Recent developments in fibres and materials for wound management

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During the last thirty years, occlusive dressings have brought a revolution in wound management. The most important advantage of an occlusive dressing is the creation of a moist wound environment which is believed to be beneficial for wound healing. This concept has resulted in a rapidly growing world-wide market for dressings with a variety of characteristics. This review focuses on the high performance fibres and materials currently used in the fabrication of wound care products. These range from natural and modified polysaccharides and proteins to synthetic materials. The products include the most popular materials currently on the market and those patented with future potential in terms of performance and commercial value. The composition, chemistry during manufacture, physical and medical characteristics, advantages and limitations during application have been reported. Based on the present research and existing products, some new and futuristic approaches, especially in the development of novel fibres for wound healing, have been proposed.

Keywords: Alginate, Chitin, Chitosan, Collagen, Wound dressings

1 Introduction

The fibres and polymers currently used to fabricate wound healing and health-care products are numerous, such as natural and modified cellulose, alginites, chitin/chitosan, collagen, hydrocolloid and synthetic fibres or hydrogels. Depending on the materials used, they can be divided into three categories, i.e. natural or modified polysaccharides, proteins and synthetic polymers. Various fibres play a very important role in the production of these products. However, due to the speciality of these fibres, there is no comprehensive review on the subject. This review will concentrate on the recent progress in the development of new wound healing products from these materials. The current developments in fibres and polymers as well as the future potential in this crucial area are reviewed and discussed.

2 Alginate

The success of alginate fibres in the manufacturing of wound-healing products is shown by the rate of growth of their use globally. In Europe, the turnover of alginate dressings was $29 million in 1993 and is expected to increase to $44 million in 19981. They are suitable for wounds with moderate to heavy wound exudate. The advantages are that they are hemostatic, highly absorbent, and suitable for full thickness wounds. They require a reduced frequency of dressing changes and promote gelation and moist healing but they still have some limitations that they always need a secondary dressing and are not suitable for dry wounds.

2.1 Structures and Properties

Alginites are naturally occurring polysaccharides in seaweed. The fibrosity of this seaweed derives from its content of long chain molecules of algamic acid or its salts. Algamic acid is a polymer of D-mannuronic acid (M) and L-guluronic acid (G) linked ~4)-ß-D-ManA-(1 and ~4)-α-L-GulA-(1 shown in Fig. 1.

![Fig. 1—Structures of β-D-mannuronic acid (M) and α-L-guluronic acid (G) residues](image-url)
These two monomers may be linked in blocks, e.g. -M-M-M-G-G-G-G-, or mixed, e.g. -M-G-G-M-G-M-G- (ref. 3). The relative proportion of mannuronic to guluronic acid in alginate fibre significantly affects the properties of the end product. Alginate forms a gel when divalent metal ions, e.g. Ca²⁺, crosslinks the neighbouring blocks. For a GG block, poly-L-guluronate, the stereochemical structure of the top repeating units, creates a space where the calcium ions can be positioned (Fig. 2). This will lead to a so-called 'egg-box' structure schematically represented in Fig. 3. However, no such binding is observed in poly-D-mannuronate blocks⁴,⁵. This is responsible for the differences in properties between high G and high M alginates. Alginates extracted from different sources differ in the relative proportions of guluronate and mannuronate, with seaweed stems usually containing a high concentration of guluronate (high G). As a result of the strong calcium binding ability, high G alginate forms stronger gels than the high M alginate.

