. As can be seen from this figure, pure PVA samples exhibits a large and sharp endothermic peak at 194°C. As the PVA content in the CECS/PVA electrospun nanofibers is reduced, the maximum related to crystalline melt gets smaller and broader. This is due to reduced crystallinity which in turn is related to the higher amounts of CECS in the nanofiber composition. On the other hand, because of the high rate of solidification in the electrospinning process the elongated chains of CECS/PVA nanofibers do not have a chance for crystallization.

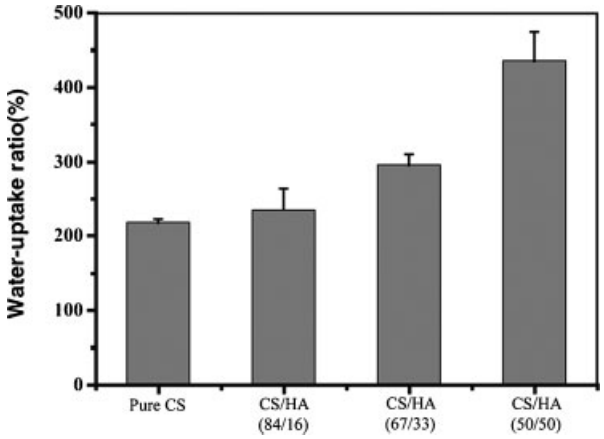


Figure 11. The effect of HA ratio on the water-uptake ability. (Reprinted from Reference [67], Copyright (2007) John Wiley & Sons, Ltd.).

Thermogravimetric analysis (TGA)

Rujitanaroj *et al.*[116] studied the heat resistance of gelatin electrospun and crosslinked (1–3 h) nanofiber mats with and

Table 7. Water contact angle of the chitosan (CS)/HA composite films (from Reference [67])

Samples	Pure CS	CS84/HA16	CS67/HA33	CS50/HA50
Water contact angles	88.1 ± 1.5	86.2 ± 0.3	84.9 ± 0.9	73.8 ± 1.6

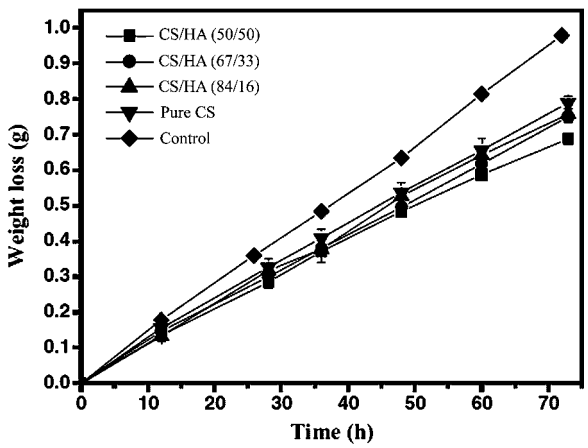


Figure 12. The weight loss of permeation bottle as a function of incubation time. The RH was controlled at 40%. (Reprinted from Reference [67], Copyright (2007) John Wiley & Sons, Ltd.).

Table 8. Water vapor permeability of the CS/HA composite films (from ref. [67])

Samples	Blank	Pure CS	CS84/ HA16	CS67/ HA33	CS50/ HA50
WVP ($mg\,cm^{-2}\,hr^{-1}$) 40% RH	11.37	9.07	8.86	8.58	8.01

without Ag by a TGA technique. The TGA thermograms are presented in Fig. 14. In all the TGA thermograms a two-stage weight loss is evident. The first stage of weight loss is due to the moisture present in the samples and the second one is because of gelatin degradation. The moisture loss for these samples occurs over a temperature ranges of ~25°C to ~90°C to ~150°C with moisture content of ~9 to ~14%, with the values for the uncrosslinked ones being the greatest (i.e. ~14% for the pure gelatin fiber mat and ~12% for the gelatin fiber mat containing $AgNO_3$). It is also seen that crosslinking of samples extends the temperature range of the weight loss to about 150°C and at the same time the weight loss due to moisture content drops to lower values. This indicates that the crosslinked samples have higher moisture retention ability. The onset of thermal degradation temperature ($T_{d,\ onset}$) for uncrosslinked pure gelatin fibers is about 269°C, while it is about 206°C for the uncrosslinked samples containing Ag; Ag promotes the degradation process of the gelatin electrospun nanofiber mats to some extent. For samples without Ag which are crosslinked for 1 and 3 hr, the $T_{d,\ onset}$ is 350°C and 354°C, respectively, while the samples containing Ag and crosslinked for the similar periods show the $T_{d,\ onset}$ at 326°C and 360°C, respectively. Consequently, crosslinked samples have relatively higher char content as compared to the uncrosslinked ones. These results indicate that the crosslinking increases the thermal stability of the gelatin nanofiber mats.

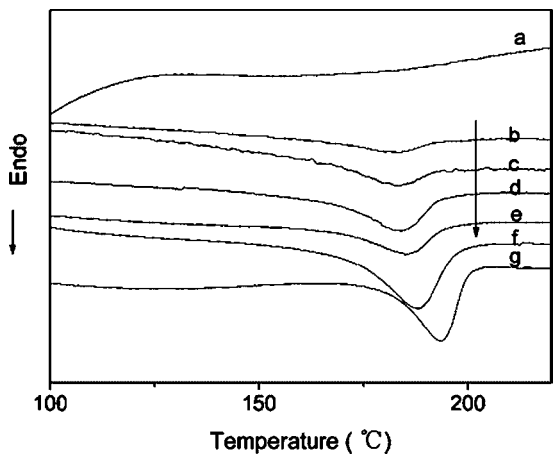


Figure 13. DSC curves of CECS, PVA, and the nanofibrous membranes with different CECS/PVA weight ratio: (a) CECS; (b) 50/50; (c) 40/60; (d) 30/70; (e) 20/80; (f) 10/90; (g) PVA. (Reprinted from Reference [121], Copyright (2008) American Chemical Society).

