International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 3, Issue 3, 2011

Review Article

POLYSACCHARIDE FIBERS IN WOUND MANAGEMENT

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Received: 12 April 2011, Revised and Accepted: 13 May 2011

ABSTRACT

The future of fiber technology for medical applications depends largely on the future needs of our civilization. The use of new fibers for healthcare textiles application has increased rapidly over the past quarter of a century. With the recent advances in tissue engineering, drug delivery, and gene delivery- alginate, chitin/chitosan and their derivatives present a novel and useful class of biomaterials. . Hence small changes in their molecular structure can bring large changes in their interactions with components of biological tissues or drugs. These polymers are excellent candidates for applications in the biomedical field because of their versatility, biocompatibility, bio absorbability and significant absence of cytotoxicity.

Wound healing rate depends mainly on proper dressing materials. Over the last few years there has been a rapidly expanding interest in polysaccharides from both a fundamental viewpoint and also from an applications viewpoint. With different varieties of polysaccharides in modern wound dressings, this article discusses the effective utilization of polysaccharide fibers like alginate, chitin and chitosan for the medical application, specifically for wound management. Further it explains the current research status and also summarizes the different findings of researchers.

Keywords: Alginate, Chitosan, Chitin, Polysaccharides, Wound management.

INTRODUCTION

The use of natural fibers in medical applications spans to ancient times. These fibers afford a bioactive matrix for design of more biocompatible and intelligent materials owing to their remarkable molecular structure. Oligosaccharides and polysaccharides are biopolymers commonly found in living organisms, and are known to reveal the physiological functions by forming a specific conformation. There has been an intensified effort in recent years in identifying the biological functions of polysaccharides as related to potential biomedical applications.

Polysaccharides appear in many different forms in plants. They might be neutral polymers or they might be poly anionic consisting of only one type of monosaccharide, or they might have two or more, up to six different monosaccharide types. They can be linear or branched and they might be substituted with different types of organic groups, such as methyl and acetyl groups. Other types of polysaccharides isolated from plants used in the traditional medicine were identified as having their biologically active sites in the complementary system, the case of arabinans and arabinogalactans[1].

Classification of polysaccharides

There are wide verities of polysaccharides available from different natural sources; they have been generally classified as follows[2].

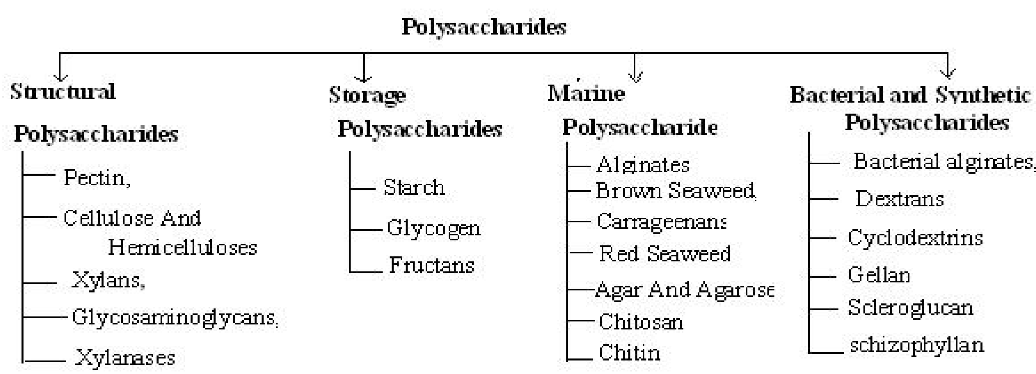

Fig. 1: Classification of polysaccharides

Polysaccharides can also be classified based on their molecular structure, like polysaccharides with

- Rod-shape molecules like alginates, xanthans and chitosans
- Linear random coil type structures like dextrans and pullulans
- Branched structures like glycogen and amylopectin
- Polyanions such as alginates, pectins, carrageenans, xanthans and hyaluronic acid
- Polycations such as dextran derivatives and chitosans
- Neutral structures such as guar, pullulan and dextran.

Virtually all of these molecules are non-toxic and harvestable at low cost in large quantities[2].

Wound management & dressing types

The wound may be defined as a loss or breaking of cellular and anatomic or functional continuity of living tissue[3]. Wound care management is an extremely complex medical operation. Dressing varies with the type of wound and wound management, and no single dressing is universally applicable.

