History of Wound Management

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Abstract- *Since the cavedweller, man has been liable to his wounds. Wound care develop from magical invocations, mixture, and ointments, to a systematic text of wound management and surgery from Hippocrates and Celsus. These promotes were lost after the fall of the Roman Empire. In Europe, the central ages were a revert of wound management back to mixture and attracts. It was'nt until the time of big armies using weapons and bombard that surgical wound management develop again. This article will briefly highlight major milestones in wound management.*

Keywords- Wound Management, ointments, surgery, Hippocrates etc.

I. INTRODUCTION

A brief history of wound management:

On ancient medical and wound management procedures, a substantial quantity of literature has been produced. These findings demonstrate that the world's oldest medical document was discovered on Sumerian clay, which is the world's oldest written history record. In this document, the "three healing gestures" were described as follows:

a. Washing the wound
b. Applying dressings
c. Bandaging the wound.[1]

During the Egyptian civilisation, more significant developments occurred. In ancient times, they made significant advances in controlling primary human illnesses and inflammation.[2] The wound treatment at the time was a linen-based textile gauze construction. The Egyptians conducted preliminary research on the use of honey, gums, resins, and plant extracts in wound care, and honey was used to coat linen textile structures to make them antimicrobial.[3-5]
Many historians have emphasised the ancient Greeks' contribution to medicine and wound treatment. The Greeks separated wounds into two groups: infected nonhealing wounds and noninfected healing wounds, in order to determine the severity of the wounds. Both Hippocrates and Galen recognised two sorts of wounds: the first is dry and clean, which is cured by the first, and the second is dirty and infected, which is healed by the second. The other is filthy, and it has to be drained before it can recover.[6-]7Galen also proposed the principle of "laudable pus." For the first time, metal powder, milk, honey, and wine were used in the gauze application in another big research in ancient Greece. It was proposed that when metallic copper was mixed with vinegar, copper acetate was formed, which has antibacterial qualities and might be used to heal wounds and skin ulcers.[8]Traditional wound dressing materials in the nineteenth century included a wide range of textile fibres (such as cotton, silk, and wool) and structures (knitted, nonwoven, and composites). Lumerie in France invented the cotton gauze soaked with paraffin as a wound treatment.[9]The discovery of bacteria and the application of antibiotics in wound and wound healing occurred in the mid-nineteenth century. During this process, Pasteur and Joseph Lister followed Semmelweis's observations on bacteria and antibiotics. Lister10 started wrapping wounds with many layers of gauze, which is a crucial element of a composite dressing, to prevent contamination. To avoid carbolic acid injury to the tissues, he inserted a layer of rather impermeable silk between the gauze layers and the wounds. Pasteur invented the "germ-free" wound environment idea. Another interesting conclusion of his research was that bodily fluid/exudate could not produce germs or diseases. He proposed that the wound be covered and kept dry to protect it from infectious germs in the surroundings.[10-11]Following Pasteur's discoveries, Koch observed a significant transfer of germs from the surgeon's hands, equipment, and bandages, as well as from the patients, during surgery or therapy.[12]Winter made history in the field of wound treatment by performing a groundbreaking procedure. He offered a wound healing model that challenged conventional wisdom. When he realised that keeping the wound environment moist enhanced healing and produced considerably better clinical results than keeping the wound environment dry, he was ecstatic.[13]The present understanding of the biological mechanisms involved in wound healing and tissue regeneration has been substantially increased and strengthened in recent years due to advances in cellular and molecular biology. The latest understanding of cellular and molecular level phenomena involved in the dynamic and complex process of wound healing, including blood coagulation, inflammation, fibroplasias, collagen deposition, and wound contraction, has resulted in a significant advancement and an ever-growing number of woundcare products being designed and developed.[14]The main aims of