X-ray analysis

A quantitative determination of nanoparticle distribution is possible by X-ray diffraction (XRD). Hong[117] studied the silver nanoparticle distribution in PVA nanofiber mats before and after thermal treatment. The related XRD patterns are shown in Figure 15. Both samples show the original peak with $2\theta = 20^{\circ}$ which is related to the 101 plane of crystalline structure of PVA.[132] The intensity of the peak for PVA film with thermal treatment is higher and shows a shift towards higher angles as compared to the PVA film without thermal treatment. Also, for the PVA films with thermal treatment, a new peak at $2\theta = 12^{\circ}$ and another peak at $2\theta = 23^{\circ}$ are observable which can be related to changes in crystallization of PVA as a result of the thermal treatment.

In the energy dispersive X-ray (EDX) test, the traces of elements in polymers can be detected. Duan *et al.*[119] studied the presence of elements in PCL nanofibers containing nanoAgZ. Figure 16 shows EDX spectrum and the conductive EDX mapping. EDX curves from nanoAgZ particles show the presence of silver, phosphorus, and zirconium in PCL fibers which contain nanoAgZ particles. Also, EDX curve for silver has a uniform distribution in the samples.

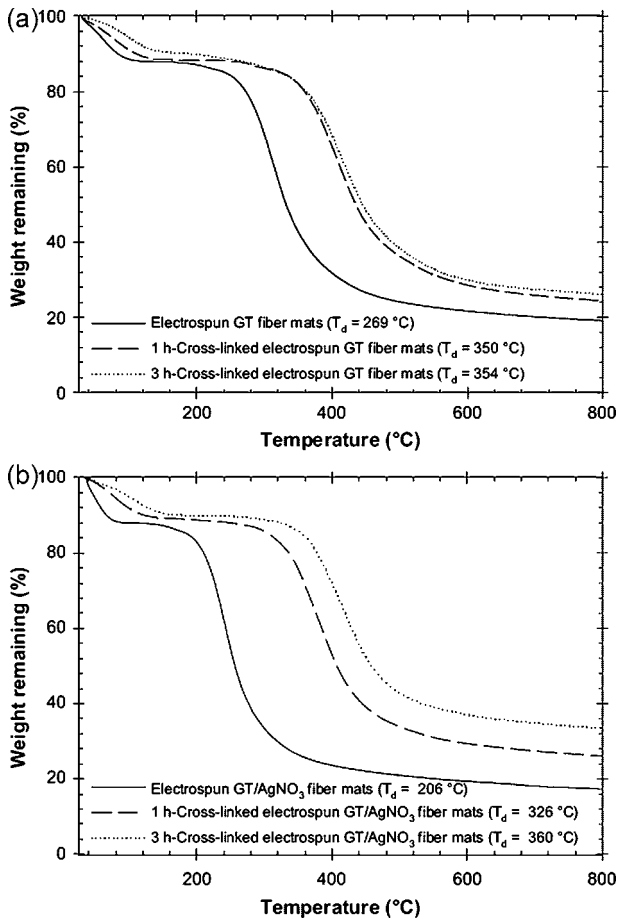


Figure 14. Thermogravimetric spectra of the electrospun fiber mats from (a) the base gelatin solution and (b) the $AgNO_3$-containing gelatin solution aged for 12 h, after having been cross-linked with moist vapor of glutaraldehyde for 1–3 h. (Reprinted from Reference [116], Copyright (2008) Elsevier Ltd. All rights reserved.).

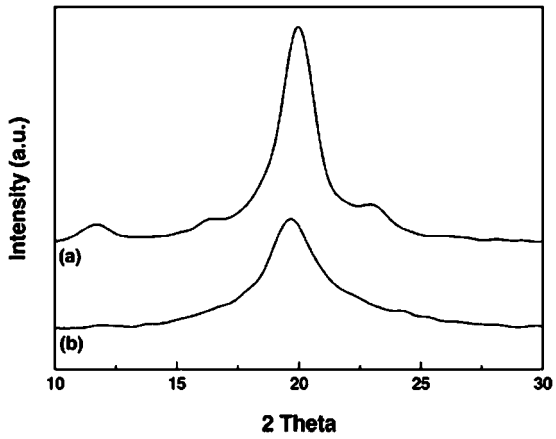


Figure 15. XRD patterns of the pure PVA films; (a) heat treated at 155°C for 3 min, (b) no heat treatment. (Reprinted from Reference [117], Copyright (2006) Society of Plastics Engineers).