Wound dressing materials are mainly classified as absorbent and non absorbent, depending on the type of fiber used[4]. Wound dressings can also be classified as Passive products, Interactive products and Bio active products, based on its nature of action[5].

Requirements of wound dressings

The successful wound dressing must satisfy several criteria like[6]

- Seal the wound and prevent introduction of external stresses and loss of energy
- Remove excess exudates and toxic components
- Maintain a high humidity at the wound dressing interface
- Provide thermal insulation
- Act as a barrier to micro organism
- Be free from particulates and toxic wound contamination
- Be removable without causing trauma at dressing change.

An insight into the article

First part of this article explains alginate fiber, which was firstly explained and presented by chemist E.C Stanford in the close of nineteenth century. In moist healing concept, alginate fiber becomes one of the most important fibers in the wound dressing[7].

The incorporation of biological agents into the fiber used for nonwoven wound dressings provide a means for directly introducing such agents to the wound without a separate application and with no additional discomfort to the patient. Many authors discussed the wound healing ability of the alginate fiber with different modification[8,9].

The Second part discusses the chitin and chitosan polysaccharides and their applications in various medical fields. The specialty of chitin and chitosan fiber is, its high biocompatibility, non toxic and ability to improve wound healing and therefore it is evaluated in a number of medical applications[10] such as drug delivery[11,12], wound dressing[13], etc.

Alginate fibers

Alginate is a natural polysaccharide extracted from brown seaweeds. Alginate is the main constituent of brown algae and is found in the cell wall and intercellular regions[14,15]. The manufacture of alginate fibers[16] consists of the following steps.

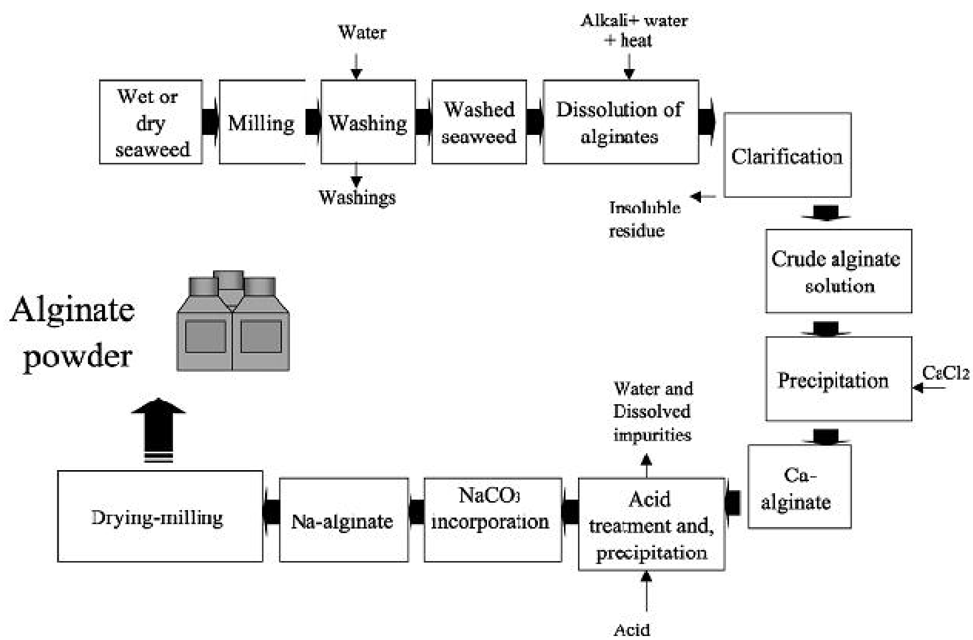

Fig. 2: Alginate manufacturing process[16]

The relative proportion of mannuronic to guluronic acid in alginate fiber significantly affects the properties of end product.

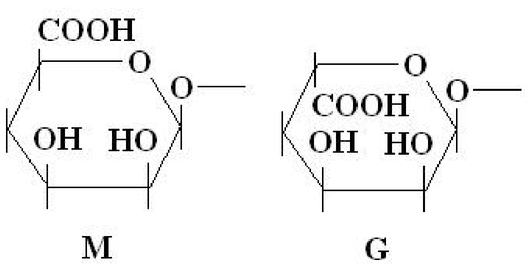

Fig. 3: Structure of β-D-mannuronic acid (M) and α-L-guluronic acid(G).[17]

Alginate fibers can be made by extruding the water-soluble sodium alginate solution into an aqueous calcium chloride bath, using a simple wet spinning process. The resultant calcium alginate fibers have been known for many years for their non-inflammability, due to the high concentration of metal ions in the fibers.