innovations are to relieve patient pain, reduce wound healing times, and solve chronic wound healing clinical difficulties. The development and testing of new wound dressing materials and procedures is an essential aspect of the world's rapidly increasing biomaterials sector.[15-17]To properly cure the wound and keep it free of infectious agents, the wound must be covered with the suitable substance. The primary purposes of wound dressings are to prevent strikethrough and to protect wound sites from infection and additional damage. A number of studies on wound-wet interactions have found that wounds that are maintained moist heal significantly quicker than those that are kept dry.[15, 18–20]The hunt for the perfect dressing continues, as there is presently no dressing that suits all patients, all wound types, or all stages of the healing process. The following are the most important needs for wound dressings:

a. The capacity to absorb fluid and contribute water to a dry wound is known as fluid control.
b. Physical barrier: to prevent strikethrough and further physical harm.
c. Infected wounds require microbial management.
d. Odour control: a wound frequently emits an unpleasant and irritating odour.
e. Low wound adhesion: excellent dressings can help eliminate wound adherence.
f. For deep cavity wounds, use aspace filler.
g. Debridement: supplying the right amount of moisture, temperature, and pH.
h. To avoid blood loss, haemostatic haemorrhage is controlled as soon as feasible.
i. Scar reduction: scar development is a significant cosmetic issue for the patient.
j. Metal ion metabolism: any metal ion shortage slows wound healing.

Medical textiles

Technical textiles are one-of-a-kind designed structures that provide superior solutions for a growing number of applications. Medical textiles is one of the most important fields in technical textiles, with a wide range of commercially accessible items including wound dressings, sutures, bandages, scaffolds, masks, surgical gowns, and so on.[21] Nonwoven fabrics are used in medical textiles because they have important properties including high absorption, porosity, and adaptability in terms of bulk and area densities. The majority of nonwoven medical goods (70%) are single-use and disposable. Because of their light weight, flexibility, increased mixing choices, and high strength, nonwoven textiles are frequently used to make composites.[22]

Wounds are complicated by nature, and there is no one-size-fits-all bandage that can be used to treat all sorts of wounds. The most appropriate wound dressing for a given wound involves expert knowledge as well as clinical assessment; nevertheless, the most appropriate wound dressing relies not only on the kind of wound but also on the stage of the healing process.[23]Many developed countries' total annual healthcare budgets include wound dressings. The potential market for healthcare and medical textiles is rapidly expanding. Advanced wound dressings are expected to have a large commercial potential, according to predictions. In 2012, yearly growth is expected to range between ten and fifteen percent.[24]Over 100,000 procedures requiring surgical wounds are done every day in the United States alone. The need for all forms of surgical intervention, notably cardiovascular, orthopedic, urological, and dermatological operations, is increasing as the population ages. The treatment of venous leg ulcers places a lot of pressure on healthcare providers all around the world. The treatment of this illness costs the NHS £650 million per year in the United Kingdom alone.[25]A wound dressing must reduce pain, absorb exudates, avoid infection and pollutant contact with the wound, maintain non-toxicity, maintain a moist environment, and have optimal gaseous permeability, temperature, and pH. A contemporary wound dressing should also have a variety of desired features, such as biodegradability, bio absorbability, and simplicity of application, as well as being flexible, comfortable, and bacteria-resistant.[26]PLA fiber is one of the most rapidly expanding biodegradable fibre types in current research, with researchers actively attempting to bring innovative application areas as a substitute for standard synthetic fibres. Sutures, scaffolds for tissue engineering, and drug delivery systems are among of the biomedical applications of PLA.[27, 28, 29]