The surface layer with a depth of 3–5 nm from the electrospun mats made from CS/PLA and quaternized CS derived (QCS, Scheme 2) *N*, *N*, *N*-trimethyl chitosan iodide blended PLA (QCS/PLA) nanofiber was analyzed by X-ray photoelectron spectroscopy (XPS).[133] Figure 17 shows the XPS spectra of these electrospun mats in the presence of the following solvents respectively: dichloromethane (DCM), triflouro acetic acid (TFA), dimethyl sulfoxide (DMSO), and dimethyl formamide (DMF). In the case of electrospun CS/PLA nanofiber mats in TFA/DCM (70/30 vol%), four elements *viz*. carbon (285 eV, C_{1s}), oxygen (532.5 eV, O_{1s}), nitrogen (399.6 and 401.6 eV, N_{1s}) and fluorine (687.9 eV, F_{1s}) were characterized which are shown in Fig. 17 (a–d), respectively. The XPS curves for QCS/PLA nanofiber mats in DMF/DMSO (60/40 vol%) confirmed the presence of the following elements: carbon (285 eV, C_{1s}), oxygen (532.3 eV, O_{1s}), nitrogen (400 and 402.6 eV, N_{1s}), and iodine (618.5 and 630 eV, I_{3d}). These elements are shown in Fig. 17 (e–h), respectively. With respect to the XPS curves related to the carbon (285 eV, C_{1s}) of CS/PLA nanofibers (Fig. 17 (a)), four peaks corresponding to $-C-H$ or $-C-C$ from PLA and also, $-C-NH_2$ from CS in binding energy 285 eV (45%), $-C-O$, $-C-OH$ and $-C-N-C=O$ from CS and also, $-C-O$ from PLA with binding energy 286.8 eV

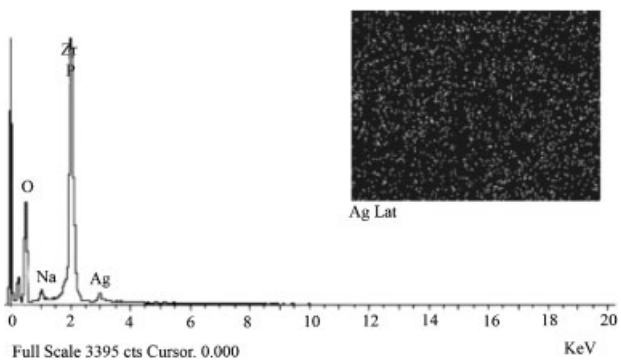
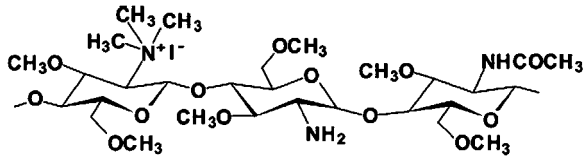


Figure 16. EDX spectrum and EDX mapping of nanoAgZ containing composite PCL fibers. (Reprinted from Reference [119], Copyright (2007) Wiley Periodicals, Inc.).



Scheme 2. Quaternized chitosan (QCS) chain sequence. (Reprinted from Reference [133], Copyright (2009) WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim).

(35%), $-O-C-O$ and $-N-C=O$ from CS with binding energy 288.4 eV (8%) and finally, $-O-C=O$ from PLA with binding energy 289.1 eV (12%) are evident, which have good correlation with the information obtained from the literature.[134,135] For the rest of elements there is a similar behavior which can be seen in Table 9. Also, the binding energy of similar elements in QCS/PLA and CS/PLA nanofibers can be compared with each other.

Mechanical properties

Tensile strength measurements were used for characterization and controlling the performance of pharmaceutical films and packaging materials.[136] A general knowledge of the mechanical properties for wound dressing materials is very important because these materials need certain tensile strength, sustainability, flexibility, bending, and elastic properties. Additionally, replacement of a wound dressing material must be carried out easily without trauma or any possible damage to new epithelial tissues.[137] These desired properties and a reasonable balance between flexibility and hardness can be determined by tensile test. During this test, a sample (usually dumbbell shaped) is placed under elongation up to ultimate break.[138] The usual mechanical properties which can be determined by this test are elongation at break, tensile strength at yield or at break, elastic modulus and compression test.

CONCLUSIONS

In the present review, new and necessary information about wounds of acute type, and their healing stages were discussed. In the classification of the wounds, two types of acute and chronic wounds are considered. In acute wounds, physical, chemical, and thermal parameters are involved, while the chronic wounds are mainly caused by some diseases, such as diabetes etc. In the healing process of a wound the following five phases were explained: hemostasis, inflammation, migration, proliferation, and remodeling. Also the role of fibrinogen in blood clotting and phagocytes in the epithelialization process was discussed. In the next section of this paper, conventional and modern wound dressing materials used for rapid healing and less infection were reviewed. In a general classification of wounds, the wound dressing materials are divided to passive, interactive, and bioactive types. Technological progress, such as wound dressing materials containing a nanostructure material, has led to new developments in this field. Electrospinning is a process which can be used for the production of biopolymeric nanofibers containing different ingredients for the control of the surface and healing process of

