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Prototypes of Primary Wound Dressing of Fibrous and Quasi-Fibrous Structure in Terms of Safety of Their Usage

Abstract
The subject of this paper is the evaluation of the critical usability parameters and the parameters characterising the safety of selected prototypes of dressing materials on featuring fibrous, quasi-fibre and hybrid structures, developed at the Institute of Biopolymers and Chemical Fibres (IBWCh). Primary sterile dressing materials were evaluated for usability, which determines the user's safety and physiological comfort according to a series of PN-EN 13726 standards, harmonised with the EU Directive on medical devices, before and after the accelerated ageing process. The scope of the research was developed based on identifying potential threats arising from the expected clinical application of the medical devices being designed. It allowed for the determination of the impact of selected physical and mechanical parameters, needed from a utility point of view, on the properties of the final medical devices, and the elaboration of the documentation of risk analysis, according to the guide described in Standard PN-EN ISO 14971:2011.

Key words: *wound dressings, fibrous structure, biopolymers, preclinical studies, risk assessment.*

Introduction

The designed medical devices must meet a line of requirements defined by the relevant Standards, harmonised with Directive EU 93/42/EEC. Physical and mechanical properties, usage comfort and safety of specific wound dressing materials are evaluated in laboratories, using carefully selected indicators, covered by the series of PN-EN 13726 Standards, which include [1]:

1. Absorption at free soaking - the total absorption in an excess of test liquid with no additional load. This parameter allows for the assessment of the accuracy of wound dressing performances when applied on abundantly or medium exudated wounds;
2. Transport of fluids - the sum of fluids absorbed and vaporised by the dressing. This parameter allows for the assessment of the fluid transport in waterproof wound dressings that are normally used for more than 24 hours. The abilities to absorb exudates and to create a suitable microenvironment are important features of wound dressings;
3. Transmission of moisture vapour in contact with both water vapour and the liquid - this parameter determines the material permeability allowing the particles of water or water vapour to escape from the skin or wound to the external atmosphere, under certain conditions of humidity and temperature. Retention of fluid in the wound dressing can be hazardous, and consequently lead to serious skin damage. It is desirable that a wound dressing has sufficient ability to transmit moisture vapour in order to prevent the accumulation of fluids beneath it;
4. The ability of the dressing to fit - the ability of wound dressings to adapt to the body's shape and movements, in terms of measuring of mechanical performance, i.e. elongation and permanent deformation;
5. Water resistance defined as the ability of wound dressings to withstand the hydrostatic pressure of a 500 mm high water column for 300 s;
6. Dispersion characteristics - the aim of the test is to distinguish fibrous wound dressings that undergo dispersion due to the moist environment of the wound under simulation with an excess of fluid simulating an exudation. Evaluation of the dispersion characteristics is useful to determine the effects of wound dressings applied on abundantly or medium exudated wounds with partial or complete saturation of the wound dressing. The study supports the process of selecting an appropriate method for removing the wound dressing from the wound. It allows also for distinguishing between the wound dressings that disintegrate under the test conditions or are easily dispersible and those that remain intact. The dispersible dressings can be removed from the wound by rinsing.

A properly selected study program, which chooses research tests that verify the presumed functionalities of developed medical devices, facilitates and speeds up the selection of the most optimal solutions, even at the preclinical tests stage. This will allow prediction of the most efficient technical solutions for biological tests (verifying both aspects of safety and the performance of medical device prototypes).

Assessing the storage time and the impact of storage conditions on the critical properties of the medical device is important when designing a wound dressing material. Many different techniques for accelerated ageing are used for the evaluation of the storage time of medical devices. These methods are mainly based on the degradation reactions of zero, first or pseudo-first-order, presented by the Arrhenius equation [3]:

$$r = {}^{dq}/_{dt} = Ae^{-E_a/kT}$$

where: r – reaction order, A - constant depending on the material type, E_a- energy of activation (eV), k – Boltzman constant (0.8617×10^{-4} ev/K), and T - temperature.