Medical applications of alginate fibers

The type of use, the method of manufacture, the form and ways of disposal govern the choice of fibers used in the medical field. In medical use one can consider alginate fibers as non-toxic, noncarcinogenic, non-allergenic, highly absorbent, haemostatic, of reasonable strength, biocompatible, capable of being sterilized, manipulatable to incorporate mendicants and using cheap nonwoven technology to process it.

Alginate fiber dressings are increasingly used for the treatment of diabetic foot ulcer. They form a hard occlusive matt over the ulcer and thus prevent continuous drainage. A collagen – alginate – fiber wound dressing is also an effective dressing for the management of foot ulcer[18].

Nonwoven alginate fabrics have attracted attention as disposable textiles especially in wound dressings. Shorter production cycles, high flexibility and versatility and low production cost are some of the claimed advantages. There are various types of nonwoven wound dressings comprising alginates[19-21]. Mahoney *et al.*[22] have described a process of producing a nonwoven fabric from crimped and staple cut alginate fibers. The web from a conventional card is built up by the sequential laying of layers of fibers, over one another, until a web of the desired weight is achieved.

The versatile alginate fiber systems are ideal for encouraging cells to recreate the tissue geometry in three dimensions. They may be modified to meet different cell requirements by, say, altering the fiber diameter, length or even the extreme step of modifying the polymer. The novel antimicrobial wound dressings can also be made by blending calcium alginate fibers with the silver-containing Xstatic fibers. In this system, the calcium alginate fibers provide the high absorbency and gelling ability, whilst the silver-containing fibers provide the sustained release of silver ions[23].

Modifications of alginate fibers can be performed to either improve or introduce novel functional properties[24-27]. Much attention has been focused on absorption, retention properties, non-immunogenic, bioerodible implantation composition and incorporation of medicants to assist the natural haemostatic property of the fiber. In this regard, Mahoney *et al.*[28] claim to have improved the absorbency of alginate fiber by 120 times its own weight. Blending of alginate with carboxymethyl cellulose with the object of improving the swelling and reducing the brittleness of alginate fibers has been attempted[29].

Recently, some active ingredients have been incorporated into alginate fiber to improve the traditional properties of the product. One of the methods was reported to incorporate the silver based antibacterial to the fiber[30]. Silver Sulphadiazine (SSD) containing alginate fiber and silver – alginate fibers were produced using various incorporation techniques. Calcium alginate dressing reduces the severity of pain to patients with burn undergoing skin grafting and is favoured by its ease of care[31].

a) b)

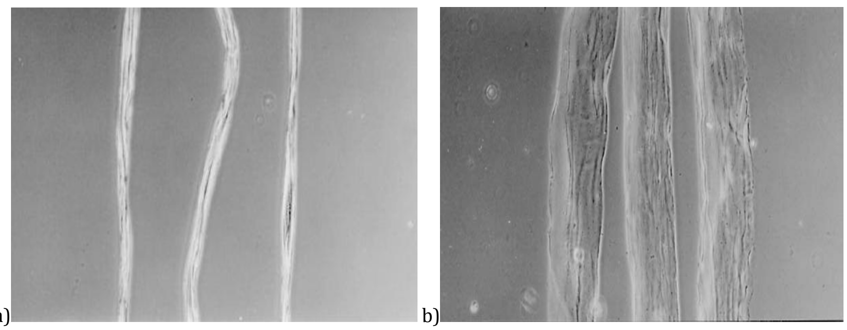

Fig. 4: Alginate fibers with a) 2.0% and b) 29.7% sodium alginate, wet in water[32]

Figure 4 shows the photomicrograph of alginate fibers with sodium content when they were placed in contact with water. It is clear that as the sodium content increases, the fibers are capable of holding more water within the fiber structure. This is important in two respects. First, as the fibers hold more water, the dressings are capable of absorbing more wound exudates, hence extending the duration of the dressing. Second, when the fiber absorbs water into the fiber structure and swells, the spaces between the fibers in the dressing are closed, thus prohibiting liquid from lateral spreading and preventing the maceration of the areas surrounding the wound surface [32].

