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Chemical Purity of Biodegradable Medical-Grade Fibres of Aliphatic Copolyesters

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Abstract
Fibres prepared on an experimental scale from biodegradable copolyester of glycolide and lactide (PLGA) and from PLGA with the addition of 9% of atactic poly([R,S]-3-hydroxybutyrate (PLGA+a-PHB) were characterised to assess their possible use in the preparation of surgery sutures. Commercial spinfinish Estesol PF 790 (Bozzetto Group, Italy) was applied on the fibres in the spinning step. A method was prepared for an organic extraction of the spinfinish from the PLGA fibres, and the process efficacy was assessed by scanning electron microscopy (SEM) and by estimating chemical purity. With spinfinish removed, the fibres were subjected to an extraction process which simulated the utilisation of the products in an aqueous medium. The aqueous extracts were analysed to estimate contamination contents. Also estimated was the time in which the fibres degrade when subjected to surplus extraction in an aqueous medium.

Key words: *biomedical polymers, PGLA fibres, chemical purity, medical devices, spinfinish non-ionic, physico-chemical analysis, chemical contamination.*

Introduction

The ever growing demand for polymeric medical devices is boosting progress in new technologies for the synthesis and processing of resins. Owing to their mechanical and physical-chemical properties like excellent processabilty, repeatability of product quality, easy sterilisation, bio-inertness, non-toxicity and non-allergenic action, polymers are displacing traditional ceramic and metallic products [1].

Copolymers play an important role in medicine. Their multicomponent structure offers a broader span of desired properties and opens new avenues of application, thus contributing to developments in medicine.

Copolymers of glycolide and lactide (PLGA) lend themselves to the preparation of medical devices thanks to their biocompatibility with the human organism and absorption in bodily fluids [2 - 4]. Products made of PLGA are well water- and vapour-permeable, and do not cause an inflammation reaction of the body. The US Food and Drug Administration (FDA) have approved the use of PLGA [5, 6]. Owing to beneficial properties, the PLGA copolymers have found a number of applications like stabilizing elements of bone splinters in maxillafascial surgery, sutures and drug carriers [7, 8].

In the human organism, PLGA undergoes resorption: lactic and glycolic acids are delivered as a result of its degradation. In further metabolic processes both acids are reduced to harmless substances: water and carbon dioxide [9 - 12]. A real asset of medical devices made of PLGA is that its structure can be tailored to degrade in a desired set time.

The proportion between the lactide and glycolide components and presence of additives are crucial in the resorption process though the medium, with the pH, molecular mass and crystallinity also playing a role [13, 14]. Many factors are to be taken into account in designing absorbable medical devices, which makes their preparation a rather complex business. One important action is the assessment of clinical risk related to the use of polymeric materials, which is made by examining the products of biodegradation [15].

Various biodegradable fibrous materials of renewable resources were prepared in the project called *"Biodegradable fibre products",* including glycolide and lactide copolymers designed for medical application. At the Centre of Polymeric and Carbon Materials of the Polish Academy of Sciences in Zabrze, the synthesis of fibre–grade PLGA was investigated. A zirconium initiator was employed in the synthesis to replace the commonly used, much more toxic compounds of tin. Also prepared was the synthesis of amorphous poly([R,S]-3-hydroxybutyrate) (a-PHB) by employing a metal ion-free initiator in the process. Further research

Table 1. *Physico-chemical properties of PLGA and PLGA+a-PHB: T_g - temperature of glass transition, T_m - melting temperature, MFI - melt flow index.*

Type of polymer	Inherent viscosity, dl/g	Content of ash, %	T_g, °C	T_m, °C	MFI $_{190°C}$, g/10min
PLGA	2.12	0.02	47.2	120.1	8.6
PLGA + a-PHB	1.5	0.04	55.53 5.84	166.5	32.7

was concerned with the technology of blending PLGA and a-PHB to obtain products with enhanced elasticity [16], which is beneficial to the post-surgery patient's recovery [17]. In the next step of the investigation, textile prototypes were prepared for use in sutures, and a scheme of testing the products was proposed based on European directives concerning medical devices [18 - 21].

