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Chitosan Medical Dressings

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1) *This article is a review of research & development works into medical dressings based on chitosan, realised in the Institute of Chemical Fibres, all of rhem initiated and directed by the late* ***Professor Henryk Struszczyk Ph.D., D.Sc.****, who also was the co-author of the scientific report and articles connected with these works.*

Abstract
Biopolymer chitosan manifests properties that open up a wide span of applications in many sectors, mainly medicine. Examples are presented of well-known uses of chitosan in medical dressings, including haemostatic preparations. On the basis of this background, a survey is made of the research and results achieved in the Institute of Chemical Fibres in the field of chitosan-based dressings.

Key words: *chitosan, medicine, wound dressings.*

Introduction

Chitosan is a high-molecular copolymer with acetyloglucosamine and glucosamine radicals in its chain. After dissolution in diluted organic and inorganic acids, it forms viscid polyelectrolytes. Solutions of chitosan are prone to yield fibres, film and coatings. Its good miscibility with other polymers means that complexes and chelates are readily formed. The presence of active groups in chitosan molecules allows for easy chemical modification. This is why chitosan is used in many fields, including medicine [1], namely its specific biological features like biodegradability, biocompatibility, antibacterial activity and ability to bind lipids, thus reducing cholesterol level (LDL).

Potential applications of chitosan in medicine can only be exploited if its usable forms are properly developed and prepared. In solution and gel, it can be used as a bacteriostatic, fungistatic and coating agent. Gels and suspensions may play the role of carriers for slow release or controlled action of drugs, as an immobilising medium and an encapsulation material. Film and membranes are used in dialysis, contact lenses, dressings and the encapsulation of mammal cells, including cell cultures. Chitosan sponges are used in dressings, and to stop bleeding of mucous membranes. Chitosan fibres there are used as resorbable sutures, non-wovens for dressings, and as drug carriers in the form of hollow fibres.

Extensive investigations are being conducted both in Poland and other countries aimed at the wider use of chitosan in wound dressings. The increasing interest in the material is caused by its biological activity resulting from its susceptibility to degradation under the influence of enzymes present in body fluids such as lysozyme and N-acetylglucosoamidase. The degradation products, being chito-oligomers, are able to stimulate macrophages and positively influence collagen sedimentation, thus accelerating the wound healing process [2].

A properly-selected chitosan also influences blood coagulability, and is therefore used in haemostatic dressings.

Dressing materials based on chitin, chitosan and derivatives are well-known on the market, and are produced mainly in Japan and the US. JEX KK Co produces composite dressings made of synthetic resins, chitosan and materials of collagen and acetylchitiosan [3, 4].

Eisai Co is manufacture of chitin dressings in sponge form (Chitopack C®) or a PET non-woven modified with chitin (Chitopack C®).

The Japanese Unitika Co offers a dressing non-woven of chitosan fibres. The American 3M proposes a chitosan gel preparation (Tegasorb®) and a hydrocolloid (Tegaderm®) designed for the healing of extensive internal wounds [5].

The University of Washington Medical Center (USA) is the producer of a chitosan dressing material to regenerate skin after serious second- and third-degree burns [6].

In 2002 a chitosan dressing for battlefield uses was devised by HemCon Bandage™ USA. It gained importance following the Iraqi war and terrorist threat. After testing at the US Army Institute of Surgical Research, the Brooke Army Medical Center and the Oregon Medical Laser Center, it was included in US Army equipment [7, 8].

Other haemostatic dressings containing chitin and chitosan as bioactive agents are also well-known, notably the Syvek patch, RDH (Marine Polymer Technologies), Clo-Sur PAD (Medtronic-Scion), Chito-Seal (Abbot), the M-Patch and Trauma DEX (Medafor) [9].

Medical application

For several years multidirectional research and development work has been conducted in the Institute of Chemical Fibres under the leadership of Professor Henryk Struszczyk, aimed at the preparation of various chitosan forms for medical application. Most of this work has been conducted in the Institute's Section of Biomedicals. The Section operates under the rules of Good Laboratory Practice (GLP); certificate No G-016 was granted in 2002.