Wound management materials

Wound dressing materials, as briefly mentioned above, can play an important part in wound healing. An excellent wound dressing not only protects the area from mechanical damage, but also speeds up the healing process and helps to avoid bacterial infection. The evolution of wound dressings may be addressed in this regard, taking into account both classic and modern (advanced, smart) dressings. Traditional wound dressings include the following essential traits and properties: keeping wounds dry and warm; avoiding strikethrough; absorbent pad; and a physical barrier such as gauzes or felt. Traditional dressings' adhesion structure is one of the most serious issues, causing genuine trauma to patients owing to their difficulties in removing them from the wound surface. There has recently been a surge in interest in the creation of low-adherence conventional dressings, such as adding a polyamide contact layer, covering viscose fibre with polypropylene (PP), and impregnating gauze with paraffin. Even while significant advances in conventional dressings have been made, they still lack the necessary qualities for complicated wound healing applications. Extensible bandages, cotton and rubber elastic bandages, elastic adhesive bandages, elastic web bandages, extension strapping, thick cotton and rubber elastic, titanium dioxide elastic adhesive bandages, and vented elastic bandages are examples of commonly used conventional wound dressings. [15,21,30,31]

Dressings made of hydrocolloid:

Hydrocolloid dressings are a kind of dressing that contains gel-forming substances such as sodium carboxymethylcellulose (NaCMC), gelatine, pectin, and alginate, and are among the most extensively used contemporary dressings. When these polymers come into touch with wound exudate, they absorb it and subsequently expand. Hydrocolloid dressings provide important qualities for wound dressing applications, including an excellent antibacterial performance. Hydrocolloid dressings are occlusive, meaning they keep water, oxygen, and germs out of the wound. This might make angiogenesis and granulation easier. Hydrocolloids also lower the pH of the wound surface, preventing bacteria from growing in an acidic environment.[33]Another advantage of hydrocolloid wound dressings is that they are conformable to the shape of the patient's body and cling well to high-friction locations like the sacrum and heels.

Semi-permeable films/foams:

The foams are porous materials with great absorption capacity and flexibility. Semi-permeable film is a sterile polyurethane sheet with an acrylic adhesive coating. It's utilised to create a sterile area in which to perform surgical incisions, and some more advanced films with different moisture/vapour permeabilities are employed for venous access sites. They can be used as a first and second dressing. Silastic, Lyofoam, Tegaderm, HyperFoam, and Shingna are some of the commercially available foam dressings. They effortlessly fit to the shape of the patient's body. The wound can be easily checked thanks to the transparency of the films. They are semi-occlusive and retain moisture due to their film structure; they facilitate autolytic debridement of necrotic wounds and provide a moist healing environment for granulating wounds.

Wound dressings made of hydrogel:

Hydrogels are cross-linked polymeric networks that swell when exposed to biological fluid and are commonly used in medication delivery and tissue/organ healing. Hydrogel dressings are made of water or glycerine. Hydrogel wound dressings may be made with CMC, agar, glycerol, and pectin. In water, hydrogel polymers may absorb up to 90% of their mass. Dermabrasion, small burns, and skin donor sites can all benefit from hydrogel dressings. Hydrogels help autolytic debridement in wounds with necrotic tissue like slough or eschar by maintaining a wet wound environment on a clean, healthy, granulating wound.

Dressings for composite wounds:

Due to the fact that wound healing involves a number of stages, a multi-functional wound dressing is required that can be successful at each step of the healing process. The goal of composite dressing development is to blend different materials to meet the diverse clinical needs and applications. The postoperative jubilee dressing (Aquacel® Surgical) is an example of a composite dressing. It consists of a hydrofibre inner layer with a viscoelastic hydrocolloid outer layer and is developed as a composite dressing for post-surgical applications such as total knee replacement.[34]

Wound dressings made of nanofibers:

Nanofiber wound dressings, according to recent research, show a lot of potential for both acute and chronic wound healing. Nanofiber-based wound dressings made of synthetic or natural polymers offer unique qualities such high surface area, volume ratio, 3-D micro porous structure, porosity, and permeability.[35, 36]These could aid in improving the extracellular matrix's capacity to be mimicked (ECM). Long-term stability of nanofibers has only been studied in a few cases. In a recent study, Tort et al attempted to combine the benefits of collagen, chitosan, and alginate, and found that the combination could speed up healing as the structure formed as nanofibers.