Presented herein are results of investigation into the assessment of the chemical purity of the fibres prepared, designed for sutures. It was an aim of the work to propose a system for controlling the chemical purity of biodegradable medical devices based on Polish standards, and European and American Pharmacopoeia. The selection of crucial information from a rich basis of documents was a substantial part of the work, which enabled the preparation of a dependable system of analysing medical devices. Another goal of the investigation was to prepare a method for selective removal of the spinfinish that would leave the molecular structure intact, which is an important factor since high quality is demanded from surgery sutures, which are expected to be free from defects and safe to use. The aim of the examination in the domain of chemical purity assessment was the characteristics of substances leached from the prototypes of medical devices under conditions that simulate standard application. Hazardous substances are identified and quantified in an analysis of chemical purity. The results give a picture of the exposure to chemical substances and are a criterion in the permission for further clinical testing of the devices. The results are compared with the directives of European and American Pharmacopeia and with published results of investigations into the chemical purity of polymeric medical devices [22 - 24]. In the works devoted to chemical purity control, proficiency in analysis and technology are important as well as a skillful knowledge of the regulatory standard documents. Also significant are the characteristics of the products and their intended medical use. The selection of crucial parameters to estimate the concentration of hazardous substances is a complex and difficult process. The experience and knowledge of people in technology and laboratories and their good cooperation lay the foundation for preparing the system of chemical purity assessment.

Various additives like catalysts and spinfinishes are implemented into polymers during their synthesis or fibre processing, which is the reason why undesired substances may be obtained from polymeric medical devices. These hazardous materials should be identified. In an examination of the chemical purity, physical-chemical parameters like the content of heavy metals and chloride & sulphate ions should be estimated based on material specifications and in accordance with standard recommendations. These substances may exert a negative impact on biochemical processes in the human body during the use of the medical devices and cause morbid effects like inflammations. The presence of heavy metals like lead or mercury is most adverse due to their toxicity when in contact with the human organism. The system of chemical purity assessment should include the estimation of pH, as its undesired values and changes may negatively affect wound healing. Any undesired effects have to be strictly avoided during the application of medical devices, and therefore quantitative estimation of water-insoluble substances eluted in the course of simulated use is equally important in the assessment of chemical purity as well as turbidity estimation of the solution, which could enable to evaluate the degradation of polymeric materials.

Materials and investigation methods

Fibres designed for medical application were examined, prepared at the Institute of Biopolymers and Chemical Fibres, Łódź, Poland on an experimental scale from biodegradable aliphatic copolyesters, provided by the Centre of Polymeric and Carbon Materials of the Polish Academy of Sciences in Zabrze. Two kinds of the copolymers were prepared with the use of zirconium catalysts [25], notably:

- Copolymer of glycolide and lactide (PLGA) (content of lactide 15% mol).
- Copolymer of glycolide and lactide with the addition of 9% of atactic poly([R,S]-3-hydroxybutyrate); a polymeric blend (PLGA + a-PHB).

Some physico-chemical properties of the copolymers are presented in ***Table 1***.

Fibres were spun from the melt with subsequent drawing. The spinning temperature was in the range of 205 - 230 °C (temperature of the polymer melt in the spinning head was 230 °C and 207 °C for PLGA and PLGA+a-PHB, respectively). The spinning output was 16 g/min at a speed of 800 m/min with a 12-hole spinneret. The fibre spun was drawn on a heated godet at 58 °C and 55 °C for PLGA and PLGA+a-PHB, respectively. The draw ratio was in the range of 2.5 - 3.0. Fibres were prepared with a linear mass in the range of 60 - 80 dtex (79 dtex for PLGA and 63 dtex for PLGA+a-PHB). The melt spinning of fibres involves the use of auxiliary agents. Commercial spinfinish Estesol PF 790 supplied by the Bozzetto Group, Italy, was employed to this end. It was applied on the fibres in the form of an aqueous solution. Poly-ethylene-glycolester is the main component of the spinfinish, which is approved by FDA and classified as an auxiliary substance suitable for medical application following examinations at the University of Medicine, Wrocław, Poland [26].