2.2 Alginate Fibres and Dressings

The development of alginate fibre spinning is attributed to Speakman and his pioneering work in 1939-1940². The general procedure of making calcium alginate fibres is now well established, i.e. extruding Na-alginate aqueous solution into a Ca²⁺ containing coagulation bath. Alginate fibre, typically calcium alginate, was originally expected to be an alternative to textile fibres like viscose rayon. The yarn made from alginate has a dry strength comparable with that of viscose rayon, but its wet strength is much lower, which makes it unsuitable as a traditional textile material. However, in the past two decades, following the moist healing concept⁶, alginate fibre has become one of the most important materials for wound dressings. The moist condition is found to be ideal for wound healing⁷. When alginate fibrous dressing absorbs exudate from wound, a jelly-like material is formed and a moist micro-environment is created during the course of healing. At the same time, calcium alginate rapidly releases calcium ions in exchange for sodium ions on contact with blood, which stimulates both platelet activation and whole blood coagulation to a greater extent than that achieved by simple contact with surgical gauze⁸. This explains the hemostatic performance of these particular fibres. The in-situ generation of a moist healing environment and the consequent high absorbency of the alginate dressings are two of the outstanding properties which make the alginate dressing one of the most versatile wound dressings available today.

Most of the commercially available dressings are fabricated into nonwoven or ropes for deeper packing. There are many alginate products currently on the market, e.g. Kaltostat, Sorbsan, Algosteril, etc. Among them, Sorbsan is a high M alginate while Algosteril and Kaltostat are high G ones. Based on an early-established technique, Kaltostat was modified to a so-called new generation calcium/sodium alginate dressing. The calcium/sodium alginate fibres are made by post-treatment of the Ca-alginate fibre spun by the normal wet spinning process. The Ca-alginate fibre is first treated with hydrochloric acid and then sodium carbonate. In this process, part of the calcium ions in the fibres are first replaced by the hydrogen ions which are then replaced by the sodium ions. Since the sodium alginate is water soluble, the resultant calcium/sodium alginate is more absorbent than the normal calcium alginate fibre. The absorbency of these fibres⁹ is shown in Table 1. Traditional gauze was used as a control.

It can be seen that the water uptake or absorbency is in the order of Ca/Na alginate > high
Table 1—The absorbency of different alginate dressings

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>High M Ca Alginate</th>
<th>High G Ca Alginate</th>
<th>High G Ca/Na Alginate</th>
<th>Gauze</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water uptake, %</td>
<td>2.91</td>
<td>1.82</td>
<td>7.70</td>
<td>1.30</td>
</tr>
<tr>
<td>Saline uptake, %</td>
<td>13.86</td>
<td>5.22</td>
<td>5.86</td>
<td>1.30</td>
</tr>
<tr>
<td>Absorbency, g/g</td>
<td>16.72</td>
<td>14.24</td>
<td>17.29</td>
<td>9.60</td>
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</table>

M alginate > high G alginate, while the saline uptake is in the order of high M alginate > Ca/Na alginate > high G alginate. This is easily understood from their structural differences.

Besides these traditional Ca or Ca/Na alginate dressings, some new products are being developed or marketed. One of such examples is Fibracol® which is produced by Johnson & Johnson Medical Inc. This is a collagen-containing alginate dressing. It was claimed that this is the first advanced dressing composed of both collagen and alginate and is suitable for foot ulcers and heel pressure sores.

Another alginate-containing dressing is fabricated in a quite different way. It comprises an absorbent pad impregnated with calcium alginate or mixture of calcium and sodium alginate. The absorbent pad is made of woven or nonwoven fabric from cotton, cellulosic fibres alone or blend with polyester or polyolefin. The pad is first dipped in 1-10% aqueous sodium alginate solution followed by treatment with 1-10% CaCl₂ aqueous solution. During the coagulation, Na⁺ ions in the impregnated pad would be partially replaced by Ca²⁺ and the pad is crosslinked at the same time. After the treatment, the pad is squeezed to remove the excess liquid and dried. The final alginate content is 5% in which 68% is Na-alginate and 32% is Ca-alginate. The dried pad needs a mechanical softening treatment before use. The benefits claimed by the inventor are desired hemostatic property, softness and cost-effectiveness.