When setting the conditions of accelerated ageing in the medical devices, the following should be taken into account:

1. Determining a reference temperature corresponding to the storage temperature range of 20 - 25 °C. For medical devices, the preferred temperature is usually 22 °C or 23 °C [2]. It is obvious that the reference temperature must be determined rationally, tak-

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ing into account the conditions under which a medical device will be stored.
2. Due to the time shortening of the test, the selection will be of the highest possible temperature of accelerated ageing with the following restrictions:
   a) Accelerated ageing temperature for the polymer materials should not exceed the glass transition temperature (T_g), softening point (T_m), or crystallisation point (T_k) [3]. These restrictions apply to all materials that the medical device consists of, including the medical packaging (which is an integral part of the medical device). For medical devices for accelerated ageing, which are designed with a number of materials, one chooses the temperature which is lower than the lowest one among the glass transition point (T_g), softening point (T_m) or crystallisation point (T_k) of the material that makes up the product or/ and medical packaging.
   b) The accelerated ageing temperature should not exceed 60 °C due to the thermal degradation of polymers, in particular biopolymers, at higher temperatures [3].

For temperatures of accelerated ageing and the reference temperature, the dependence of accelerated ageing time and the time of storing at the reference temperature takes the form of [3]:

$$t_{T1} = t_{RT} / Q_{10}^{(T_{T1}-T_{RT})/10}$$

where

T_{T1} – temperature of accelerated ageing,
T_{RT} – reference temperature,
Q_{10} – factor of ageing process, t_{T1}- time of accelerated ageing, and t_{RT}- time of storing at the reference temperature.

The aim of this study was to estimate the risks arising from the clinical use of the developed primary wound dressings and to verify the acceptability of the identified risks, using rationally selected research methods that simulate the presumed aspects of the application. It was necessary to develop such procedures, which, under the basic requirements, are both quick and efficient in terms of using resources and equipment.

The prototypes of wound dressing materials developed at the Institute of Biopolymers and Chemical Fibres (IBWCh) and dedicated to the treatment of wounds at particular stages of healing have been tested. The tests were executed on:

1. Sponge made of microcrystalline chitosan, intended to accelerate wound healing [3];
2. Sponges of quasi-fibrous structure, made of chitosan/carboxymethylcellulose fibrids, dedicated to healing the wounds (healing stage I) [4].

As part of this study, the potential risks associated with the usage characteristics of the developed primary wound dressings were evaluated, and the research methods allowing the verification of the named features under *in vitro* conditions were selected. Such execution of the research program allows for the rational implementation of the research process in terms of verification, which is only associated with presumed clinical use, and the functional properties of the developed medical devices.

The above-designed research programme rationally allows carrying out the project in scope of the verification of the performance aspects connected only with the assumed clinical use of medical devices. A properly carried out risk analysis allows for developing medical devices yielding only residual risk reduced to an acceptable level for both the manufacturer and the end-user [5]. In addition, the identification of the risk and its levels at the stage of preclinical test selection allows for conducting a thorough optimisation of the functionality and safety, so that only the best possible prototypes were included in the clinical trials. The risk analysis must be supported by the results of tests that indicate the possibility of the safe use of the developed medical devices.

In order to determine the suitability of a medical device, which is intended to enter the market for presumed clinical use, it is necessary to assess the safety of the product, including the risk acceptability, considering the generally acceptable current state of knowledge and technology [5].

The confluence of a properly conducted risk analysis with selected research methodology, which at the level of preclinical tests verifies the accuracy of established guidelines regarding the structure and usage properties, even after the presumed period of storage, is - as stated in the work - an essential tool to effectively achieve the objective of the project at the optimum distributed resources.

Materials

Chitosan

Chitosan from Primex (Iceland) was used for the research.

The physical and chemical parameters of the chitosan were as follows:
$\overline{M}_v$ = 358 kD,
deacetylation rate (DD) = 81%,
ash content = 0.22%,
protein content = 625 ppm,
heavy metals content:
As < 0.1 ppm, Cd < 0.1 ppm,
Pb = 0.27 ppm, Zn = 0.80 ppm,
Hg < 0.05 ppm.

Microcrystalline chitosan (MCCh/G)

The microcrystalline chitosan was made according to the method developed at IBWCh [6].

Characteristics of its physical and chemical parameters: M_v = 339 kD, DD = 81%, polymer content = 3.58 wt%.

Chitosan/carboxymethylcellulose microfibrids

The microfibrids of chitosan/carboxymethylcellulose were made under dynamic conditions, according to the method developed at IBWCh [7]. The physical and chemical parameters are: solid content = 10.04 wt%, including the chitosan content = 50%. The developed method allows for producing fibrids with a length of 100 - 200 μm and diameter of 5.0 – 25.0 μm (wet state) and 0.7-5.0 μm (dry state).