Commercial products were selected as reference materials: Resomer GL 903 – a copolymer of glycolide and lactide made by BOEHRINGE INGELHEIM (Germany), and surgery sutures MEDSORB, made from a copolymer of glycolide and lactide, supplied by the Turkish company MEDEKS.

Extraction of chemical substances from PLGA fibres

A dynamic extraction method was employed that simulates standard application according to Standard PN-EN ISO 10993-12:2009 [20], and to the requirements of USP 38 NF33 concerning the preparation of aqueous extracts for polymeric materials [23].

The process was performed in a shaker with a thermostat (Water Bath SW 23 by

Julabo Co, Germany) at a temperature of 37 ± 0.1 °C (human body temperature) for 24 ± 2 hours. Water for injection (quality certificate QC/2/0072/10) was used as an extractant. The materials tested were also underwent surplus extraction aimed at increased delivery of the chemical components in comparison to the amount delivered at simulated conditions in accordance with Standard PN-EN ISO 10993-12:2009 [20]. Mixtures containing 10 g of the fibre and 100 cm^3 of purified water were used. The process was carried out in an autoclave at 121 °C until complete degradation of the samples tested.

Estimation of the spinfinish by an extraction method

A method to leach the spinfinish from the copolymer fibres was prepared in accordance with Standard PN-P-04607:1983, Point B "*Estimation of non-fibrous substance by extraction with shaking"* [27].

An organic solvent was first sought to effectively remove the spinfinish to leave the fibre structure unaffected, for which methanol was chosen, which selectively leaches the Estesol PF 790 spinfinish without affecting the fibre structure. The process of spinfinish removal was carried out in a shaker with a thermostat (Water Bath SW 23 by Julabo Co, Germany) at a temperature of 25 ± 0.1 ºC and 150 r.p.m. The process was run in two steps: first for 15 minutes and next for 45 minutes.

After the methanol extraction, the oil-free fibres were underwent water extraction in a shaker with a thermostat at 150 r.p.m. in conditions that simulated standard use (T = 37 ± 0.1 °C, t = 24 ± 2 h). Chemical purity of the aqueous extracts prepared was assessed.

In identifying the exposures and assessing the risk involved from the application, a control system was elaborated based on standards and characteristics of the substrates and technology processes. Only those parameters were defined that are crucial in the assessment of products designed for the preparation of sutures.

The following parameters of chemical purity were estimated in two parallel tests: turbidity, and the content of sulphate and chloride ions, water-soluble substances, foaming agents, and heavy metal ions and pH.

The pH was measured by means of a pH-meter (Schott Instruments, Germany) and Blue Line 14 pH electrodes equipped with an integrated temperature sensor (Schott Instruments, Germany) according to Standard PN-EN ISO 3071:2007 [28] with a measuring accuracy of 0.1 pH units at ambient temperature.

Turbidity (NTU, nephelometric turbidity units) was estimated by the turbidimetric method according to FP VII [29] by measurement of scattered light with the use of a Unicam 5625 UV/VIS Spectrophotometer (ATI Unicam, UK). A suspension of formazine was used as a basic reference standard equal to 4000 NTU; it is a blend of hydrazine sulfate and hexamethylenetetramine (urotropine). The relationship between turbidity and concentration has to be defined by drawing an analytical curve. The instrumental assessment of turbidity is much more accurate than the visual one; moreover it enables to monitor quality and to control industrial processes.

The method of estimating sulfate ions in the aqueous extracts was based on Standard PN-P- 04781/04:1987 [30], consisting in the precipitation of sulphate ions with $BaCl_2$ under standard conditions, and comparing the turbidity of the extract tested with the turbidity of a reference solution containing a known amount of $[SO_4]^{2-}$ ions. The measurement was made with a 5625 UV/VIS spectrophotometer (ATI Unicam, UK). The limit of detection of the method is 0.001 mg of $[SO_4]^{2-}$ ions per 1g of the medical device.

Estimation of the chloride ion $[Cl]^-$ content was performed according to Standard PN-P-04895:1984 [31]. The method employs argentometric titration of aqueous solutions with an $AgNO_3$ solution at a concentration of 0.01 mol/dm^3 in the presence of dithiofluorescein. The limit of detection of the method is 0.003 mg $[Cl]^-$ ions per 1 g of the medical device.