The following matters have been included in the investigations:
- fibres from chitosan and derivatives;
- multifunctional dressing materials in the forms of sponges, gel and film;
- dietetic and anti-cholesterol preparations;
- anti-cancer preparations;
- dentistry preparations;
- veterinary preparations.

While conducting its research, the Institute has enjoyed the support of and co-operation with many scientific centres, to name just a few: the Medical Academies in Wrocław and Kraków, the Tissue Bank of the Blood Donor Centre in Katowice, the Technical University of Łódź, and Tricomed Co. in Łódź.

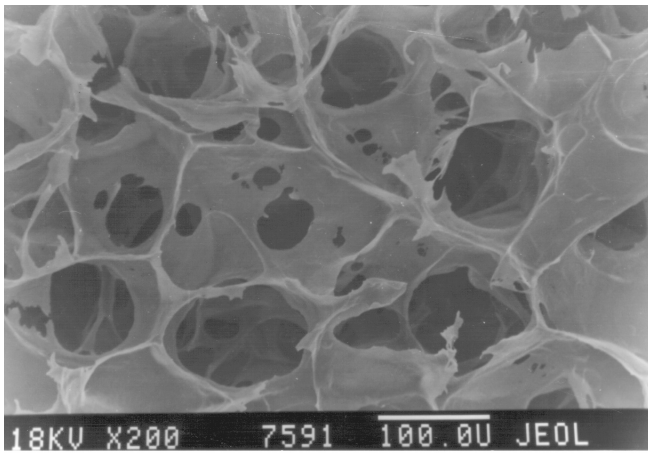

Figure 1. *SEM picture of sponge dressing surface.*

Figure 2. *ChorioChit dressing in sterile package.*

As a result of cooperation between the Institute and Viscoplast Co, Wrocław, a technology was elaborated to produce chitosan fibres for dressings [10-13]. Chitosan staple fibres that can be made according to the method lend themselves to the manufacture of a non-woven for wound-healing dressings. Due to changes introduced in the production profile of the Viscoplast company, the manufacture of the fibres was implemented in the Institute of Chemical Fibres in Łódź.

Viscose fibres modified with microcrystalline chitosan were also devised for the same purpose, that is, the manufacture of dressings. Such fibres manifest anti-bacterial activity against E. coli [14, 15].

As part of a UN project in cooperation with the Technical University of Łódź, a technology was elaborated to produce fibres from dibutyrylchitin and cellulosic fibres with the addition of dibutyrylchitin. Both fibres are designed for dressings [16, 17].

In the Institute, investigations are under way to prepare combined chitosan-alginate fibres for use in multifunctional dressings [18].

One of the most important, purpose-oriented materials developed by Prof. Struszczyk is a gel-like suspension of microcrystalline chitosan (MCCh), made by aggregation of the polymer macromolecules from suspension [19-21]. MCCh preserves all the advantageous properties of the initial chitosan such as biocompatibility, biodegradability, non-toxicity and hydrophilicity, and moreover displays an ability to produce film directly from an aqueous suspension; it is also well miscible with other polymers and substances. The opportunity is afforded to tailor the molecular and supermolecular structure of MCCh during its manufacture. Such properties predispose MCCh very well to medical uses, in particular dressings [22, 23].

The ChorioChit sponge is a biological dressing obtained by lyophilisation of human placenta blended with MCCh [24, 25]. The material is a result of cooperation with the Tissue Bank of the Blood Donor Centre in Katowice and the Silesian Medical Academy in Katowice. ChorioChit is characterised by good handiness, good wound isolation and an ability to limit the growth of pathogenic bacterial flora. The dressing's considerable usefulness was confirmed in the test healing of difficult wounds, mainly shin ulceration. Thanks to its composition and form, the material exerts a biostimulating and bacteriostatic action, and also absorbs wound exudates. The ChorioChit dressing won the gold medals at the innovation exhibitions Eureka'99 in Brussels and Genius'2002 in Budapest.

The Tissue Bank and Institute of Chemical Fibres have recently prepared a new biological dressing called ChitoFib, composed of MCCh and fibrinogenic tissue glue. The new material is designed to heal extensive, grievous injuries of the parenchymal organs such as the liver, lungs and spleen, which require quick surgical intervention to save the patient's life. The dressing was also tested on animals after physical-chemical tests. The testing results indicate the high haemostatic potential of the dressing as well as its ability to absorb wound blood. Further testing is required both in the laboratory and the clinic. ChitoFib was honoured with a gold medal at the Eureka 2004 innovation exhibition in Brussels.