Wound dressings made with alginate:

In general, it is used to treat heavily exuding wounds such as chronic leg ulcers, pressure ulcers, fungating carcinomas, and acute wounds like abrasions, lacerations, and post-surgical wounds. Commercial alginate wound dressings include AlgiDERO, AlgiSite, CarraSorb, Kaltostat, and SorbSan. Brown sea algae such as Macrocystis pyrifera, Laminaria hyperborean, Sargassum, Durvillaea Antarctica, Ecklonia maximum, Lessonia nigrescens, and Ascophyllum nodosum are the main sources of alginates. [39–42]Alginate fibres have a number of advantages over other fibres, including high absorbency, biodegradability, gelling, and biocompatibility.Alginates are unbranched binary copolymers made up of 14 linked -D-mannuronic acid (M) and -L-guluronic acid (G) residues with a wide range of composition and sequence.[45]Alginate was discovered to be a genuine block copolymer, consisting of homopolymeric areas of M- and G-blocks, respectively, interspersed with regions of alternating structure.[46, 47]The proportion of M to G units and their configurations in each polymer differ according on the algal source, which influences the polymer's physical strength and other physical qualities. [40, 48, 49] Calcium ions in high-M alginates are less firmly connected to the molecules than those in high-G alginates, allowing sodium ions to replace them more easily. This causes the alginate fibres to absorb more fluid and swell faster. Each alginate molecule has hydroxyl groups that contribute to its hydrophilicity, and it is widely known that alginates swell when they come into contact with liquids. When the dressing comes into touch with wound exudates, it undergoes an ion exchange process between the calcium ions in the dressing and the sodium ions in the wound exudates. The fibre swells and partially dissolves once a considerable proportion of the calcium ions present in the fibre are replaced by sodium. The amount of swelling is determined by the alginate's chemical composition, which is determined by its botanical source. Because of its high exudate absorption, it is commonly utilised in wound dressing applications.[50] When alginate dressing comes into contact with wound exudates, it absorbs the exudates and, thanks to its gel-forming property, creates a desirable wound moist environment. It also allows adequate exchange of water vapour and oxygen, which is an important property for wound healing, and the moist environment promotes rapid granulation and reepithelialization.[50-52]

Alginate's gelling characteristic aids in the painless removal of dressings. Alginate dressings are used to treat moderate to heavy exudates since it can absorb 15 to 20 times its weight in fluid.[53] Alginate dressings have been shown to activate human macrophages, causing them to release pro-inflammatory cytokines linked to faster healing.[54]When alginate is utilised in medicinal applications, it must undergo further purifying processes.These include mechanically washing the seaweed stems and chemical and physical procedures for removing endotoxins and protein.[55] Cotton and chitosan have been used to mix alginate with other textile fibres. Edward and colleagues investigated the use of cotton and alginate as a dressing material. They wanted to combine the advantages of cotton and alginate in a single dressing. Alginate is extremely biocompatible and has a number of appealing characteristics, including non-toxicity, non-irritability, simplicity of use and mixing, increased absorbency, and swelling; but, it has poor dimensional stability and is untidy to work with.[56, 57,58]

Wound dressings made of hydrofibre:

ConvaTec Ltd, USA, created Aquacel™, a well-known hydrofibre-containing dressing, in 1997. Sodium carboxymethyl cellulose is present in the dressings. This is a type of hydrocolloid with higher absorbent qualities, capable of absorbing up to 25 times its own weight and expanding to a high degree. These are the most sought-after characteristics in wound dressings. A significant number of microorganisms may grow on and/or in the wound when the skin is ruptured. CMC wound dressings have the potential to absorb enormous amounts of bodily fluids, eliminating a large volume of exudate in this scenario. This may result in a reduction in the number of microbes on the wound surface.[21,60] Due to its conformability and high water absorbency, the CMC-containing nonwoven dressing may maintain the patient's soft and comfortable sensation while also providing excellent wound healing performance. CMC resembles alginates in appearance and gel-forming characteristics, and it provides similar wound healing effects. When the CMC nonwoven dressing comes into direct contact with liquid, it absorbs it, but not through the conventional capillary action method. Even when the fibre is compressed, the absorbed fluid is kept within the structure of the fibre. Fluid wicking across the dressing is limited in the lateral area. The dressing quickly transforms from a dry dressing to a soft cohesive gel sheet as it absorbs exudates. CMC fibre helps wound healing by maintaining a moist environment, aiding autolysis debridement, and being easily removed with little or no injury to freshly produced tissue.[52]