The properties of alginate fibers can be modified in many ways. For example, in order to make the alginate fibers more absorbent, sodium ions can be introduced into the calcium alginate fibers through chemical treatment. In this process, the calcium alginate fibers can be first washed with hydrochloric acid to replace part of the calcium ions with hydrogen ions. The hydrogen ions are then replaced with sodium ions by a treatment with sodium carbonate or sodium hydroxide [33,34]. Highly absorbent calcium sodium alginate fibers can also be made by treating the fibers with aqueous solutions containing different amount of Na_2SO_4. The Na_2SO_4 is used because the solubility of $CaSO_4$ in water is only 0.209 g per 100 ml at 30°C, hence it can easily replace calcium ions from the alginate fibers[35].

Alginate in wound dressings

Physical and chemical properties of alginate dressing depend on the relative content of calcium and sodium ions and the relative concentration and arrangements of the mannuronic and guluronic monomers. Dressing rich in guluronic acid react readily with sodium ions and form stronger gels. On the other hand, mannuronic acid rich dressings form fewer gels. Alginate fibers have a unique ion exchange property[36]. On contact with wound exudates, the calcium ions in the fiber exchange with the sodium ions in the body fluid and as a result, part of the fiber becomes sodium alginate. Since sodium alginate is water soluble, this ion-exchange leads to the swelling of the fiber and the *in-situ* formation of gel on the wound surface. This unique property makes alginate fiber one of the ideal materials for the production of 'moist healing' wound dressings,

Now a days there are various types of alginate fibers and dressings available, utilizing the diversified properties of the different types of alginate extracted from different sources of seaweeds and the availability of many types of salts of alginate, such as zinc and silver alginate, which are used for zinc-deficient people and for antimicrobial properties respectively[36,37]. Due to their unique properties and the fact that the dressings can be used in the dry form or hydrated form, alginate dressings can be used for a wide range of wounds, providing a cost-effective treatment that involves a minimum number of dressing changes. Table 1 lists the Commercial Alginate-based wound dressings[38].

Table 1: Commercial alginate-based wound dressings

Product	Manufacturer
AlgiDERM	Bard
AlgiSite	Smith & Nephew, Inc
Algosteril	Johnson & Johnson
CarraSorb H	Carrington
CURASORB, CURASORB Zinc	Kendall
Dermacea	Sherwood-Davis & Geck
FyBron	B. Braun
Gentell	Gentell
Hyperion Advanced Alginate Dressing	Hyperion Medical, Inc.
KALTOSTAT	ConvaTec
KALGINATE	DeRoyal
Maxorb	Medline
PolyMem	Ferris Mfg.
Restore	Hollister
SORBSAN	Dow Hickam
SeaSorb	Coloplast Sween Corp.
Tegagen HG, Tegagen HI	3M Health Care

Chitin and chitosan fibers

Chitin and chitosan are known biodegradable natural polymers based on polysaccarides, which are extracted from various animals and plants. Chitin is one of the most abundant organic materials easily obtained from natural sources, e.g., the shells of crustaceans (lobsters, shrimps, crabs, and etc.) or the broth from the industrial fungal processes[39, 40].

Chitin fiber was first reported in 1926[41]. Like chitin, chitosan is also known to have wound-healing acceleration properties and a number of studies have shown that chitosan fibers have unique properties as a suture and wound dressing material[42].

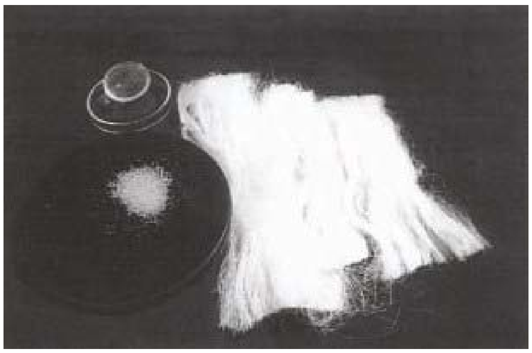

Fig. 5: Chitin gels, fibers and beads (dehydrated)[42]

Chitosan, the fully or partially deacetylated chitin, is soluble to acetic acid and other organic solvents. Due to its good solubility, chitosan, as the modified biopolymer, has the wide scale of the application field[43]. N-acetylglucosamine is common structural unit in chitin and hyaluronic acid, a material necessary in wound repair. It is therefore likely for the chitinous material to promote tissue regeneration and repair. Chitin and chitosan having many key properties relevant to the biomedical application,[44] were shown in Table 2.