Methodology

Producing sponge-like dressing materials featuring a quasi-fibrous structure from MCCh/G

A polymer composition which contained a water suspension of - 1 part by weight of MCCh and 0.5 parts by weight of plasticiser (glycerine), with a chitosan dry content of 2.5 wg%, was used to design the wound dressing sponge. The resulting formulation was homogenised thoroughly and then dried in an ALFA 1-4 laboratory lyophiliser (CHRIST). Lyophilisation was carried out at the temperature range from -20 to 10 °C and a vacuum of 0.1 up to 0.7 mbar. Under these conditions, the total time for the drying of wound dressings was 20 to 24 hours, depending on the batch size.

Preparation of dressing materials in the form of a sponge made of fibre chitosan/carboxymethylcellulose (FibCh-C/G)

For the design of wound dressings in the form of sponge, a mixture was used, consisting of:

- chitosan/carboxymethylcellulose microfibrids - 1 part by weight,
- microcrystalline chitosan – 10 wt%, related to the complex,
- plasticiser - 0.5 parts by weight (based on the dry polymer content),

The polymer content of the dry weight was 4 wt%.

The addition of microcrystalline chitosan (10 wt%) to the fibrids allowed for the uniform distribution of the mixture on a shelf of lyophiliser, and consequently resulted in a uniform defect-free sponge structure.

Research on the structure and evaluation of the porosity of wound dressing materials

Research on the external surface and cross-section of prepared wound dressing materials, as well as the evaluation of porosity, was executed with the scanning electron microscope Quanta 200 (FEI Co./USA). Analysis software from Soft Imaging Systems was used for assessment of wound dressing sponge porosity

Sterilisation of wound dressing materials

Sterilisation of wound dressing materials was executed by radiation, with an accelerated electron dose of 25 kGy.

The method of sterilisation was chosen taking into account the susceptibility of the materials used for the wound dressing prototype to the sterilising agent and the potential risk resulting from its use. For porous medical devices, radiation is the most acceptable method of sterilisation. Ethylene oxide may introduce additional risks arising from the accumulation of ethylene oxide and its derivatives by a porous product. Additionally, when using plasticiser (glycerine), toxic derivatives of the reaction of ethylene oxide with the hydroxyl groups of glycerol may be produced. The application of another acceptable method, steam sterilisation, leads to the degradation of biopolymers that are main components of the wound dressing, which has a negative impact on the expected functional properties.

Table 1. The applied parameters of accelerated ageing.

Ageing temp.	Environment temp.	Pattern		Days of ageing process corresponding to 1 year at the environment temperature	Weeks of ageing process corresponding to 1 year at the environment temperature
		Days of year	Ageing coefficient		
60 °C	23 °C	365	$2^{3.7}$	28	4

Sterilisation was carried out in the Institute of Applied Radiation Chemistry, Lodz University of Technology.

Evaluation of the effectiveness of wound dressing sterilisation

Evaluation of the effectiveness of wound dressing sterilization was carried out [1] on the basis of:

- Microbiological purity (bioburden) assessment of the designed wound dressing before sterilisation by direct inoculation methods;
- Assessment of sterility.

The research was conducted in accordance with the Polish Pharmacopoeia, ed. V, volume III, and volume I, ed. VII.

Assessment of wound dressing material storage time (accelerated ageing) [2]

Assessment of the time of storage on the usage properties of the designed dressings was carried out in accordance with the guidelines of the ASTM F1980:2002 Standard [3], which makes use of the Von'Hoff theory on accelerating the ageing of the product by increasing the storage temperature ***Table 1***.

The maximum allowable temperature was taken as the temperature of accelerated ageing, as the so-called "the worst case". This temperature was determined by taking into account the types of materials used for the manufacturing of wound dressings (especially biopolymers susceptible to thermal degradation) and thermoplastic polymers, which are key components of the packaging of wound dressings, as well as guidelines described in [3].

Assessment of performance of wound dressing materials before and after the accelerated ageing process [2]

Assessment of the functional parameters of wound dressing materials before and after accelerated ageing process was carried out in accordance with the following standards:

- Transportation of fluids PN-EN 13726-1:2005 (p.3.3).
- Absorption under free soaking in g PN-EN 13726-1:2005 (p.3.2).
- Characteristics of dispersion PN-EN 13726-1:2005 (p.3.6).
- Moisture vapour transmission (MVTR) in $g \cdot m^{-2} \cdot 24^{-1}$ PN-EN 13726-2:2005
  - in contact with water vapour;
  - in contact with fluid.
- Watertightness PN-EN 13726-3:2005.
- Conformability PN-EN 13726-4:2005.