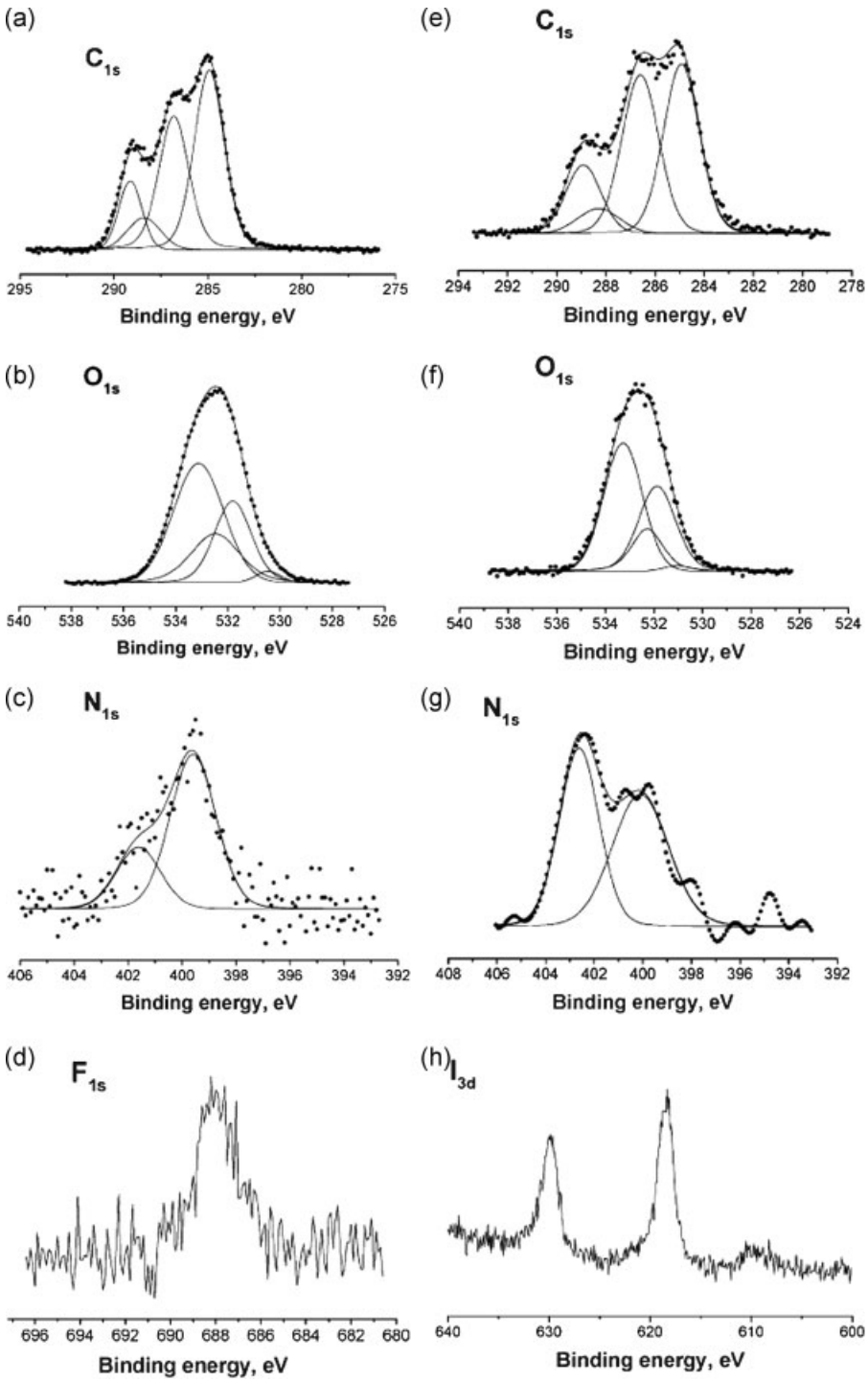


Figure 17. XPS peak fittings for electrospun CS/PLA mat (CS/PLA (50:50 wt%)) [C_{1s} (a), O_{1s} (b), N_{1s} (c), and F_{1s} (d)] and for electrospun QCS/PLA mat (QCS/PLA (30:70 wt%)) [C_{1s} (e), O_{1s} (f), N_{1s} (g), and I_{3d} (h)]. (Reprinted from Reference [133], Copyright (2009) WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim).

a wound. Electrospun polymeric membranes are the most advanced and efficient wound dressing materials compared to other modern bandages such as hydrocolloids, hydrogels, and alginates. These membranes, due to their very high surface area to volume ratio, have extraordinary abilities such as controlled release of drugs, cultivation in the physiological environment of the cells, a very high increase in the reproduction and growth of live cells, etc. All these characteristics have highly extended their applications on different wounds as compared to traditional wound dressing materials. In the next stage of this work, standard tests which are directly related to wound dressing materials were explained. The results of these tests can be used

Table 9. XPS peak fitting information for electrospun CS/PLA (50:50 wt%) and QCS/PLA (30:70 wt%) (from ref. [133])

	CS/PLA nanofibrous mats			QCS/PLA nanofibrous mats		
Element	Bindings	Binding energy (eV)	Intensity (%)	Bindings	Binding energy (eV)	Intensity (%)
C_{1s}	$-C-H$ or $-C-C$ of PLA $-C-NH_2$ of CS	285	45	$-C-H$ or $-C-C-$ of PLA $-C-NH_2$ of QCS	285	39
	$-C-O$, $-C-OH$ and $-C-N-C=O$ of CS $-C-O$ of PLA	286.8	35	$-C-O$, $-C-OH$, $-C-OCH_3$ and $-C-N-C=O$ of QCS $-C-O$ of PLA	286.6	38
	$-O-C-O$ and $-N-C=O$ of CS	288.4	8	$-O-C-O$ and $-N-C=O$ of QCS	288.3	7
	$-O-C=O$ of PLA	289.1	12	$-O-C=O$ of PLA	288.9	16
O_{1s}	$-C-OH$ and $-O-C-O$ of CS	532.5	—	—	—	—
	$-O-C$ of PLA	533.1	—	—	—	—
	$-O=C$ of PLA	531.8	—	—	—	—
	$-N-C=O$ of CS	530.5	—	—	—	—
N_{1s}	$-N-C=O$ and $-NH_2$	399.6	72	$-N-C=O$ and $-NH_2$	400	51
	$-NH_3^+$	401.6	28	$-N^+(CH_3)_3$	402.6	49
F_{1s}	Salts formation by reaction of TFA with amino groups of CS	687.9	—	—	—	—
I_{3d}	—	—	—	$I_{3d5/2}$	618.5	60
	—	—	—	$I_{3d3/2}$	630	40