Table 2: Biological properties of chitin and chitosan

- Bio compatible: natural polymer; Biodegradable to normal body constituents; safe and non toxic
- Binds to mammalian and microbial cells aggressively
- Regenerative effect on connective gum tissue
- Accelerates the formation of osteoblasts, responsible for bone formation
- Hemostatic
- Bacteriostatic
- Fungistatic
- Spermicidal
- Antitumor
- Anticholesteremic
- Central nervous system depressant
- Immunoadjuvant

Chitin and chitosan are the only basic polysocrides with pH values below ~ 6.5. chitosan solution carries a positive charge.[45] Chitosan exists naturally only in a few species of fungi. Chitin and chitosan consist of 2-acetamido-2-deoxy-β-D-glucose and 2-amino-2-deoxy-β-D glucose as repeating units respectively. Chitin is chemically identical to cellulose except that secondary hydroxyl group on the alpha carbon atom of the cellulose molecule is substituted with acetoamide groups, as shown in Figure 6. Chitin and Chitosan fibers are unique as they carry an acetamido/amino functionality that impart many biological properties. Chitosan fiber is unlike other fibers is unique: it carries a positive ionic charge, it has remarkable affinity to proteins, it can be functionalized and it is renewable [46].

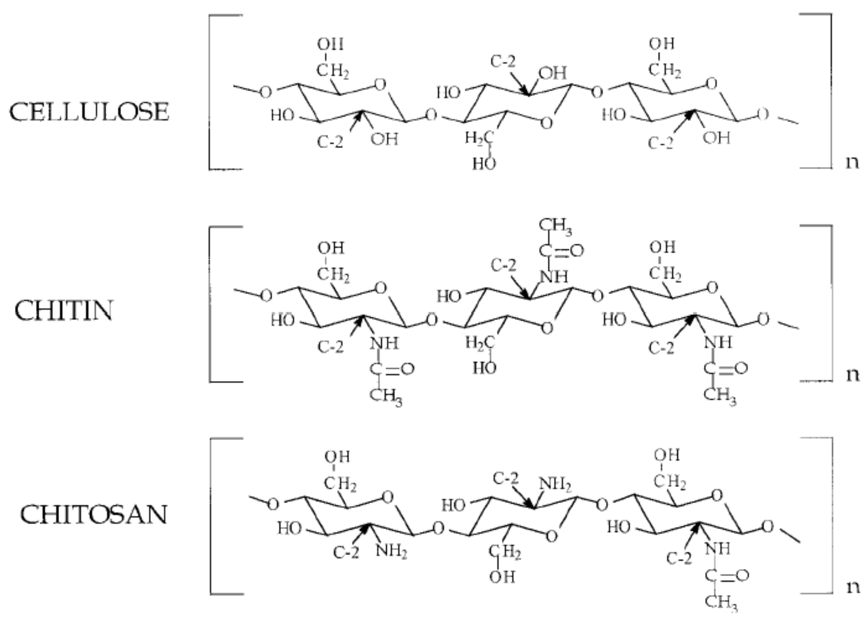

Fig. 6: Molecular structures of cellulose, chitin, chitosan [47]

Chitin and chitosan fibers are produced by a wet-spinning process, but rarely by a dry-spinning process. When using wet-spinning process to produce the fibers, the two polymers firstly are dissolved in a solvent and then the polymer solution is extruded via fine holes (especially through a viscose-type spinneret[48]) into a non-solvent (coagulant) at 45-50 ^{0}C. The polymer precipitates out in the form of a filament, which can be washed, drawn, and dried to form the fibers.

Chitin and chitosan in wound dressings

Especially using the two polymers in medical applications has attracted interest because of having a lot of advantages as being natural renewable resources, being the most abundant polymeric material in the earth, biocompatibility, biodegradability, easy availability, nontoxicity,

the ability to chelate heavy metals, Interestingly, some antibacterial and antifimgal activities have been described with chitosan and modified chitosan derivatives. Due to the antimicrobial property both Chitin and chitosan has long been known as being able to accelerate the wound-healing process. It has been shown that by applying chitin dressings, the wound healing process can be accelerated by up to 75% [50].