The content of water-soluble substances was determined according to Standard PN-P-04781/06:1988 [32]. The amount of dry residue in the water extract is estimated in this method, being the sum of water-soluble and insoluble matter (turbid extracts).

Detection of forming agents in the PLGA and PLGA+a-PHB water extracts was made according to Standard PN-P-04781/14:1989 [33]. The method of detecting foaming agents in aqueous extracts consists in measuring the height of the froth after shaking of the sample. The appearance of, at least, one single full circle of air bubbles around the wall of the test tube witnesses the presence of foaming agents.

Heavy metal ion content, including Cd, Cr (sum of all oxidation states), Pb, Zn, and Hg, was determined by atomic absorption spectrometry using a SCAN-1 spectrometer (Thermo Jarrell ASH Co., USA) [19]. Cd, Cr, Pb and Zn were directly determined in aqueous extracts by the flame method ASA (FAAS) at the following parameters:

- Cd: wave length λ = 228.8 nm, flame - acetylene-air, limit of detection - 0.02 mg/dm^3,
- Cr: wave length λ = 357.9 nm, flame - acetylene N_2O, limit of detection - 0.2 mg/dm^3,
- Pb: wave length λ = 217.0 nm, flame - acetylene-air, limit of detection - 0.2 mg/dm^3,
- Zn: wave length λ = 213.9 nm, flame - acetylene-air, limit of detection - 0.01 mg/dm^3.

Mercury was determined by the method of cold vapour atomic spectroscopy ASA (CVAAS) using an Atomic Vapor Accessory 440 (Thermo Jawell ASH, USA) at the following parameters: wave length- λ = 253.7 nm, reductive solution - 5% $SnCl_2$ in 20% HCl, carrier gas-Ar, limit of detection- 0.01 mg/dm^3.

Scanning electron microscopy (SEM)

Fibres prepared from PLGA were SEM-tested by means of a microscope - Quanta 200 (USA) delivered by FEI Co. Samples powdered with a 20 nm layer of gold were tested in a high vacuum at electron-beam-accelerating voltage of 5 KV.

Results and discussion

The aim of the investigation into chemical purity was assessment of the profile of substances that are leached under conditions of simulated application from prototypes of textile medical products prepared from the copolymers of lactide and glycolide PLGA, and PLGA with the addition of poly([R,S]-3-hydroxybutyrate). In the first step, parameters were adopted for the identification and content of hazardous substances. Analytical methods were prepared to assess material quality parameters in accordance with directives in force.

Table 2. *Content of spinfinish (oil phase) applied on PLGA and PLGA + a-PHB fibres after 15 and 45 minutes of methanol extraction: *Relative Standard Deviation.*

Time of extraction, min.	Fibre PLGA with spinfinish					Fibre PLGA+a-PHB with spinfinish				
	Content of spinfinish, %									
	measurement			average	RSD*, %	measurement			average	RSD*, %
	I	II	III			I	II	III		
15	0.326	0.326	0.342	**0.340**	5.6	1.070	1.010	1.030	**1.040**	2,9
45	0.033	0.033	0.034	**0.033**	1.7	0.011	0.010	0.010	**0.010**	5,6

Table 3. *Results of chemical purity examination under conditions simulating standard application of PLGA fibres with spinfinish after methanol extraction (t = 15 and 45 min) and of fibres from below the spinneret without spinfinish.*

Sample	pH	Content of foaming agents, cm	Content of ions, mg/g product		Dry residue of aqueous extract, %wt	Turbidity, NTU
			$[SO_4]^{2-}$	$[Cl]^-$		
Fibres with spinfinish	2.7	1.00	0.008	0.090	0.93	5.2
Fibres afterextraction, 15 min.	3.5	0.19	0.003	0.040	0.03	none
Fibres after extraction, 45 min.	4.2	0.01	0.001	0.030	0.01	none
Fibres without spinfinish	6.6	0.01	0.003	0.030	0.02	none