for the evaluation of antibacterial wound dressings in contact with common bacteria on the surface of the burned wounds such as *E. coli*, *P. aeroginosa* etc. Also, proliferation tests of cells, culture, and adhesion of cell in the cultivating environment could be elucidated. In the next section of this paper, quantitative observations are made by histological images showing the healing process of a wound covered with different wound dressing materials. Also, the methods for determination of WVP, which is a highly important factor in the moisture control and keeping the wound wet under the nanofibrous wound dressing materials, were discussed. The results showed that the rate of moisture and oxygen release from the surface of a wound must be in the range of 8–10 mg/(cm^2 hr). Finally, various tests which are carried out depending on the use of a wound dressing material in different environments were discussed. The tests such as DSC, used for determination of crystallization rate of nanofibers and their flexibility, TGA, which is done for measurements of heat resistance of crosslinked nanofibers, and X-ray diffraction patterns for study of dispersion state of nanoparticles in electrospun nanofiber mats were explained. Ultimately, the mechanical properties such as tensile strength, elastic modulus, and elongation at break were discussed briefly.

This paper provides detailed basic information about wound dressing materials and summarizes the latest developments in this field. The results show that the combination of nanotechnology with electrospinning process can open up new doors for development of the next generation of wound dressing materials with highly desirable properties.