Risk analysis for the evaluated wound dressings

The risk analysis for the selected wound dressings was performed according to the guide described in Standard PN-EN ISO 14971:2011 and selected parts of Standard PN-EN ISO 22442-1:2008 using the FMEA method (Failure Mode and Effect Analysis).

The analytical methods

Determination of average molecular weight of chitosan (Mv) - Viscometric method

The average molecular weight of chitosan was calculated on a basis of the intrinsic viscosity [η]. Viscosity was measured with capillary viscosimeter with capillary No. 1, K ≈ 0.01, according to the SPR/BPB/5 procedure (IBWCh) [8].

Determination of the chitosan deacetylation degree (DD) - a method of first derivative of UV spectrum

The degree of deacetylation (DD) was determined by spectrophotometric methods, consisting of the determination of a maximum of the first derivative curve of the UV spectrum and mathematical calculation of DD according to the procedure SPR/BLF/21 (IBWCh) [9].

Determination of the ash content

The ash content in chitosan was determined at the temperature of 800 °C, according to the procedure IBWCh - SPR/BLF/6 [10].

Determination of heavy metals

The content of heavy metals was determined by Atomic Absorption Spectrometry.

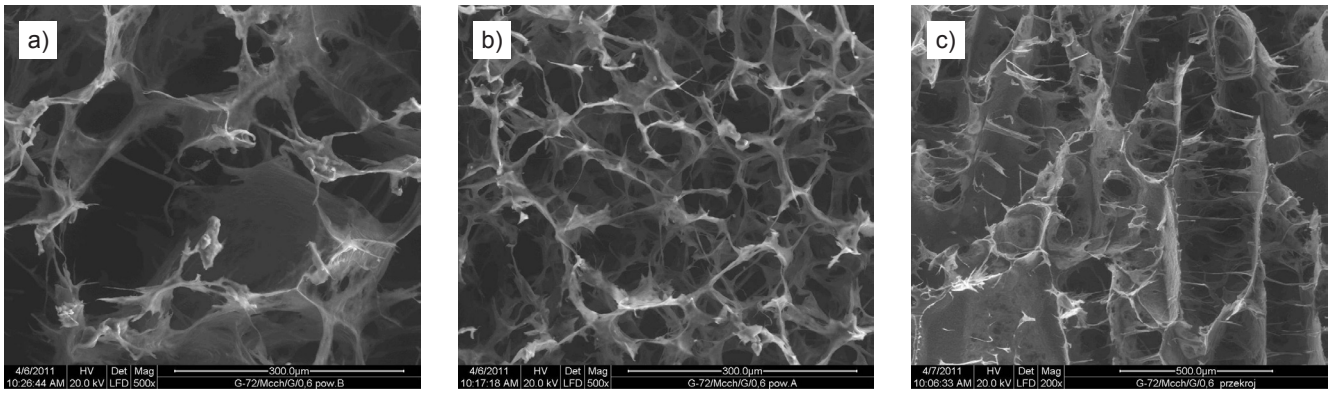

Figure 1. *SEM microphotographs of structure of the sponge dressing prototype, made of MCCh/G; a) surface A 500×, b) surface B 500×, c) cross-section 200×.*