Quite recently, some active ingredients have been incorporated into alginate fibres to improve the traditional properties of the products. One of the methods was to incorporate silver-based antibacterial to the fibre. Silver sulphadiazine (SSD) containing alginate fibres and silver-alginate fibre were produced using various incorporation techniques. SSD was introduced either during the preparation of the spinning solution or incorporated at the coagulation stage.

3 Chitin/Chitosan
3.1 Structures and Biomedical Properties

Chitin is one of the most abundant polysaccharides found in nature. At present, the commercial source of chitin is from shrimp shells but it also occurs in many fungi. Chitosan is the partially deacetylated form of chitin. A sharp nomenclature border between them has not yet been defined. They are composed of two common sugars, D-glucosamine and N-acetyl-D-glucosamine, as shown in Fig. 4. Chitin and chitosan key properties relevant to biomedical applications are listed in Table 2 (refs 13 & 14).

These properties result from the unique structures of chitin and chitosan. Most commercial polysaccharides, e.g. cellulose, pectin, alginic acid,
starch, etc. are neutral or acidic. Chitin and chitosan are the only basic polysaccharides. At pH values below ~6.5, chitosan in solution carries a positive charge. This makes it readily react with a variety of negatively charged materials or polyanions. Chitin and chitosan can be fabricated into many desired forms, such as solution/gel, beads, film/membrane, sponge, fibres, etc. Among them, film and fibre forms are very important in the production of wound dressings. Although both chitin and chitosan can be made into fibres and films, chitosan fibre is much easier to make due to its much better solubility.

### 3.2 Spinning Techniques of Chitin/Chitosan Fibres

Numerous methods of spinning chitin fibre have been reported since Von Weimann reported the first solution of chitin that could be formed into a 'ropy-plastic' state in 1926. He prepared the solution using inorganic salts capable of strong hydration\(^{15}\), such as LiCNS, Ca(CNS)\(_2\), CaI\(_2\), CaCl\(_2\), etc. After that a great number of solvent systems including organic or mixture of inorganic salts and organic solvents were introduced\(^{17-22}\). Some of the solvent systems and chitin fibre properties are listed in Table 3 (ref. 23).

Although some of these systems could result in high quality spinning dopes and fibre properties, the solution preparation and fibre spinning and post-treatment process are quite complicated and time-consuming. In contrast to chitin, chitosan has much better solubility due to the ease of forming ammonium salts in aqueous dilute acid solution, typically acetic acid. The preparation of aqueous chitosan solution in acetic acid was first reported by Rigby\(^{24}\). However, some other acids were also explored by many researchers, such as formic, 10% citric, pyruvic and lactic acids\(^{25}\). The properties of chitosan fibres are comparable to those of chitin fibres\(^{26}\). The chitosan fibres

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<table>
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<tr>
<th>Table 2—Chitosan's biological properties</th>
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<tr>
<td><strong>Biocompatible:</strong> natural polymer; biodegradable to normal body constituents; safe and non-toxic</td>
</tr>
<tr>
<td><strong>Binds to mammalian and microbial cells aggressively</strong></td>
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<tr>
<td><strong>Regenerative effect on connective gum tissue</strong></td>
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<td><strong>Accelerates the formation of osteoblasts, responsible for bone formation</strong></td>
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<tr>
<td><strong>Hemostatic</strong></td>
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<td><strong>Bacteriostatic</strong></td>
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<td><strong>Fungistatic</strong></td>
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<tr>
<td><strong>Spermicidal</strong></td>
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<tr>
<td><strong>Antitumor</strong></td>
</tr>
<tr>
<td><strong>Anticholesterolemic</strong></td>
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<tr>
<td><strong>Accelerates bone formation</strong></td>
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<td><strong>Central nervous system depressant</strong></td>
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<td><strong>Immunoadjuvant</strong></td>
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<table>
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<th>Table 3—Spinning conditions and fibre properties</th>
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<tr>
<td><strong>Solvent (v/v)</strong> Coagulation</td>
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<tr>
<td><strong>1st</strong></td>
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<tr>
<td>Solvent (v/v)</td>
</tr>
<tr>
<td>Coagulation</td>
</tr>
<tr>
<td>EtOAc</td>
</tr>
<tr>
<td>iPE</td>
</tr>
<tr>
<td>Stretch ratio</td>
</tr>
<tr>
<td>Tenacity, g/den</td>
</tr>
<tr>
<td>Dry (20°C, 65% R H)</td>
</tr>
<tr>
<td>Wet (20°C, 100% R H)</td>
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<tr>
<td>Elongation, %</td>
</tr>
<tr>
<td>Dry (20°C, 65% R H)</td>
</tr>
<tr>
<td>Wet (20°C, 100% R H)</td>
</tr>
<tr>
<td>Knot strength, g/den</td>
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<tr>
<td>Denier</td>
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</table>