REFERENCES

[1] G. Majno, *The Healing Hand: Man and Wound in the Ancient World*. Harvard University Press, Cambridge, **1975**.
[2] S. Thomas, *Wound Management and Dressing*. Pharmaceutical Press, London, **1990**.
[3] J. Doshi, D. H. Reneker, *J. Electrostatics* **1995**, *35*, 151.
[4] A. Formhals, US patent, 1975504, **1934**.
[5] S. R. Bhattarai, N. Bhattarai, H. K. Yi, P. H. Hwang, D. I. Cha, H. Y. Kim, *Biomaterials* **2004**, *25*, 2595.
[6] G. S. Lazarus, D. M. Cooper, D. R. Knighton, D. J. Margolis, E. R. Percoraro, G. Rodeheaver, M. C. Robson, *Arch. Dermatol* **1994**, *130*, 489.
[7] J. N. Percival, *Surgery* **2002**, *20*, 114.
[8] K. Moore, R. McCallion, R. J. Searle, M. C. Stacey, K. G. Harding, *Int. Wound J.* **2006**, *3*, 89.
[9] K. G. Harding, H. L. Morris, G. K. Patel, *Brit. Med. J.* **2002**, *324*, 160.
[10] M. C. Ferreira, P. Tuma, V. F. Carvalho, F. Kamamoto, *Clinics* **2006**, *61*, 571.
[11] J. H. Musset, A. J. Winfield, *Wound Management, Stoma, and Incontinence Products*, (Eds. A. J. Winfield R. M. E Richards), Churchill Livingstone, London, **1998**, pp. 176–187.
[12] F. Strodtbeck, *New Inf. Nurs. Rev.* **2001**, *1*, 43.
[13] R. A. F. Clark, *The Molecular and Cellular Biology of Wound Repair*. Plenum, New York, **1996**.
[14] L. Russell, *Br. J. Nurs.* **1999**, *9*, 10.
[15] B. A. Mast, *The Skin in Wound Healing: Biomedical and Clinical Aspects*, (Eds. I. K. Choen R. F. Diegelmann W. Lindblad), Saunders, Philadelphia, **1999**, pp. 344–355.
[16] J. S. Boateng, K. H. Matthews, H. N. E. Stevens, G. M. Eccleston, *J. Pharm. Sci.* **2008**, *97*, 2892.
[17] B. D. Ratner, A. S. Hoffman, F. J. Schoen, J. E. Lemons, *Biomaterials Science: An Introduction to Materials in Medicine*. Academic Press, California, **1996**.
[18] P. Martin, *Science* **1997**, *276*, 75.
[19] T. K. Hunt, *Wound Healing and Wound Infection: Theory and Surgical Practice*. Appleton-Century-Crofts, New York, **1980**.
[20] K. Inngjerdingen, C. S. Nergard, D. Diallo, P. P. Mounkoro, B. S. Paulsen, *J. Ethnopharmacol* **2004**, *92*, 233.
[21] A. Y. Mensah, P. J. Houghton, R. A. Dickson, T. C. Fleischer, M. Heinrich, P. Bremner, *Phytother. Res.* **2006**, *20*, 941.
[22] S. K. Purner, M. Babu, *Burns* **2000**, *26*, 54.
[23] L. Van Rijswijk, *J. Wound Care* **2006**, *15*, 11.
[24] S. Thomas, *Wound and Wound healing in: Wound Management and Dressings*. Pharmaceutical Press, London, **2004**.
[25] G. D. Winter, *Nature* **1962**, *193*, 294.
[26] C. D. Hinman, H. Mainbach, *Nature* **1963**, *200*, 377.
[27] D. Queen, H. Orsted, H. Sanada, G. Sussman, *Int. Wound J.* **2004**, *1*, 59.
[28] A. F. Falabella, *Dermatol. Ther.* **2006**, *19*, 317.
[29] V. J. Jones, *Int. Wound J.* **2006**, *3*, 79.
[30] A. M. Jones, L. San Miguel, *J. Wound Care* **2006**, *15*, 65.
[31] M. J. Hoekstra, M. H. Hermans, C. D. Richters, R. P. Dutrieux, *J. Wound Care* **2002**, *11*, 113.
[32] S. Thomas, P. Loveless, *Pharm. J.* **1988**, *240*, 785.
[33] R. E. S. Maricia, M. C. R. Castro, *Clin. Dermatol.* **2002**, *20*, 715.
[34] D. A. Morgan, *Pharm. J.* **1999**, *263*, 820.
[35] A. Moody, *Br. J. Comm. Nurs.* **2006**, *11*, S12.
[36] J. Fletcher, *Nurs. Times* **2005**, *101*, 51.
[37] C. Dealey, *Br. J. Nurs.* **1993**, *2*, 358.
[38] A. Heenan, *World Wide Wounds* **1998**, *1*, 1.
[39] S. Thomas, *J. Wound Care* **1992**, *1*, 27.
[40] S. Thomas, *J. Wound Care* **2000**, *9*, 56.
[41] C. K. Kuo, P. X. S. Ma, *Biomaterials* **2001**, *22*, 511.
[42] S. Ichioka, K. Harii, M. Nakahara, Y. Sato, *Scand J. Plast. Reconstr. Surg. Hand Surg.* **1998**, *32*, 311.
[43] G. Blaine, *Ann. Surg.* **1947**, *125*, 102.
[44] J. M. N. Ramshaw, J. A. Werkmeister, V. Glatteur, *Biotechnol. Rev.* **1995**, *13*, 336.
[45] S. H. Liu, R. S. Yang, R. Al-Shaikh, J. M. Lane, *Clin. Orthop. Res.* **1995**, *318*, 265.
[46] S. Meaume, D. Vallet, M. N. Morere, L. Teot, *J. Wound Care* **2005**, *14*, 411.
[47] H. J. T. Rutten, P. H. A. Nijhuis, *Eur. J. Surg.* **1997**, *163*, 31.
[48] Y. Sawada, M. Ara, T. Yotsuyanagi, K. Sone, *Burns* **1990**, *16*, 347.
[49] Y. Sawada, O. Tadashi, K. Masazumi, S. Kazunobu, O. Koichi, J. Sasaki, *Br. J. Plast. Surg.* **1994**, *47*, 158.
[50] S. Ganlanduik, W. R. Wrigtson, S. Young, S. Myers, H. C. Polk, *Am. J. Surg.* **1997**, *63*, 831.
[51] T. R. S. Kumar, M. V. Bai, L. K. Krishnan, *Biologicals* **2004**, *32*, 49.
[52] A. Komarcevic, *Med. Pregl.* **2000**, *53*, 363.
[53] H. H. Steenfos, *J. Plast. Reconstr. Surg.* **1994**, *28*, 95.
[54] D. G. Greenhalgh, *J. Trauma Inj. Infect. Crit. Care* **1996**, *41*, 159.
[55] E. Wallace, *Br. J. Nurs.* **1994**, *3*, 662.
[56] M. Linda, *Nutritional Biochemistry and Metabolism with Clinical Applications*. Appleton & Lange, East Norwalk, **1991**.
[57] R. P. da Rocha, D. P. Lucio, T. D. L. Souza, S. T. Pereira, G. J. M. Fernandes, *Aesthet. Plast. Surg.* **2002**, *26*, 197.
[58] H. Osieki, *Nutrients in Profile*. Bioconcepts, Queensland, **1995**.
[59] G. Kirschmann, J. Kirschmann, *Nutrition Almanac*. McGraw-Hill, New York, **1996**.
[60] M. Ignatova, N. Manolova, I. Rashkov, *Eur. Polym. J.* **2007**, *43*, 1609.
[61] L. G. Ovington, *J. Clin. Dermatol.* **2007**, *25*, 33.
[62] G. Luo, J. Tang, W. He, J. Wu, B. Ma, X. Wang, X. Chen, S. Yi, X. Zhang, X. Li, *et al. Wound Rep. Reg.* **2008**, *16*, 800.
[63] M. Kokabi, M. Sirousazar, Z. Muhammad Hassan, *Eur. Polym. J.* **2007**, *43*, 773.
[64] B. Baskovich, E. M. Sampson, G. S. Schultz, L. K. Parnell, *Int. Wound J.* **2008**, *5*, 543.
[65] A. Gupta, R. Kumar, N. K. Upadhyay, P. Surekha, P. K. Roy, *J. Appl. Polym. Sci.* **2009**, *111*, 1400.
[66] R. Singh, M. P. Chacharkar, A. K. Mathur, *Int. Wound J.* **2008**, *5*, 7.
[67] H. Xu, L. Ma, H. Shi, C. Gao, C. Han, *Polym. Adv. Technol* **2007**, *18*, 869.
[68] M. Wang, L. Xu, H. Hu, M. Zhai, J. Peng, Y. Nho, J. Li, G. Wei, *Nucl. Instrum. Meth. B* **2007**, *265*, 385.
[69] H. J. Yoo, H. D. Kim, *J. Biomed. Mater. Res. B* **2008**, *85*, 326.
[70] D. J. Vachon, D. R. Yager, *J. Biomed. Mater. Res. A* **2006**, *76*, 35.
[71] N. Yusof, A. H. Ainul Hafiza, R. M. Zohdi, M. Zuki, M. Z. A. Bakar, *Radiat. Phys. Chem.* **2007**, *76*, 1767.
[72] C. T. Chiu, J. S. Lee, C. S. Chu, Y. P. Chang, Y. J. Wang, *J. Mater. Sci. Mater. Med.* **2008**, *78*, 2503.
[73] J. M. Yang, S. J. Yang, H. T. Lin, T. H. Wu, H. J. Chen, *Mat. Sci. Eng. C-Bio. S.* **2008**, *28*, 150.