CMC dressings are used to treat chronic wounds like leg ulcers and pressure ulcers, as well as acute wounds including abrasions, lacerations, incisions, donor sites, and first and second degree burns.

The dressing can also be used to treat surgical or traumatic wounds that have been left to heal on their own due to secondary intent.

It's used to treat wounds that are prone to bleeding, such as those that have been deteriorated mechanically or medically, donor sites, and traumatic wounds.

PCL (Polycaprolacton):

Wound dressings are made up of absorbent and cross-linked polymer networks in general. Polycaprolactone (PCL), semi-crystalline polyester that is biodegradable and biocompatible, is one of the current polymers. The FDA has approved a number of PCL-based medication delivery devices and implants. The use of PCL on wound and burn dressings, tissue engineering, scaffold production, drug targeting, and 3D wound dressings has been the subject of numerous investigations (1-A). Muwaffak et al. used hot melt extrusion to successfully construct 3D printed wound dressings in collaboration with Ag, Cu, and Zn into PCL filaments.[38]

Polylactic acid (PLA):

Unlike typical synthetic polymers, which rely on oil and gas reserves, polylactic acid (PLA) is a linear aliphatic thermoplastic polyester generated entirely from renewable natural sources such as corn and crops. It has outstanding qualities such as biocompatibility, compostability, and minimal human toxicity.[61-65] PLA fibre is one of the most rapidly expanding biodegradable fibre types in current research, with researchers attempting to provide new applications as an alternative to synthetic fibres.[28] The polymer is biodegradable and is made by either direct condensation of lactic acid or ring opening of a cyclic intermediate dimer. PLA fibres can be processed using the traditional melt spinning method. When PLA is composted, carbon dioxide is eliminated from the atmosphere. Natural and manmade polymers electrospun into fibres, such as PLA fibre, are also used in tissue engineering.[66-68] PLA fibres have similar features to many other thermoplastic fibres, such as low moisture resorption and a smooth surface. PLA's commercial potential as a textile fibre is significant. Its mechanical qualities are comparable to normal PET, and its low melting and softening temperatures are comparable to polypropylene fibre. PLA has a lower specific gravity than other natural fibres (1.25gcm-3). Tenacity at break is higher (32-36 cN tex-1) than for other natural fibres. PLA has good wickability, fluid spreading speed, and drying speed. PLA fibres do not have antibacterial characteristics unless they are treated properly.[29, 69, 70]

II. CONCLUSION

Wound healing is a multi-step, multi-factor physiological process. Because of the complication of these phenomena, the healing process is extremely arduous and unpleasant. A number of external pathways become active during repair and aid tissue healing, in addition to cellular and molecular components. During the healing phase of wounds, wound dressing is one of the most important external effectors. The main difficulties with wound dressings have been identified in this review.

REFERENCES

[1] Majno G. The Healing Hand: Man and Wound in the Ancient World. Cambridge: Harvard University Press; 1975. p. 600.

[2] Nicholson PT, Ian S. Ancient Egyptian Materials and Technology. Cambridge: Cambridge University Press; 2000. p. 1–19.

[3] Majno G. The Swnw (Egypt): The Healing Han. Man and Wound in the Ancient World. Massachusetts: Harvard University Press; 1975. p. 571.