Abbreviations: FA—formic acid; DCA—dichloroacetic acid; iPE—isopropyl ether; EtOAc—ethyl acetate; Ace—acetone; and AcOH—acetic acid.
obtained from the above methods could be converted into chitin again after fibre formation.

3.3 Chitin- and Chitosan-based Dressings

As described above, chitin/chitosan have many distinctive biomedical properties and have been applied in many different industrial areas already, such as food, cosmetic and pharmaceutical industries. However, chitin-based wound healing products are still at the early stage of research. Most of these work showed positive results when chitin or chitosan was used in accelerating wound healing. Biagini et al.27 developed a chitosan derivative, N-carboxybutyl chitosan, dressing for treating the plastic surgery donor sites. The solution of N-carboxybutyl chitosan was dialysed and freeze-dried to produce a soft and flexible pad, which was sterilised and applied to the wound. They reported that this dressing could promote ordered tissue regeneration. Compared to control donor sites, better histoarchitectural order, better vascularization and the absence of inflammatory cells were observed at the dermal level, whilst fewer aspects of proliferation of the malpighian layer were reported at the epidermal level.

Another research group at the British Textile Technology Group (BTTG) patented a procedure for making chitin-based fibrous dressing.28-31 However, in their method the chitin/chitosan fibres were not made by the traditional fibre-spinning technique and the raw materials were not from shrimp shell but from microfungi instead. Their procedure can be summarised as follows:

(i) Micro-fungal mycelia preparation from a culture of Mucor mucedo growing in a nutrient solution,
(ii) Culture washing and treatment with NaOH to remove protein and precipitate chitin/chitosan,
(iii) Bleaching and further washing,
(iv) Preparation of the dispersion of the fibres using paper-making equipment, and
(v) Filtration and wet-laid matt preparation; mixing with other fibres to give mechanical strength.

This is a very novel method which uses non-animal source as the raw material and the resulting microfungal fibres are totally different from the normal spun fibres as shown in Fig. 5. They have highly branched and irregular structures. The fibres are unmanageably brittle when they are allowed to dry and a plasticiser has to be associated with the whole process and a wet-laid matt is the basic product.

Another surgical dressing was developed by Sparkes and Murray32. This dressing is made of chitosan-gelatin complex. The procedure involves dissolving the chitosan in water in the presence of a suitable acid, resulting in a pH in solution of about 2-3, followed by adding the gelatin dissolved in water. The weight ratio of chitosan and gelatin is 3:1 to 1:3. To reduce the stiffness of the resulting dressing a certain amount of plasticisers such as glycerol and sorbitol could be added into the mixture. Dressing film was cast from this solution on a flat plate and dried at room temperature. It was claimed that in contrast to the conventional biological dressings this experimental dressing displayed excellent adhesion to subcutaneous fat.