[74] L. Wang, E. Khor, A. Wee, L. Y. Lim, *J. Biomed. Mater. Res. B* **2002**, *63*, 610.
[75] T. T. Reddy, A. Kano, A. Maruyama, M. Hadano, A. Takahara, *Biomacromolecules* **2008**, *9*, 1313.
[76] W. G. Payne, J. Posnett, O. Alvarez, M. B. Etris, G. Jameson, R. Wolcott, H. Dharma, S. Hartwell, D. Ochs, *Ostomy Wound Manag.* **2009**, *55*(2), 50.
[77] D. H. Reneker, I. Chun, *Nanotechnology* **1996**, *7*, 216.
[78] G. I. Taylor, *Proc. Roy. Soc. London* **1969**, A313.
[79] T. Subbiah, G. S. Bhat, R. W. Tock, S. Parameswaran, S. S. Ramkumar, *J. Appl. Polym. Sci.* **2005**, *96*, 557.
[80] J. Manee-in, M. Nithitanakul, P. Supaphol, *IPJ* **2006**, *15*(4), 341.
[81] S. Koombhongse, W. Liu, D. H. Reneker, *J. Polym. Sci. Part B: Polym. Phys.* **2001**, *39*, 2598.
[82] L. Wannatong, A. Sirivat, P. Supaphol, *Polym. Int.* **2004**, *53*, 1851.
[83] K. Sombatmankhong, N. Sanchavanakit, P. Pavasant, P. Supaphol, *Polymer* **2007**, *48*, 1419.
[84] P. Wutticharoenmongkol, N. Sanchavanakit, P. Pavasant, P. Supaphol, *Macromol. Biosci.* **2006**, *6*, 70.
[85] R. Jaeger, M. M. Bergshoef, C. M. I. Batlle, S. Holger, G. Vancso, *J. Macromol. Symp.* **1998**, *127*, 141.
[86] K. Arayanarakul, N. Choktaweesap, D. Aht-ong, C. Meechaisue, P. Supaphol, *Macromol. Mater. Eng.* **2006**, *291*, 581.
[87] V. Pornsopone, P. Supaphol, R. Rangkupan, S. Tantayanon, *Polym. Eng. Sci.* **2005**, *45*, 1073.
[88] P. Taepaiboon, U. Rungsardthong, P. Supaphol, *Eur. J. Pharm. Biopharm* **2007**, *67*, 387.
[89] P. Supaphol, C. Mitt-Uppatham, M. Nititanakul, *J. Polym. Sci. Part B: Polym. Phys.* **2005**, *43*, 3699.
[90] H. Fong, W. Liu, C. Wang, R. A. Vaia, *Polymer* **2002**, *43*, 775.
[91] K. H. Lee, H. Y. Kim, Y. M. La, D. R. Lee, N. H. Sung, *J. Polym. Sci. Part B: Polym. Phys.* **2002**, *40*, 2259.
[92] N. Choktaweesap, K. Arayanarakul, D. Aht-Ong, C. Meechaisue, P. Supaphol, *Polym. J.* **2007**, *39*, 622.
[93] P. P. Tsai, H. Gibson, P. Gibson, *J. Electrostat.* **2002**, *54*, 333.
[94] J. Sutasinpromprae, S. Jitjaicham, M. Nithitanakul, C. Meechaisue, P. Supaphol, *Polym. Int.* **2006**, *55*, 825.
[95] J. Kim, D. S. Lee, *Polym. J.* **2000**, *32*, 616.
[96] E. R. Kenawy, G. L. Bowlin, K. Mansfield, J. Layman, D. G. Simpson, E. H. Sanders, G. E. Wnwk, *J. Control. Release* **2002**, *81*, 57.
[97] W. Ritcharoen, Y. Thaiying, Y. Saejeng, I. Jangchud, R. Rangkupan, C. Meechaisue, P. Supaphol, *Cellulose* **2008**, *15*, 435.
[98] M. Bognitzki, W. Czado, T. Frese, A. Schaper, M. Hellwig, M. Steinhart, A. Greiner, H. Wendorff, *Adv. Mater.* **2001**, *13*, 70.
[99] C. J. Buchko, L. C. Chen, S. Yu, D. C. Martin, *Polymer* **1999**, *40*, 7397.
[100] C. Meechaisue, P. Wutticharoenmongkol, R. Waraput, T. Huangjing, N. Ketbumrung, P. Pavasant, P. Supaphol, *Biomed. Mater.* **2007**, *2*, 181.
[101] S. Chuangchote, A. Sirivat, P. Supaphol, *Nanotechnology* **2007**, *18*, 1.
[102] A. Moradzadegan, S. O. Ranaei-Siadat, A. E. Habibi, M. Taghizadeh, M. Barshan-Tashnizi, R. Jalili, K. Khajeh, *Eng. Life Sci.* (in press). DOI: 10.1002/elsc.200900001
[103] P. Sangsanoh, P. Supaphol, *Biomacromolecules* **2006**, *7*(10), 2710.
[104] M. Spasova, N. Manolova, D. Paneva, I. Rashkov, *E-Polymers* **2004**, *056*.
[105] M. Spasova, D. Paneva, N. Manolova, P. Radenkov, I. Rashkov, *Macromol. Biosci.* **2008**, *8*, 153.