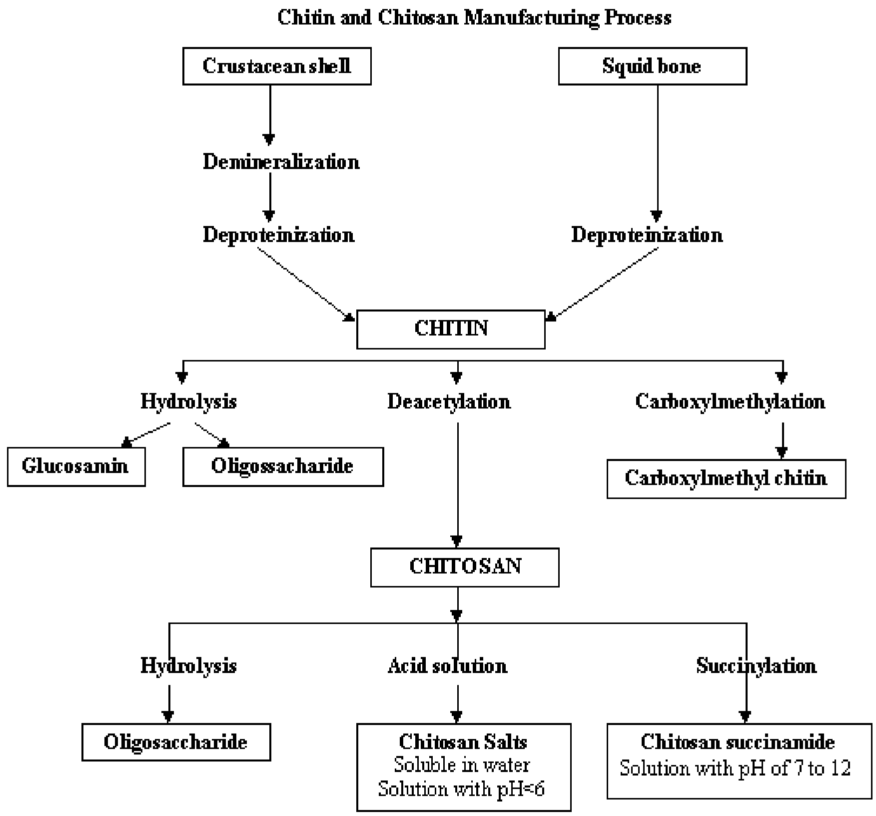

Fig. 7: Chitin and chitosan manufacturing process[49]

The origins for chitin being propounded as a candidate for wound healing can be traced back to the breakthrough paper by Prudden et al. [51] Based on their study of the use of cartilage in accelerating wound healing, they deduced that the active component was N-acetyl-glucosamine. To verify their hunch, chitin obtained from shrimp and fungal sources were applied as topical powders on wounds. Eventually, results confirmed chitin's accelerating effect in wound healing. The authors proposed that the chitin powders released N-acetyl-glucosamine as a consequence of the breakdown of chitin by the enzyme lysozyme, abundantly present in fresh and healing wounds. It is of significance to note that fungal chitin was resorbed twice as fast as shrimp chitin.

In another study, a chlorhexidine containing chitosan-based wound dressing was shown to have antibacterial efficacy towards the primary wound bed bacteria, *Pseudomonas aeruginosa* and *Staphyloccocus aureus.*[52]

Chitosan can be easily dissolved in aqueous solutions of almost all the organic and inorganic acids because of the primary amine group on the C-2 position of the glucose residue. Chitosan fibers can be made by first dissolving it in an aqueous acidic solution and then extruding the solution through fine holes into a coagulation bath of a dilute alkali solution. Chitosan precipitates out in the form of a filament which can be washed, stretched and dried to form fibers for the production of wound dressings [53].

K. S. Pillai et al[54] reported that The electrospinning technology opens up enormous possibilities for the preparation of chitin and Chitosan mats for antimicrobial and wound healing applications. Spasova and coworkers propose that the Chitosan nano-fibrous obtained by electrospun mats are promising for wound healing applications as they could demonstrate the antibacterial activity of the photo-crosslinked electrospun mats against Staphylococcus aureus and Escherichia coli [55]. A naturally occurring antibacterial agent was derived from chitosan obtained from gab cell. It was effective against both pathogenic Bram positive and Gram negative bacteria and also prevented from forming offensive odours.