Nara et al.33 patented a wound dressing comprising a nonwoven fabric composed of chitin fibres made by wet spinning technique. In one of the examples, chitin powder (available from Kyowa Yushi Co. Ltd.) was ground to 100 mesh and treated in 1N HCl for 1 h at 4°C. It was then heated to 90°C where it was treated for 3 h in a 3% NaOH solution to remove calcium and protein in the chitin powder, and rinsed repeatedly followed by drying. The resultant chitin had a viscosity of 256 cP at 30°C when it was dissolved in a dimethylacetamide solution containing 8 wt% NaOH.
lithium chloride to form a 0.2 wt% solution. The chitin was dissolved in a dimethylacetamide solution containing lithium chloride of 7 wt% to form a 7% dope. After filtering and holding to allow defoaming to occur, the dope was transported to a nozzle having a diameter of 0.06 mm and 200 holes from a charged tank under pressure by a gear pump and extruded into butanol at 60°C at the rate of 2.2 g/min. The chitin was coagulated and collected at the speed of 10 m/min. The resultant strand was rinsed with water and dried to obtain a filament of 0.74 dtex with a strength of 2.8 g/den. The filaments were then cut into staple fibres. Nonwoven dressings were made by using polyvinyl alcohol as a fibrous binder.

Muzzarelli recently introduced another chitosan derivative which was believed to be very promising in medical applications. This derivative is 5-methylpyrrolidinone chitosan which was made by a series of chemical reactions. He claimed that this polymer is compatible with other polymer solutions including gelatin, poly(vinyl alcohol), poly(vinyl pyrrolidone) and hyaluronic acid. The advantages claimed by the inventor include healing of wounded meniscal tissues, healing of decubitus ulcers, depression of capsule formation around prostheses, limitation of scar formation and retraction during healing. Some wound dressing samples were prepared in his work from the aqueous solution of this 5-methylpyrrolidinone chitosan which was dialysed and laminated between stainless steel plates and freeze-dried to yield fleeces. It is also claimed that this material could be fabricated into many different forms, such as filaments, nonwoven fabrics, etc. Once applied to a wound, 5-methylpyrrolidinone chitosan becomes immediately available in the form of oligomers produced under the action of lysozyme.

Another chitin derivative, dibutyrylchitin, was spun into fibre recently by a research group at the University of Leeds. Dibutyrylchitin was prepared by treatment of krill chitin with butyric anhydride in the presence of perchloric acid as a catalyst of reaction carried out at 25-30°C. Samples of polymers with molecular weights high enough to form fibres were obtained, and dibutyrylchitin fibres were made by a simple method of dry spinning 20-22% solution in acetone. The results showed that the fibres had tensile properties similar to or better than those of chitin and some chitin derivatives. An attempt to convert dibutyrylchitin fibres to chitin fibres was made. It was claimed that chitin fibres with good tensile properties could be obtained by alkaline hydrolysis of dibutyrylchitin fibres without destroying the fibre structure. However, no more information was given about the uses of this fibre.

As far as chitin-based commercial wound dressings are concerned, in Japan one product (Beschitin®, Unitika) is commercially available, which is a nonwoven fabric manufactured from chitin filaments. At present, very few commercial dressings based on chitin or chitosan fibre are available in the market.

4 Synthetic Fibre-based Products

In many high performance dressings, synthetic fibres are incorporated or blended to enhance the properties of the final products, such as absorbency, strength, antibacterial performance, etc.

One of these products was developed by Cheil Synthetics of Kyungsan, Korea. The procedure can be summarised as follows:

(i) Dissolving a mordenite (0.5-2.5% based on the final yarn), a class of antibacterial zeolite, into a polyurethane with dimethylformamide, and
(ii) Spinning the solution into fibres by wet spinning technique.

It may be noted that before being dissolved, the mordenite is boiled in a strong acid to give a silica/alumina molar ratio of 12-33. It is then ion-exchanged with an antibacterial metal, Ag, Cu or Zn, having a controlled average particle size ranging from 0.5 μm to 2.0 μm. The mordenite (zeolite) is a porous material with a very high surface area. The metal ion is firmly bonded to the zeolite so the resistance to bacterial attack is effective for a long time.