[4] Wang T, Xiao-Kang Z, Xu-Ting X, et al. Hydrogel sheets of chitosan, honey and gelatin as burn wound dressings. Carbohydrate Polymers. 2012;88(1):75–83.

[5] Meri JW. Medieval Islamic Civilization: An Encyclopaedia. UK: Routledge; 2006. p. 300.

[6] Dealey C. Wound healing in Moorish Spain. EWMA Journal. 2002;34:32–34.

[7] Gorbach SL. Good and Laudable Pus. J Clin Invest. 1995;96(6):2545.

[8] Caldwell MD. Topical wound therapy-an historical perspective. J Trauma. 1990;30(12 Suppl):116–122.

[9] Cavendish M. Inventors and inventions. Marshall Cavendish Coorp, New York; 2007.

[10] Savin JA. Joseph Lister: a neglected master of investigative dermatology. Br J Dermatol. 1995;132(6):1003–1007.

[11] Lawrence G. Surgery (traditional). In: Bynum WF, Companion Encyclopedia of the History of Medicine. London, New York: Routledge, 1993;2:961–983.

[12] Wells TS. Some cause of excessive mortality after surgical operations. British Medical J. 1864;196(2):384–388.

[13] Bryan J. Moist wound healing: a concept that changed our practice. J Wound Care. 2004;13(6):227–228.

[14] Lee YH, Chang JJ, Yang MC, et al. Acceleration of wound healing in diabetic rats by layered hydrogel dressing. Carbohydrate Polymers. 2012;88(3):809–819.

[15] Dee KC, Puleo DA Bizios R. An introduction to Tissue-Biomaterial Interactions. New York: Wiley & Sons; 2002.

[16] Zahedi P. A Review on Wound Dressings with an Emphasis on Electronicspun Nanofibrous Polymeric Bandages. Polymer Advanced Technologies. 2010;21(2):77–95.

[17] Qin Y. Advanced wound dressings. J Textile Institute. 2001;92(2):127–138.

[18] Bolton LL, Monte K, Pirone LA. Moisture and Healing: Beyond the Jargon. Ostomy Wound Manage. 2000;46(1A Suppl):51S–62S.

[19] Mabrouk A. Moist occlusive dressing (AquacelW Ag) versus moist open dressing (MEBOW) in the management of partial-thickness facial burns: A

comparative study in Ain Shams University. Burns. 2012;38(3):396–403.

[20] Morton LM, Phillips TJ. Wound Healing Update. Semin Cutan Med Surg. 2012;31(1):33–37.

[21] Anand SC, Kennedy JF, Miraftab M, et al. Medical textiles and biomaterials for healthcare. Cambridge: Woodhead publishing; 2006. p. 499–508.

[22] Ajmeri JR, Ajmeri CJ. Nonwoven materials and technologies for medical applications. In: Bartels VT, editor. Handbook of medical textiles. Cambridge: Woodhead Publishing; 2001. p. 106–131.

[23] Bentley J. Understanding the wound healing process. Practice Nursing. 2004;15(4):181–188.

[24] Rajendran S, Anand SC. Woven textiles for medical applications. In: Gandhi K, editor. Woven textiles: Principles, technologies and applications. Cambridge: Woodhead Publishing; 2012. p. 414–441.

[25] Morrell CJ. Cost effectiveness of community leg ulcer clinics: randomised controlled trial. British Medical J. 1998;316:1487.

[26] London AP, Tonelli AE, Hudson SM, et al. Textile composite wound dressing. IEEE. USA; 1995.

[27] Amass AJ, N Goala KLR, Tighe BJ, et al. Polylactic acids produced from l- and dl-lactic acid anhydrosulfite: stereochemical aspects. Polymer. 1999;40(18):5073–5078.

[28] Lunt J. Polylactic Acid Polymers for Fibers and Nonwovens. International Fiber J. 2000;55:48–52.