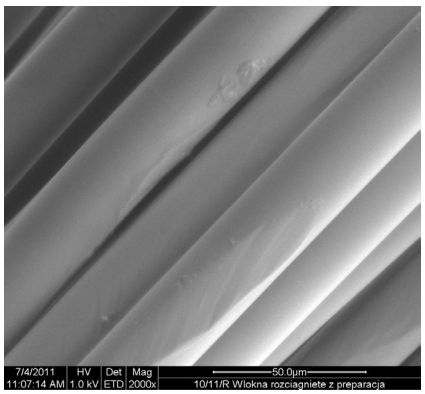

Figure 1. *Fibres PLGA with spinfinish (magnification 2000×).*

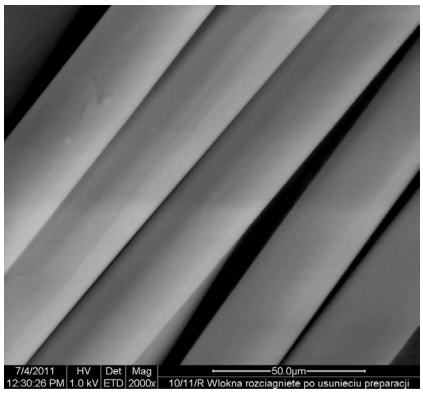

Figure 2. *Fibres PLGA after methanol extraction (magnification 2000×).*

Estimation of the content of substances leached from fibres made of PLGA and PLGA + a-PHB with commercial spinfinish Estesol PF 790 applied

Fibres were extracted with methanol in two steps: the first step - 15 minutes, and second step - 45 minutes [18]. Results of the spinfinish content measurements are presented in ***Table 2***.

The content of the spinfinish in the second 45 minutes of extraction was less than 10% of the amount leached in step one. The results are in accordance with the requirements of Standard PN-EN ISO 10993-12 [20]. Most of the spinfinish applied is removed in the course of the first extraction step (15 minutes), while in the second step the fibre is purified of residual amounts of the oil phase. After the first phase of methanol extraction (15 minutes), the content of toxic substances was analysed in the PLGA fibre. The process was accomplished under conditions simulating standard use (T = 37 ± 0.1 °C; t = 24 ± 2 h) in aqueous medium. Results of the examination are shown in ***Table 3***. The PLGA+ a-PHB fibres were subjected to extraction by the two step methanol process, the results of which are presented in ***Figure 3***.

It issues from the investigation results of chemical purity assessment of PLGA fibres after extraction simulating standard use that the level of impurities of the individual parameters for fibres after 45 minutes of extraction is comparable with those of the fibres without spinfinish. It was found that the prolonged extraction selectively removes the spinfinish from the fibre. SEM observation is proof that the extraction does not cause any damage to the fibre structure (***Figures 1*** & ***2***), which is also confirmed by the repeatable measurement results of the spinfinish contents obtained in the second step of methanol extraction (***Table 2***). The selective removal of the spinfinish is a more important process. For toxicological assessment of the products, fibres devoid of the spinfinish were in, a consecutive step, subjected to an extraction that simulated standard use, which is the reason why an intact structure ought to be preserved in the products tested.

Investigation into the chemical purity of PLGA and PLGA + a-PHB fibres

PLGA and PLGA+ a-PHB fibres after selective two-step removal of the spinfinish and commercial copolymer Resomer GL 903 as reference were extracted with water in a a procedure that simulated standard application (T = 37 ± 0.1 °C, t = 24 ± 2 h).

The aqueous extracts obtained were colourless and free of foaming agents, which means the absence of allergenic or irritating substances. The presence of a foaming substance in aqueous extracts is not permissible, as stated in standardisation documents [33].

Turbiditimetric analysis showed that the solutions are transparent. The results are close to those of water for injection, which satisfies the requirements of European Pharmacopeia and USP 38 NF33 [22, 23]. As per the Pharmacopoeia, a solution is transparent if its turbidity does not exceed 6 NTU.

pH of the aqueous extracts

pH was measured in the aqueous solutions obtained by extraction of the fibres examined, the results of which are presented in ***Figure 3.a***.

Solutions with pH < 4 and pH > 8 carry the risk of causing chemical- borne irritation [24]. Results close to the reference material were measured in the extracts from PLGA fibres (pH 4.3). The addition of a-PHB brings the pH down to a level at which the irritation of tissue might occur. It is therefore recommended to check if sutures made of the fibres examined still reveal a low pH level after the simulation extraction.