Another similar idea, patented recently in a US patent, is to treat acrylic or modacyclic fibre with a copper compound containing a borate, carbonate or a mixture thereof. Besides acrylic fibres, some other fibres can also be used as a substrate, such as polyester, polyamide, etc. They may be graft-polymerised with acrylonitrile prior to treatment with a copper compound. Another technique of developing antibacterial fibres is by incorporating...
antibacterial additives into the spinning solution or melt. A technique developed by Filament Fibre Technology, Salisbury, North Carolina, USA, is to add bacteriostat of Microban into polypropylene followed by extrusion.

Another class of synthetic materials is synthetic biodegradable fibres. One of such examples was introduced by Unitika, Osaka, Japan. The biodegradable fibres were made from poly-ε-caprolactone (PCL) and/or poly-β-propiolactone (PPL) of 0.89-6.7 dtex. Researchers at Du Pont developed another biodegradable material based on a polyester comprising a copolymer of a non-aromatic diacid, e.g. adipic and glutaric acid, and containing alkali metal or alkali earth metal sulpho groups such as metal 5-sulphospiophthalic acid derivatives. When compared to the previous routes, this method is more cost-effective.

The research and development of superabsorbent (SA) polymers and fibres have become active areas for medical and hygiene products. Normally, these materials are not used alone but combined with other materials as a liquid absorbent component. Compared with particulate products, SA fibres show many advantages, e.g. high surface area, fast absorption, flexible handle, and ease of formation of soft products with different shapes to fit the contour of the wound or body. SA fibres have been available since the late 1980s. Currently, there are three different ways of making these fibres of which the first is to fix SA powders onto or into a fibre substrate. The second is to modify non-SA fibres to increase their absorbency significantly, such as cellulose, acrylic fibres, etc. The last one is to synthesise SA polymers which can be spun into fibres by normal spinning techniques and then crosslink them.

A recent example of the first type combines SA powders and thermoplastic fibres made from polyolefin, PET, polyamides or copolymers of ethylene and acrylic/methacrylic acid, or ethylene and vinyl acetate into a nonwoven matrix. The nonwoven fabric and SA powders are thermal bonded by those thermoplastic fibres present. Another superabsorbent nonwoven was made by a similar method except using wet-laying instead of using the bonding technique. The wet matt was made from the mixture of SA particles, fibres (wood pulp and polyester), and acrylic adhesives. The SA particles were synthesised with acrylic or vinyl monomers and slightly crosslinked by polyfunctional reagents. The wet matt was dried at 250°C to form a nonwoven fabric.

The earliest products developed by modifying non-superabsorbent fibres (method two above) were based on modified cellulose, such as cross-linked cellulose or cellulose derivatives, grafted cellulose, etc. Crosslinked cellulose is obtained by combining at least two inter- or intra-molecular hydroxyl groups. A variety of crosslinking agents are available such as formaldehyde, methylolated nitrogen compounds, dicarboxylic acids, disiocyanates, etc. Crosslinked carboxymethyl cellulose (CMC) is another way to improve the absorbency of CMC fibres. Alternatively, grafting to cellulose may enhance water absorbency and offers another technique. Monomers such as acrylonitrile, acrylamide and various acrylate and methacrylate esters and their mixtures may be grafted following by saponification to sodium polyacrylate. More recently, acrylic fibres have been used as a raw material and hydrolysed to convert nitrile groups into carboxylic acid groups, thus yielding a superabsorbent fibre.

The last method mentioned above is to synthesise superabsorbent polymers directly. These include crosslinked polyacrylates, poly(maleic anhydride), poly(vinyl alcohol), poly(ethylene oxide), etc. Fig. 6 is a typical example of crosslinked polyacrylate.