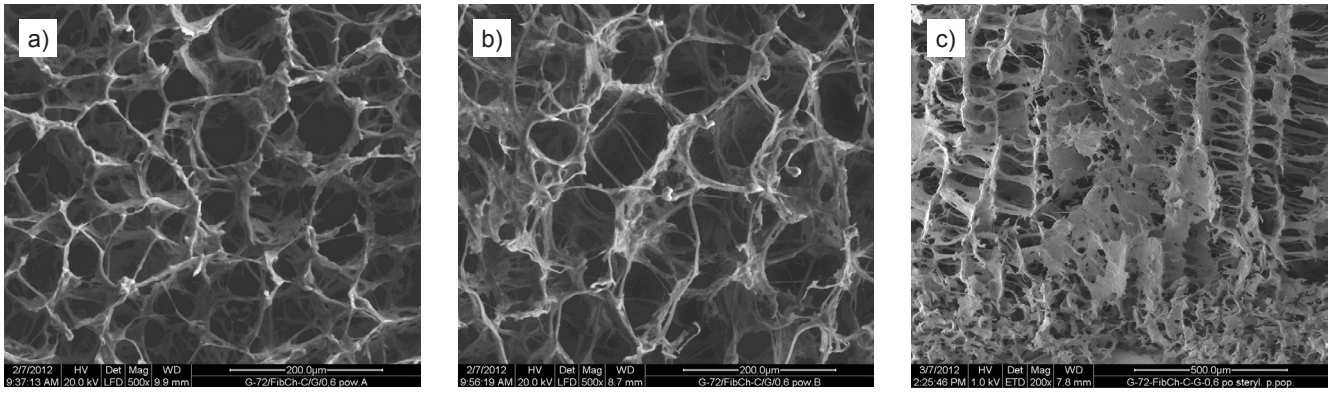

Figure 2. *SEM microphotographs of the structure of the sponge dressing prototype, made of chitosan/carboxymethylcellulose fibrids [FibCh-C]; a) surface A 500×, b) surface B 500×, c) cross-section 200×.*

Table 2. *Measurement of the pore diameter of the spongy dressing materials.*

Symbol	Sponge composition	Mean diameter of pores, µm	Min. µm	Max, µm	Standard deviation, µm
MCCh/G	MCCh -1 part by weight; plasticizer – 0,5 part by weight	30.06	10.55	61.09	14.01
FibCh-C/G	chit./carboxymethylcellulose microfibrids - 1 PBW; plasticiser – 0.5 part by weight, MCCh – 10wt% related to complex	58.94	32.75	85.79	17.26

Determination of the protein content

The index of protein content in chitosan was determined by the Lowry method, according to procedure SPR/BBP/7/1 (IBWCh) [1].

Determination of the chitosan content in suspension

The contents of chitosan in suspensions were determined according to procedure SPR/BPB/11 (IBWCh) [12].

Research results

Research of the structure of selected prototypes of spongy dressings

Structure studies of selected wound dressings were carried out using a scanning electron microscope. The studies included research into the external surface as well as the cross-section of sponge dressings (***Figures 1, 2*** and ***Table 2***).

The obtained results indicated that the lyophilisation process allows for preparation of both usable forms of the polymers, the material having a strictly regular three-dimensional (3-D), quasi-fibrous structure. Both the outer surface and the cross-section of wound dressings (***Figures 1, 2***) have a high porosity with a very uniform distribution of regular shaped pores. One should note that the walls of pores are not formed by an unceasing layer of the polymer, but have an open-work structure. Visually, the internal structure of the sponges is largely similar to the structure of the conventional fibrous material, with a 3-D knit. The research also showed some differences in the sponge structure, in terms of the pore sizes (***Table 2***). Dressing sponges made of fibrous forms of chitosan/carboxymethylcellulose composite in the form of microfibrids featured a porous material of about 57 - 93% larger pore size compared to sponges made of microcrystalline chitosan. Structured forms of fibrids are especially visible in ***Figure 2.c***. The results of these studies confirm the validity of the initial presumptions taken when designing the wound dressing, which stated that fibrids are a usable form of polymer that is useful for the production of wound dressing materials dedicated for stage I of wound healing. It requires the application of wound dressings of a highly enhanced internal surface and increased absorptivity.

Assessment of microbiological purity and sterility of sponge prototypes

The prototypes of dressing sponges prepared for tests were exposed to sterilisation with a dose of 25 kGy of accelerated electrons. The effectiveness of sterilisation was assessed by examining the ste-

rility according to the Polish Pharmacopoeia, Volume III.

Preliminary study (***Tables 3*** & ***4***) showed that such a sterilisation method is effective and provides a sterility of the designed wound dressing.

The initial amount of the microorganisms on the designed spongy dressing, as the input data for estimation of the effectiveness of the sterilization process, is shown in ***Table 4***.

Moreover, the risk of immunological reaction against the bacterial particles remained after sterilisation was determined by the bioburden (microbiological contaminations) before the process of the sterilisation (***Table 4***).

Table 3. *Tests of sterility of the spongy dressing materials.*

Sample symbol	Microorganisms (medium)	Time of incubation, days	Temperature of incubation, °C	Result
MKCh/G	anaerobic	14	37	no growth, sterile sample
	aerobic		25	
	aerobic		25	
FibCh-C/G	anaerobic		37	
	aerobic		25	

Table 4. *Bioburden tests of sponge dressings by the direct inoculation method before sterilisation.*

Sample symbol	Microorganisms (medium)	Time, days	Temperature of incubation, °C	Number of microorganisms, jtk/g
MKCh/G	bacteria	5	30-35	< 0.5
	fungi		20-25	< 0.5
FibCh-C/G	bacteria		30-35	< 0.5
	fungi		20-25	< 0.5

Assessment of the performance of selected sponge dressing prototypes

Selected sterile prototypes of spongy dressings were evaluated towards appropriately selected properties which simulate clinical usage before and after accelerated ageing corresponding to 12 months of storage at real conditions. The results are shown in ***Table 5***.