[29] Farrington DW. Poly (lactic acid) fibers. In: Blackburn RS, editor. Biodegradable and sustainable fibres. Cambridge: Woodhead Publishing; 2005.

[30] Anand SC. Medical textiles 96. Cambridge: Woodhead Ltd; 1997. p. 149.

[31] Menaker GM. Wound Dressings at the Turn of the Millennium. Curr Problem Dermato. 2001;13(2):86–89.

[32] Capanemaa SVN, Mansura AAP, Jesusa A, et al. Superabsorbent crosslinked carboxymethyl cellulose-PEG hydrogelsfor potential wound dressing applications. International J Biological Macromolecules. 2017;106:1218–1234.

[33] Vowden K, Vowden P. Wound dressings: principles and practice. Surgery. 2017;29(10):491–495.

[34] Burke NG, Green C, McHugh G, et al. A prospective randomised study comparing the jubilee dressing method to a standard adhesive dressing for total hip and knee replacements. J Tissue Viability. 2012;21(3):84- 87.

[35] Natu MV, De Sousa HC, Gil MH. Effects of drug solubility, state and loading on controlled release in bicomponent electrospun fibers. Int J Pharm. 2010;397(1–2):50–58.

[36] Aduba DC, Hammer JA, Yuan Q, et al. Semi-interpenetrating network (sIPN) gelatin nanofiber scaffolds for oral mucosal drug delivery. Acta Biomater. 2013;9(5):6576–6584.

[37] Tort S, Acartürk F, Beşikci A. Evaluation of Three-layered Doxycycline-collagen Loaded Nanofiber Wound Dressing. Int J Pharm. 2017;529(1–2):642–653.

[38] Muwaffak Z, Goyanes A, Clark V, et al. Patient-specific 3D scanned and 3D printed antimicrobial polycaprolactone wound dresings. Int J Pharm. 2017;527(1–2):161–170.

[39] Goh CH, Heng PWS, Chan LW. Alginates as a useful natural polymer for microencapsulation and therapeutic applications. Carbohydrate Polymers. 2012;88(1):1–12.

[40] Wee S, Gombotz WR. Protein release from alginate matrices. Adv Drug Deliv Rev. 1998;31(3):267–285.

[41] Andersen IL, Skipnes O, Smidsrød O, et al. Some biological functions of matrix components in benthic algae in relation to their chemistry and the composition of seawter. ACS Symp Ser. 1977;48:361–381.

[42] Thu HE, Zulfakar MH, Ng SF. Alginate based bilayer hydrocolloid films as potential slow-release modern wound dressing. Int J Pharm. 2012;434(1–2):375–383.

[43] Chapman DJ. Algin and alginates. Seaweeds and their uses. New York: Chapman and Hall; 1980.

[44] Stanford EC. Alginate. British Pat. No. 142, UK; 1881.

[45] Draget KI, Smidsrod O, Break GS. Alginates from algae. In: Steinbuchel A, Rhee SK, editors. Polysaccharides and polyamides in the food industry, Production and patenrs. Germany: Wiley-VCH, Weinheim; 2005. p. 771.

[46] Painter TJ, Smidsrod O, Haug A. A computer study of the changes in composition distribution occurring durng random depolymerisation of a binary linear heteropolysaccharide. Acta Chem Scand. 1968;22(5):1637–1648.

[47] Larsen B, Olav S, Terence P, et al. Calculation of th nearest-neighbour frequencies in fragments of alginate from the yields of free monomers after partial hydrolsis. Acta Chem Scand. 1970;24(2):726–728.

[48] Gaserod O, Smidsrod O, Skjak-Braek G. Microcapsules of alginate-chitosan-I. A quantitative study of the interaction between alginate and chitosan. Biomaterials Cilt. 1998;19(20):1815–1825.

[49] Lee YH, Chang JJ, Yang MC, et al. Acceleration of wound healing in diabetic rats by layered hydrogel dressing. Carbohydrate Polymers. 2012;88(3):809–819.