[106] H. Penchev, D. Paneva, N. Manolova, I. Rashkov, *Macromol. Biosci.* **2009**, *9*, 884.
[107] Y. Kim, D. H. Reneker, *Polym. Eng. Sci.* **1999**, *39*, 849.
[108] Z. Jun, H. Hou, A. Schaper, J. H. Wendorff, A. Greiner, *E-Polymers* **2003**, *009*.
[109] Y. Zhang, C. T. Lim, S. Ramakrishna, Z. M. Huang, *J. Mater. Sci. -Mater. M.* **2005**, *16*, 933.
[110] S. E. Dabney, The use of electrospinning technology to produce wound dressings, *PhD Dissertation*, The University of Akron, May, **2002**.
[111] D. Martindale, *Sci. Amer. July* **2000**, 34.
[112] E. Chiellini, H. Gil, G. Braunegg, J. Buchert, M. Van der Zee, *Biorelated Polymers: Sustainable Polymer Science and Technology*. Kluwer Academic/Plenum Publisher, New York, **2001**.
[113] J. Venugopal, S. Ramakrishna, *Appl. Biochem. Biotech.* **2005**, *125*, 147.
[114] R. Samatham, K. J. Kim, *Polym. Eng. Sci.* **2006**, *46*, 954.
[115] K. H. Hong, J. L. Park, I. H. Sul, J. H. Youk, T. J. Kang, *J. Polym. Sci. Part B: Polym. Phys.* **2006**, *44*, 2468.
[116] P. O. Rujitanaroj, N. Pimpha, P. Supaphol, *Polymer* **2008**, *49*, 4723.
[117] K. H. Hong, *Polym. Eng. Sci.* **2007**, *47*, 43.
[118] L. Yao, T. W. Haas, A. Guiseppi-Elie, G. L. Bowlin, D. G. Simpson, G. E. Wnek, *Chem. Mater.* **2003**, *15*, 1860.
[119] Y. Y. Duan, J. Jia, S. H. Wang, W. Yan, L. Jin, Z. Y. Wang, *J. Appl. Polym. Sci.* **2007**, *106*, 1208.
[120] Y. Liu, P. R. Cooper, J. E. Barralet, R. M. Shelton, *Biomaterials* **2007**, *28*, 1393.
[121] Y. Zhou, D. Yang, X. Chen, Q. Xu, F. Lu, J. Nie, *Biomacromolecules* **2008**, *9*, 349.
[122] C. H. Su, C. S. Sun, S. W. Juan, H. O. Ho, C. H. Hu, M. T. Sheu, *Biomaterials* **1999**, *20*, 61.
[123] J. P. Chen, G. Y. Chang, J. K. Chen, *Colloid. Surface A* **2008**, *313–314*, 183.
[124] H. M. Powell, D. M. Supp, S. T. Boyce, *Biomaterials* **2008**, *29*, 834.
[125] M. S. Khil, D. I. Cha, H. Y. Kim, I. S. Kim, N. Bhattarai, *J. Biomed. Mater. Res. B* **2003**, *67*, 675.
[126] S. Thomas, G. Hughes, P. Fram, A. Hallett, *SMTL Rep.* **2005**, 1–124.
[127] E. D. Walton, Test method for water vapor permeability of thin films, *Surgical Materials Testing Laboratory Report*, Wales, UK, **2002**.
[128] L. Ostlund, *British Standards BS EN 13726-1. Test methods for primary wound dressings. Part 1: Aspects of Absorbency, section 3.3 Fluid Handling Capacity*, **2002**.
[129] P. Wu, A. C. Fisher, P. P. Food, D. Queen, J. D. S. Gaylor, *Biomaterials* **1995**, *16*, 171.
[130] L. R. Cardona, Y. D. Sanzgiri, L. M. Benedetti, V. J. Stella, E. M. Topp, *Biomaterials* **1996**, *17*, 1639.
[131] Y. B. Wu, S. H. Yu, F. L. Mi, C. W. Wu, S. S. Shyu, C. K. Peng, A. C. Chao, *Carbohyd. Polym.* **2004**, *57*, 435.
[132] N. Koji, Y. Tomonori, I. Kenji, S. Fumio, *J. Appl. Polym. Sci.* **1999**, *74*, 133.
[133] M. Ignatova, N. Manolova, N. Markova, I. Rashkov, *Macromol. Biosci.* **2009**, *9*, 102.
[134] E. Kiss, I. Bertoti, I. Vargha-Butler, *J. Colloid Interface Sci.* **2002**, *245*, 91.
[135] I. F. Amaral, P. L. Granja, M. A. Barbosa, *J. Biomater. Sci. Polym. Ed.* **2005**, *16*, 1575.
[136] J. E. Lee, J. C. Park, Y. S. Hwang, J. K. Kim, J. G. Kim, H. Sub, *Yonsei Med. J.* **2001**, *42*, 172.
[137] D. A. Morgan, *Pharm. J.* **1999**, *263*, 820.
[138] J. Boateng, *PhD Thesis*, University of Strathclyde, **2005**.