However, most of the products obtained from the last method are not in fibrous form. The problem is that once crosslinking has occurred in a polymer, it is not possible to convert it into a fibre. Without crosslinking, however, the material is not stable enough when wetted. One solution to this problem was discovered during the late 1980s and involved producing the fibre first and then crosslinking it to produce a network of closely tied polymer chains with a huge internal surface area. Courtaulds (Coventry, UK) and Camelot Superabsorbents Ltd (Alberta, Canada) are believed to be the leading companies in commercialising these fibres. Courtaulds, working jointly with Allied Colloids Ltd, has developed a series of SA fibres initially from a substantially linear polymer from a water-soluble ethenically...
unsaturated monomer blend. The polymer contained carboxylic acid and hydroxylic groups linked by ester linkages. Due to its brittleness, a plasticising monomer should be added, such as an alkyl ester of (meth)acrylic acid or other unsaturated carboxylic acid, as well as vinylacetate, etc. After the initial achievement, they launched their second generation product and market it as Oasis°79.°8 2. The superabsorbent fibre Fibersorb®, made in Camelot, is based on salts of olefin/alkyl carboxylate copolymers.

5 Collagen- and Other Protein-based Dressings

5.1 Structure and Properties of Collagen

Collagen is the principal structural protein in the vertebrate body. The extracellular proteins of the main connective tissues consist of 90% or more collagen in tendon and bone and more than 50% in the skin. Thus, collagen has an excellent biocompatibility which makes it a popular choice as a major component of artificial tissue and wound dressings 83 - 85. Collagen is composed of three polypeptide chains which form a triple-chain helix 86. These triple-chain helices assemble into microfibrils and then fibrils 87. Native fibrillar collagen is the most important polymorphic form of collagen, which makes the fibrous dressing product possible. The methods for isolation and purification of collagen vary and are largely dependent on the sources, but they should keep the helix structure essentially intact. Soluble collagen may be obtained by chemical or enzymatic methods and the procedures for preparing and

characterising soluble collagen have been reviewed 88,89. Extensively crosslinked collagen forms, e.g. skin or tendon, can be dispersed as a fine fibrillar suspensions. However, collagen in solution can be reconstituted into fibrils that have a structure similar to that of native fibrils from which it was originally extracted 90. The most interesting applications of collagen are biomedical which are summarised in Table 4 (ref. 86).

The attractiveness of collagen as a biomaterial is largely due to the fact that it is a natural material of low immunogenicity and is therefore seen by the body as a normal constituent rather than foreign matter. However, the conversion of collagen into a useful form for generating products unavoidably changes its properties more or less and may lessen its apparent advantage over other polymers. It is here that the challenge exists at the present time.

5.2 Dressings Manufacturing

Collagen-based wound dressings have been shown to inhibit wound contraction in vivo 91. Morphological studies suggest that collagen-based wound dressings enhance the deposition of oriented organised collagen fibres characteristic of the remodelling phase of wound healing 92. One Israeli company has revealed that it has developed a wide spectrum of collagen-based products, including biological wound dressings, bone implants, cosmetics, hemostatic sponges, etc. They claim that product prototypes are already completed and tested in pre-clinical trials 93.

Researchers at Robert Wood Johnson Medical School have reported a technique of improving the mechanical properties of collagen fibres by
crosslinking. They used severe dehydration at elevated temperatures (dehydrothermal crosslinking) to crosslink the collagen fibres. Based on the relationship between mechanical properties and crosslinking times and temperatures, the optimum mechanical properties were obtained in 5 days at 110°C. The strength and modulus were 91.8 and 896 MPa respectively.94

Besides the naturally occurring collagen fibres, some synthetic collagen or polypeptide fibres have been reported. A synthetic collagen fibre was introduced in University of Medicine and Dentistry of New Jersey95. Crosslinked fibres with diameter of 20-50 µm were embedded in an uncrosslinked loose matrix. Normally, there is a certain degree of degradation observed during the preparation of polypeptide solution. This problem was solved by the researchers at Du Pont96. They prepared a spinnable 5-30% polypeptide solution using a mixed solvent system containing hexafluoroisopropanol, formic acid and at least one lithium halide (LiCl or LiBr). Ideally, the solution should be liquid crystalline and the spinning dope could be extruded into a liquid coagulation bath or an inert gas.