The main purpose of the studied sponge dressings is to use them for wounds in the first phase of the healing process. Wound dressings of this type are required to be adequately absorptive, permeable and able to absorb exudates. The designed dressing prototypes meet all of the above-mentioned requirements after the sterilisation process.

Based on the obtained results, it was found that the selected wound dressing prototypes after the sterilisation process demonstrate:

a) the ability to close the transport of fluids, the value is about 18 g after 24 h of testing, and 20 g after 48 h;
b) sufficient capacity for the transmission of both fluids and steam. The value of this parameter for the fluids for the MCCh sponges is 15,000 $g \cdot m^{-2} \cdot 24^{-1}$, whereas the sponges made of chitosan/carboxymethylcellulose microfibrides characterised by the parameter reaches a nearly two-fold higher value. The ability of a wound dressing to transmit water vapour is at the level close to ca. 5000 $g \cdot m^{-2} \cdot 24^{-1}$. Conventional wound dressings used clinically have values of MVTR close to those of the MCCh/G dressings, both in contact with water vapour (1953 $g \cdot m^{-2} \cdot 24^{-1}$ [13] or 7305 $g \cdot m^{-2} \cdot 24^{-1}$ [14]), and in contact with the fluid (20019 $g \cdot m^{-2} \cdot 24^{-1}$ [13]). High levels of MVTR of a FibCh-C/G dressing prototype in contact with the liquid may bring a risk of rapid (excessive) draining of the wounds with little exudate, which may be particularly suitable for a wound with high exudate, by optimum evaporation of the excess (reduction of maceration risk and usability prolongation);
c) suitable absorption properties, ranging from 28 up to 38 g/100 cm^2 of wound dressing;
d) inadequate surgical handling (conformability), resulting from the lack of drape, expressed by a measurement of mechanical properties, i.e. tensile and permanent deformation;
e) lack of watertightness, which results from the porous structure of the wound dressing.

The estimated properties allow the identification of potential risks connected to the clinical application of the designed wound dressing, as well as to the elaboration of preliminary guidelines and indications for further clinical applications.

The accelerated ageing process did not cause significant changes in the usage properties of wound dressings (***Figures 3*** and ***Table 8***), which determine the safety and physiological comfort of the patients. The designed wound dressings retain their performance during simulated one year storage under conditions of accelerated ageing, according to the guidelines of Standard ATSM F 1980:2002.

The only drawback of these wound dressings is inadequate clinical conformability, expressed by poor draping on the skin's surface. It should be considered that the materials selected for the study take the form of a sponge, which has a high degree of porosity that significantly reduces the values of certain parameters, i.e. the elongation or permanent deformation. However, this problem can be solved by strengthening the wound dressing with an elastic layer, using a hybrid design of

Table 5. *Assessment of performance of dressing sponge prototypes; * - the results are the mean value of measurement of 10 samples, ** - the results are the mean value of measurement of 5 samples.*

Process	Symbol of wound dressing	Absorptivity at free soaking*, g/100 cm^2	Transportation of fluids**, g		Characteristics of dispersion	Transmission of moisture vapours**, $g \cdot m^{-2} \cdot 24^{-1}$		Conformability	
			24h	48h		in contact with water vapour	in contact with fluid	Tensility, $N \times cm^{-1}$	Permanent deformation, %
after sterilisation	MCCh/G	7.10/28.42	18.27	19.79	not dispersible (-)	4992 ± 355	14980 ± 622	absence	absence
	FibCh-C/G	9.65/38.61	18.30	20.67	+	5394 ± 426	29305 ± 6178		
after accelerated ageing	MCCh/G	5.97/23.89	16.06	20.70	dispersible (+)	5369 ± 208	14278 ± 813		
	FibCh-C/G	8.21/32.84	17.80	20.26	+	5663 ± 500	32875 ± 4409		