In cooperation with the Institute of Pulp and Papermaking in Łódź, a polypropylene-chitosan non-woven was prepared according to a wet paper method (see Figure 3). Tests made in the Institute's Microbiological Laboratory have documented the bacteriostatic action of the chitosan-containing non-woven against E. coli [26, 27]. No cytotoxic nor intracutaneous irritating action could be detected during the testing carried out in the Department of Experimental Surgery and Biomaterial Investigation of the Wrocław Medical Academy. On the other hand, it was found during animal testing that the non-woven stimulates fibroblast division and accelerates wound healing. See Figure 4 [28].

The PP/chitosan non-woven won a gold medal at the Eureka 2001 exhibition of inventions in Brussels.

In cooperation with the Institute of Textile Engineering in Łódź, investigations were made to prepare dressings containing chitosan as a carrier of kyotorphin with ?analgesic properties. The dressing is given the form of a sponge or film, to be used on open wounds, scalds and ulcers.

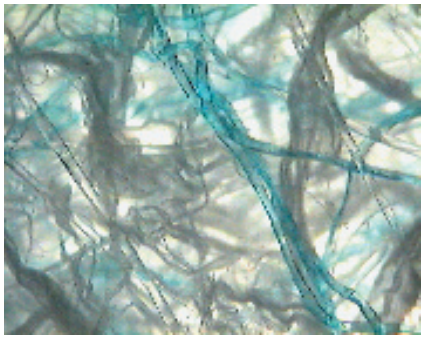

Figure 3. *The surface of the PP/chitosan non-woven Chitosan fibres blue tinted.*

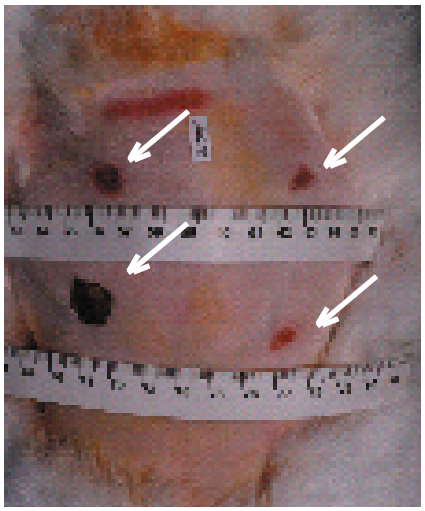

Figure 4. *The appearence of wounds after 15 days; left - reference material- aseptic agent+gauze right - PP/chitosan non-woven.* ***Remark:*** *This figure is presented in colour in the internet-editor of the journal (www.fibtex.lodz.pl).*

As part of a research agreement between the Institute and a US pharmaceutical company, a medical chitosan device was elaborated [29-31] which was approved by the Federal Drug Administration (FDA) and produced for practice in the USA in the form of a haemostatic dressing Chito-Seal [32].

Following other research, a chitosan preparation with optimised physico-chemical properties was devised for use in preventing blood coagulation [33].

Presently, in the Institute of Chemical Fibres, further projects are under way, related to various chitosan materials for dressing applications. In preparation, amongst others, are composite materials based on MCCh, fibroin and natural silk-derived protein. Such biomaterials, in sponge and film forms, are made by conventional or sublimation drying. Other research works concern the preparation of composite non-wovens (chitosan/fibroin) designed for dressings.

Investigations are also under way regarding the preparation of chitosan micro- and nanofibrides useful in the construction of non-woven dressing materials and sponges. A dressing sponge can be obtained by lyophilisation, and the non-woven material by wet forming of a fleece. Other projects are devoted to the preparation of dressing sponges and non-wovens based on chitosan fibrides and bioactive PP fibres. Lyophilisation and both wet and dry fleece forming will be employed in the manufacture of such materials. The objective of these projects is the preparation of surgical nets designed for the treatment of ruptures. Both chitosan fibres and other chitosan forms are being investigated for such uses.

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