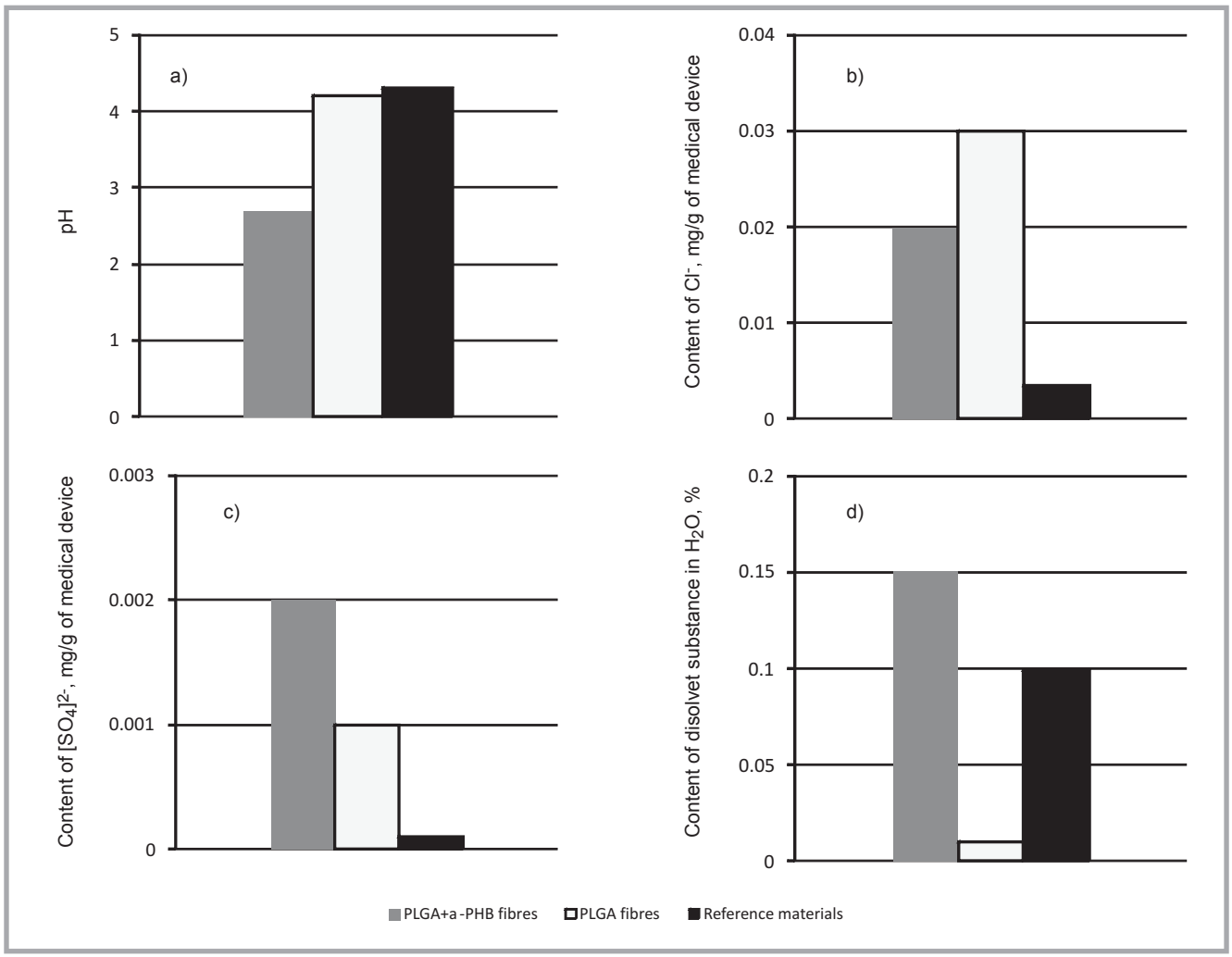

Figure 3. *a) pH of aqueous extracts obtained, b) content of chloride ions in aqueous extracts, c) content of sulfate ions in aqueous extracts, d) content of substance dissolved in aqueous extracts from the reference sample and from PLGA and PLGA + a-PHB fibres after the removal of spinfinish.*

Determination of chloride ion content in the aqueous extracts

Chloride ions count as main impurities which are admixed to medical devices in the course of their manufacture e.g. by the use of auxiliary agents in textile processing or by the addition of various chemicals in polymer synthesis [15]. The estimation of chloride ion content during simulated application of the medical device is therefore essential. Measurement results of $[Cl]^-$ contents in the aqueous extracts are presented in ***Figure 3.b***.