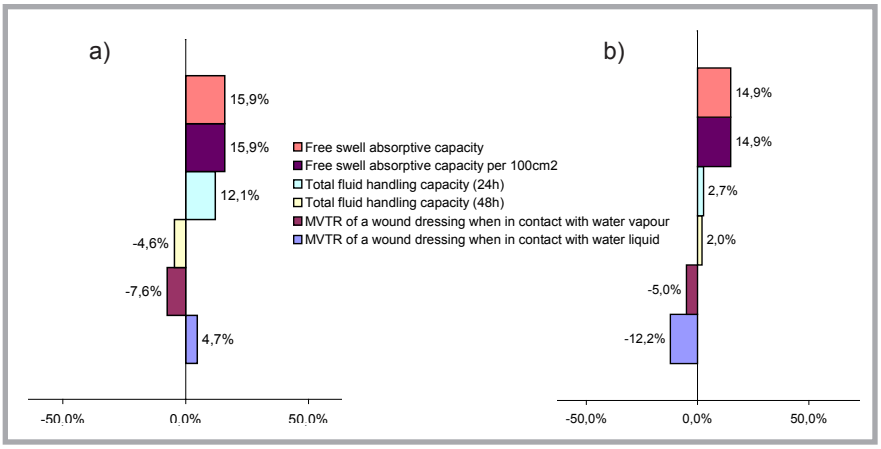

Figure 3. *Changes usable parameters of sponge wound dressing: a) MCCh/G and b) FibCh-C/G/0,6 after accelerated aging in relation to initial parameters (0 level).*

Table 6. *FMEA method - qualitative levels of severity.*

Qualitative levels of severity	Description	Weight
Catastrophic	The result is death of a patient	5
Critical	The result is a permanent disability or life-threatening injury	4
Serious	The result is injury or disability, which requires professional medical attention	3
Minor	The result is a temporary injury or impairment, which does not require professional medical intervention	2
Negligible	Temporary inconvenience or slight pain	1

Table 7. *FMEA method - semi-quantitative probability levels.*

Semi-quantitative probability levels	Ranges of probability	Weight
Frequent	$\geq 10^{-1}$	5
Possible	$< 10^{-1}$ i $\geq 10^{-2}$	4
Sporadic	$< 10^{-2}$ i $\geq 10^{-3}$	3
Isolated	$< 10^{-3}$ i $\geq 10^{-4}$	2
Unlikely	$< 10^{-4}$	1

Table 8. *Semi-quantitative matrix of risk;* ■ *- unacceptable risk,* ■ *- consider possibility of further reduction in the risk level,* □ *- acceptable risk.*

		Qualitative levels of severity				
		Negligible -1	Minor -2	Serious -3	Critical -4	Catastrophic -5
Semi-quantitative probability levels	Frequent - 5					
	Possible -4					
	Sporadic - 3					
	Isolated - 2					
	Unlikely - 1					

wound dressing, a sponge/mesh support made of synthetic fibres, and by including detailed information about method of applying and handling the dressing in the instructions for use (IFU).

Risk analysis for the evaluated wound dressings

On the basis of test results obtained over the course of the project, a risk analysis was performed in accordance with the methodology of tests, using the qualitative levels of severity (***Table 6***) and semi-quantitative probability levels (***Table 7***).

As part of the analysis, first the hazards were identified, the risk impacts were determined, and the risk control measures were designated (***Table 9,*** see page 148) for the selected prototypes of wound dressings. Then, an analysis of the risks arising from the hazards was carried out (***Table 10***).

The study showed that the risk level for prototypes of primary spongy dressings made of microcrystalline chitosan as well as those of chitosan/carboxymethylcellulose fibrids, known and defined for making up processes, was rated below an unacceptable risk, with the recommendation of further reducing the risks of 1.6 (absence of conformability). Within the scope of this analysis, the risk assessment carried out proved a higher level of benefits than risks arising from the use of selected prototypes of the medical device.

Summary

The study proved that prototypes of primary spongy dressings, prepared from the microcrystalline form of chitosan as well as from fibrids made of a chitosan-carboxymethylcellulose complex, demonstrate adequate functional properties (performance), such as absorption, permeability, and ability to absorb exudates.

The storage period of 12 months does not significantly affect the evaluated parameters. The values of these parameters ensure the safe application of the designed primary wound dressings by patients. Levels of risk of producing selected prototypes of wound dressings were below the unacceptable one. The only drawback limiting the safety, which would need to be improved in the manufacturing process, is the ability to adapt to the skin's surface. The reason for this apparently lies in the fact that the tested biomaterials are in the form of a sponge that is highly porous, which determines very good properties such as absorptivity or the transport of fluids, but conversely lowers the mechanical parameters – tensile and permanent deformation. However, this problem can be solved by reinforcing the elastic layer of wound dressings with the application of a hybrid structure, i.e. primary wound dressing sponge/mesh made of synthetic fibres.