Ignotava et al prepared fibrous poly(L-lactide) (PLLA) and bicomponent PLLA/poly(ethylene glycol) mats by electrospinning and then were coated with Chitosan [56]. Microbiological studies against Staphylococcus aureus revealed that the Chitosan coating imparts antibacterial activity to the hybrid mats. The combined haemostatic and antibacterial activities render these novel materials suitable for wound-healing applications . Torres-Giner et al. studied the effect of a number of parameters (including solvent nature, polymer origin, molecular weight and spinning conditions) on the morphology to ascertain the antimicrobial properties of the generated biofibers of Chitosan and to relate them to its chemical structure [57].

Researchers are focusing on the modification of the structure of chitin polysaccharides with a view of enhancing their mechanical and chemical property. Chitin with enhanced tensile strength and modulus was produced from chitin/chitosan acetate/formate polymer. At present very few commercial dressings based chitin and chitosan fibers available in market.[58] As far as chitin based commercial wound dressings are concerned, in Japan one product is commercially available called Beschitin®, which is a non woven fabric manufactured from chitin filament.

Chitin and chitosan in tissue engineering

Chitosan is among one of the many candidates suitable as a biodegradable polymer to form scaffolds in Tissue Engineering[59]. It is readily fabricated into various shapes and sizes, processed into fiber, knitted and woven. This provides the capability of pre-fabricating the scaffold in the shape of desired tissues or organs that can include 3-D scaffold structures. Chitosan is also insoluble at the physiological pH of 7 and therefore maintains its structure once formed. Furthermore, its monomeric constituent is similar to the extracellular matrix environment of humans, and when biodegraded, should generate non-toxic, non-harmful residues. Finally, the prospect to chemically modify chitosan at its C-6 and N-2 positions to impart desired features offers great flexibility to this biopolymer. Chitin can be transformed into various forms of scaffolds in future may include oligomeric and derivatized forms of chitin as vehicles to organize cells or even tissue in the Tissue Engineering endeavor.

Chitin and chitosan in drug delivery

Controlled drug delivery is described as phasing of drug administration to the needs of the condition at hand so that an optimal amount of drug is used to cure or control the condition in a minimum Time[60]. Some early investigations of chitin as possible drug delivery vehicles involve the preparation of chitin and chitosan gels. In a typical preparation, chitin was first dissolved in hexafluro-2- propanol and a solubilized drug was added. Subsequent evaporation of solvent and drying gave the drug containing chitin gel. Dried chitosan gels were similarly obtained except the solvent used was aqueous acetic acid.

The influence of film type and thickness on drug release was studied by Kanke et al[61] involving a drug loaded chitosan monolayer (ML) film, a double layered (DL) film comprising of an ML film plus a drug free ML film and a double layered DL-N film where the chitosan in the drug containing ML film was N-acetylated. TM *In vitro* release studies showed that the best sustained-release profile was obtained with the DL-N film. Chitin and chitosan have also been used as tableting agents to enhance the dissolution properties of poorly soluble drugs[62.] Tokura et al have summarized the possibility of carboxymethyl-chitin (CM-chitin) as a candidate for drug delivery in pro-drug platforms, adsorption and entrapment material or a combination of adsorption and entrapment [63].

In current days the chitin community has become increasingly enthusiastic over the biomedical opportunities for this material. As a result, the breadth of biomedical applications spanned by chitin and chitosan continues to expand, making chitin a material increasingly impossible to ignore. The possibilities appear endless. The surge of chitin in the biomedical direction is rooted from the postulation that there would be better acceptance of the material by the human biological system due to its natural origins and close analogy to body constituents. Together with the potential of limitless supply of this renewable material, these major influences have perpetually thrust chitin to the forefront as a biomaterial.

CONCLUSION

Textile materials are very important in all aspects of medicine, surgery and healthcare and extend of applications to which the materials used because of the versatility of textile materials. Advances in fiber sciences have resulted with a new breed of wound dressing, which contributing healing process in an effective way. In this paper, a brief overview of application of the polysaccharide fibers in wound management was presented. Further it discusses about the different properties and requirements of various polysaccharide fibers to the healing of different wounds. In particular special properties of Alginate, chitin and chitosan were summarized with the various experimental results of different researchers.

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