In both fibres tested, chloride ion contents are higher than in the reference. However, the higher $[Cl]^-$ contents remain within the permissible limit, which for medical devices is set at 0.04 mg/g in accordance with earlier investigations concerning the chemical purity of polymeric medical products [24].

Determination of sulfate ion content in the aqueous extracts

Figure 3.c presents measurement results of the $[SO_4]^{2-}$ content in aqueous extracts from the reference sample and fibres tested. Spectrophotometry was also applied in the measurements.

In both fibres tested, sulfate ion contents are higher than in the reference. However, the results obtained fall within the permissible limit according to European Pharmacopoeia No 8.0, where 0.01 mg/g is quoted for $[SO_4]^{2-}$ in Sulphate Standard Solution [22]. Very high purity is featured by the reference polymer, which probably involves costly purification procedures.

Content of dissolved substance

The amount of water-soluble substances was estimated during the process of simulated application of fibres from PLGA, the results are of which shown in ***Figure 3.d***.

Much lower than in the reference was the amount of soluble substances in the aqueous extracts from PLGA fibres. There was an insignificant difference in the soluble matter between the fibres from PLGA+a-PHB and the reference. The content of water-soluble substances affects turbidity. In both polymer variants investigated, the parameter falls within the permissible limit, which is proof of a low content of impurities, which are delivered in the course of simulated application.

Table 4 (see page 148) shows results of the chemical purity determination of aqueous extracts prepared from PLGA and PLGA + a-PHB fibres devoid of spinfinish. Results for the reference polymer are also given, as well as permissible values according to standards and research reports.

Table 4. *Results of chemical purity determination for PLGA and PLGA+a-PHB fibres devoid of spinfinish, and for the reference sample: *[24], **[22].*

		Symbol of Samples		
		Fibres PLGA	**Fibres PLGA + a-PHB**	**Reference materials**
pH		4.2	2.7	4.3
Cl^-, mg/g of medical device **Acceptance criteria <0.040***		0.03	0.02	0.003
$[SO_4]^{2-}$, mg/g of medical device **Acceptance criteria <0.010****		0.001	0.002	<0.001
Content of dissolved substance in H_2O, %		0.01	0.15	0.10
Cd	mg/100 cm³ of the aqueous extract	<0.002	<0.002	<0.002
Cr		<0.02	<0.02	<0.02
Pb		<0.02	<0.02	<0.02
Zn		0.006	0.009	0.006
Hg		<0.0002	<0.0002	<0.0002

Table 5. *Content of heavy metals in the aqueous extract after the degradation of PLGA and PLGA+a-PHB fibres with spinfinish applied, and MEDSORB sutures.*

Content of heavy metal ions, mg/100 cm³ of the aqueous extract	**Symbol of sample**		
	Fibres PLGA with spinfinish	**Fibres PLGA + a-PHB with spinfinish**	**Sutures MEDSORB**
Cd	< 0.002	< 0.002	< 0.002
Cr	< 0.02	< 0.02	< 0.02
Pb	< 0.02	< 0.02	< 0.02
Zn	0.142	0.040	0.047
Hg	< 0.0005	< 0.0005	< 0.0005

The results contained in ***Table 4*** indicate that the content of heavy metals in PLGA and PLGA+a-PHB fibres and in the reference polymer is below the limit of determination. Zinc contents are close to that in the reference. Zinc is active in the wound healing process and exerts an anti-radical action. Hence its presence and slow-release may enhance post-surgery recovery [34, 35]. The reference polymer is of very high purity. The fibres prepared from the polymers examined are, without additional purification, characterised by acceptable chemical purity in accordance with standardisation documents and literature announcements [22, 24].