[50] Lloyd LL, Kennedya JF, Methacanona P, et al. Carbohydrate polymers as wound management aids. Carbohydrate Polymers. 1998;37(3):315–322.

[51] Morgan DA. Wound management products in the Drug Tariff. The Pharmaceutical Journal. 1999;7072:820–825.

[52] Williams C. Algosteril calcium alginate dressing for moderate/high exudate. Br J Nurs. 1999;8(5):313–317.

[53] Bello YM, Philips TJ. Recent advance in wound healing. JAMA. 2000;283(6):716–718.
[54] Thomas A, Harding KG, Moore K. Alginates from wound dressings activate human macrophages to secrete tumor necrosis factor-α. Biomaterials. 2000;21(17):1797–1802.
[55] Dusseault J, Tam SK, Ménard M, et al. Evaluation of alginate purification methods: effect on polyphenol, endotoxin and protein contamination. J Biomed Mater Res A. 2006;76(2):243–251.
[56] Thomas S. Wound Dressings. In: Rovee TD, Maibach HI, editors. The Epidermis in wound healing. CRC Press LLC, New York, USA; 2004. p. 408.
[57] Edwards JV, Bopp AF, Batiste SL, et al. Human neutrophil elastase Inhibition with a novel cotton-alginate wound dressing formulation. J Biomed Mater Res. 2003;66(3):433–440.
[58] Draget KI, Taylor C. Chemical, physical and biological properties of alginates and their biomedical implications. Food Hydrocolloids. 2011;25(2):251–256.
[59] Thomas S. Alginate dressing in surgery and wound management. J Wound Care. 2000;9(2):56–60.
[60] Duteille F, Jeffery SL. A phase II prospective, non-comparative assessment of a new silver sodium carboxymethylcellulose (AQUACELW Ag BURN) glove in the management of partial thickness hand burns. Burns. 2012;38(7):1041–1050.
[61] Jung YK, Lee SY. Efficient production of polylactic acid and its copolymers by metabolically engineered Escherichia coli. J Biotechnol. 2011;151(1):94–101.
[62] Mehta R, Vineet K, Haripada B, et al. Synthesis of poly (lactic acid): a review. J Macromol Sci Polym Rev. 2005;45(4):325–349.
[63] Vink ETH, Rábago KR, Glassner DA, et al. Applications of life cycle assessment to NatureWorksTM polylactide (PLA) production. Polym Degrad Stab. 2003;80(3):403–419.
[64] Kolstad JJ, Vink ETH, Wilde BD, et al. Assessment of anaerobic degradation of Ingeo polylactides under accelerated landfill conditions. Polymer Degradation & Stability. 2012;97(7):1131–1141.
[65] Goycoolea MV, Muchow DC, Sirvio LM, et al. In search of missing links in otology. II. Development of an implantable middle ear drug delivery system: initial studies f the sustained ampicillin release for the treatment of otitis media. Laryngoscope. 1991;101(7):727–732.
[66] Pitarresi. Electrospinning of a,b-poly(N-2-hydroxyethyl)-DL-aspartamidegraft-polylactic acid to Produce a Fibrillar Scaffold. Macromolecular Nanotechnology. 2010;46(2):181–184.
[67] Edwards JW, Diller GB, Goheen C. Modified fibers with medical and specialty applications. Springer, Dordrecht, Netherlands; 2005.
[68] Li Y, Chen F, Nie J, et al. Electrospun poly(lactic acid)/chitosan core– shell structure nanofibers from homogeneous solution. Carbohydrate Polymers. 2012;90(4):1445–1451.
[69] Mang M. Poly (lactic acid): Performance Materials from Renewable Resources. NPE 2000 Conference, Chicago, USA; 2000.
[70] Mascheroni E, Guillard V, Nalin F, et al. Diffusivity of propolis compounds in Polylactic acid polymer for the development of anti-microbial packaging films. J Food Engineering Cilt. 2010;98(3):294–301.