Another protein-based material, gelatin, has been used widely in some commercial hydrocolloid dressings. Gelatin is a denatured collagen and is obviously a biocompatible material. However, no further information could be obtained regarding the possibility of fibrous wound dressings based on this material. Quite interestingly, some attempts were made 60 years ago to convert this material into sheets, films, or even filaments97. Some distinctive properties could be predicted, such as automatic gelation, high absorbency, etc. More importantly, the raw material supply is well established and inexpensive.

Quite recently, Collagen Corp. (Palo Alto, California, USA) patented a technique of improving the properties of collagen products98. In the existing commercially available products, the non-crosslinked fibrillar collagen composites tend to contain a broad range of fibre sizes. When they are used to prepare covalently crosslinked conjugates, the crosslinking is not as efficient, complete or strong as might be desired. In this technique, at least 80% of the collagen fibres are 10 µm or less in diameter. They can be conjugated to functionally activated polymers to produce collagen-synthetic conjugates with unique physical and chemical characteristics.

In contrast to the dressing products mentioned above, another wound dressing based on protein fibres was developed by Niigate Hi-Spinners99. With the awareness of the abundance of resources and biocompatibility, they used wool fibres as raw material and modified them by stripping off the outer keratin layers and exposing the non-keratin layers which are hydrophilic and have better affinity for the wound. The keratin layers were stripped away using an oxidising agent under acidic conditions and the treated fibres showed a superior absorption of wound exudate, blastema formation and epithelain regeneration.

6 Miscellaneous

Natural cotton and viscose rayon have been used as wound dressings, e.g. traditional gauze, for a very long time. However, still many modifications have been undertaken to improve their performance.

A patented technique has enabled the cellulose fibre sheet to be more absorbent by mixing cellulose fibres with the CMC powders and low density polyethylene which are attracted by the former due to the static electrical charge100. Crosslinking of the sheet matrix was achieved by compressing it between a pair of heated rollers. A membrane (low density PE film or polyhydroxypropyl cellulose film or CMC film), which is permeable to air and vapour, is laminated onto the absorbent matrix. Solvent spun cellulose fibres have been commercialised by Lenzing AG in Austria and Courtaulds in UK. These fibres have been significantly noticed for uses in medical and hygiene products101.

Finally, two very recent techniques involve the manufacturing of antimicrobial or antibacterial fibres, e.g. Hoechst Celanese’s MicroSafe AM and Fuji Spinning Co.’s Chitopoly fibres102.

7 Summary

Although the primary scientific literature does not contain much fundamental information relating to fibres used for medication and especially for wound management, a large number of fibres has been used or developed for various applications. In
addition, a significant number of published patents disclose many novel techniques for the production of fibres for medical uses. This review has attempted to increase the understanding of the importance and characteristics of these fibres. Polymers from natural sources, e.g. polysaccharides and polypeptides, are becoming more and more important especially for the contact layers in dressing adjacent to the body due to their desirable biomedical properties. In view of the products and techniques discussed in this review, the following aspects will be of great interest both for industrial and academic institutions:

- Exploration of the advantages of new materials which have distinctive biomedical properties and well-established production techniques and raw material supplying chains;
- Improvement in the performance of the existing products, such as those based on alginate, in terms of liquid and odour absorbency, integrity and wound healing properties by structural modification and incorporation of reactive ingredients; and
- Fabrication of novel structures and even "smart" dressings to enhance their suitability for the treatment of various wound types and give indications of their performance during the wound-healing process.

References
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