Time of degradation

Fibres of the copolymer of lactide and glycolide are bio-resorbable, which means that when in contact with human body fluids they undergo hydrolysis with the delivery of lactic-and glycolic acids. Commercially available are sutures with varied time of resorption in the human body, selected for treatment according to the maintenance time required.

The fibres tested were subjected to degradation in aqueous medium in an autoclave at a temperature of 121 °C. The aim of that kind of extraction was to increase the amount of chemical substances liberated from the copolymer fibres. Chemical transformation in the material tested and substance extracted are permissible during the process [20]. The content of heavy metals was estimated in the aqueous extracts from PLGA and PLGA+a-PHB fibres with applied spinfinish after their complete degradation to assess the hazard to which patients might be exposed. A comparison was made with commercial fast absorbable sutures MEDSORB PLGA (***Table 5***). It is envisaged in further research to carry out an examination after the implantation of sutures made of the copolymer fibres.

PLGA and PLGA + a-PBH fibres degraded in 5 and 12 hours, respectively. A time of 5 hours was also needed to degrade MEDSORB sutures. The addition of a-PBH doubled the degradation time in comparison to PLGA fibres and the reference material.

In the aqueous extracts after complete resorption, pH was also estimated for fibres made of PLGA and PLGA+a-PBH. In the aqueous extracts, pH was 1.4 and 1.6 for both fibres and the reference accordingly.

The content of heavy metals in the aqueous extracts after complete resorption of the copolymer fibres is comparable with that of the reference. The spinfinish applied does not contain hazardous metal ions which would exert a toxic activity. The zinc content in PLGA fibres is triple that in the reference, which may favour wound healing since zinc is active in the process by exerting anti-radical activity and by controlling cell division [34, 35]. Because copolymers were prepared with the use of a low-toxic zirconium initiator, the content of Zr was not estimated [36].

Conclusions

It may be concluded from the results of the chemical purity analysis obtained that the content of toxic substances in the fibres tested is comparable with that of the reference materials. The polymeric fibres examined satisfy the requirements of medical materials set by European Pharmacopoeia No 8.0 and American Pharmacopoeia USP 38 NF33. They are also in accordance with published results of investigations into thechemical purity of medical devices. The copolymer fibres tested in this respect lend themselves to further works aimed at the manufacture of sutures.

A low pH was measured in the aqueous extracts of PLGA+a-PBH fibres. The PLGA fibres revealed a low pH as well; however, the value in thios case is comparable with that of the reference and only insignificantly exceeds the limit set by Pharmacopoeia USP 38 NF 33 for bacteriostatic water for injection. It is worth noting that a number of substances are commercially available with low pH (pH=3.2-4.2) that are anti-bacterial and favour wound healing [37]. A very low pH was also found in the aqueous extracts of commercial MEDSORB sutures.

It was found that after the second step of extraction (45 minutes) with methanol the spinfinish Estesol PF 790 applied during fibre spinning was selectively removed. The process carried out in a water bath with shaking is safe and does not cause any damage in the fibre molecular structure, thus providing the chance of an accurate analysis of the influence of the material on the process of its application. Hence an assessment is possible of the impurities which might cause an allergenic and inflammatory reaction in the tissue. Methanol extraction can be adopted as a purification step of the fibres to remove the spinfinish, whose use was indispensable in the spinning.

PLGA fibres with applied Estesol PF 790 spinfinish undergo complete degrada-

tion in the aqueous medium in surplus extraction in the same time as the reference material. The addition of a-PBH doubles the degradation time, providing the chance of tailoring the degradation time in the devices and thus offering the possibility of designing devices for special purposes.

The content of heavy metals after complete resorption was estimated for fibres with spinfinish applied in comparison to the reference. The higher content of zinc in the aqueous extract of PLGA fibres may affect the wound healing process beneficially.

It may be concluded that the fibres of PLGA and PLGA+a-PHB prepared satisfy the requirements of chemical purity in polymeric medical devices. The conclusion opens to way to further works aimed at the preparation of sutures.

Acknowledgments

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