Editorial notes

1) *The tests were executed in the accredited Laboratory of Microbiology at IBWCh.*
2) *The tests were executed in the accredited Laboratory of Microbiology at Institute of Security Technologies MORATEX.*

Acknowledgments

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Table 9. *Risk analysis of primary sponge dressing prototypes MCCh/G and Fib-C/G.*

Item	Risk identification	Results of risk	Risk control measures - risk reduction
1	**Functional properties of the final product before and after the ageing process**		
1.1	Improper level of parameter: transportation of fluids	Inappropriate wound microenvironment - the wound too wet (risk of maceration) or too desiccated.	1) tests according to PN-EN 13726-1:2005 Standard (p.3.3)
1.2	Improper level of parameter: absorptivity at free soaking	Impossible to apply the wound dressing on the abundant or medium exuding wounds.	1) tests according to PN-EN 13726-1:2005 Standard (p.3.2);
1.3	Improper level of parameter: characteristics of dispersion	Rapid disintegration of wound dressing in contact with the wound exudated excessively. In case of partial disintegration - hindered removal from a wound.	1) tests according to PN-EN 13726-1:2005 Standard (p.3.6); 2) IFU should include information on how to remove the wound dressing from a wound
1.4	Improper level of parameter: transmission of moisture vapours	Inadequate permeability of the arrangement preventing the particles of water or water vapour moving from skin or a wound to the environment or affecting the excess evaporation under certain conditions of humidity and temperature. In case of excessive moisture retention under the wound dressing - serious damage to the skin, maceration. In an opposite case - the possibility of excessive drying of wound.	1) tests according to PN-EN 13726-2:2005 Standard
1.5	Improper level of parameter: watertightness	No resistance to external-acting water (rain, direct contact with running water, washing, etc.).	1) tests according to PN-EN 13726-3:2005 Standard; 2) IFU should include information on lacking watertightness of the wound dressing
1.6	Improper level of parameter: conformability	Wound dressing inability to adapt to the shape and the movements of the body or partial adaptation of wound dressing to the shape and movements of the body.	1) tests according to PN-EN 13726-4:2005 Standard; 2) necessity to modify the wound dressing - multilayer dressing with a flexible layer; 3) IFU should include information on fitting problems; 4) necessity to apply an intermediate wound dressing – for fixing.
1.7	Improper level of parameter: strength properties	Accidental mechanical damage of wound dressings during storage, clinical application, etc.	1) tests according to PN-EN ISO 4593:1999 and PN-EN ISO 527-3:1998 Standards
2	Sterilisation process chosen improperly regarding loss of functional properties	Lost the usable properties (mechanical properties), disintegration of the wound dressing	1) 1) tests according to PN-EN ISO 4593:1999 and PN-EN ISO 527-3:1998 Standards in aspects effects of the sterilization agent on the usable properties (mechanical behaviour)
3	Inadequate microbiological purity of semi-product undergoing the sterilization	Immunological adverse effects, lost quality, pirogenicity	Bioburden (microbiological purity) tests, verification of the sterility (FP VII)

Table 10. *Risk analysis of selected prototypes of primary sponge dressing.*

Item	Risk		Severity [D]		Probability [P]		Risk acceptability	
			MCCh/G	Fib-C/G	MCCh/G	Fib-C/G	MCCh/G	Fib-C/G
1.1	Improper level of parameter:	transportation of fluids	4	4	1	1	YES	YES
1.2		absorptivity at free soaking	4	4	1	1	YES	YES
1.3		characteristics of dispersion	4	4	1	1	YES	YES
1.4		characteristics of gelation	1	1	1	1	YES	YES
1.5		transmission of moisture vapours	4	4	1	1	YES	YES
1.6		watertightness	1	1	1	1	NO	NO
1.7		ability to fit itself	5	5	1	1	YES	YES
1.8		strength properties	3	3	1	1	YES	YES
2	Sterilisation process chosen improperly regarding loss of functional properties		3	3	1	1	YES	YES
3	Inadequate microbiological purity of semi-product undergoing the sterilization		4	4	1	1	YES	YES

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