Biodegradable shape memory polymers for medical purposes

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Introduction

"Shape memory" is a term which denotes a material's ability to return from a programmed, "frozen" temporary shape to the original, permanent shape as a result of external physical stimuli (temperature, light, IR radiation, electric or magnetic field), or chemical factors (changes of pH, ionic strength of selective solvents or addition of chemical compounds) [1÷4].

The first materials in which the shape memory effect has been observed were metal alloys *(shape memory alloys SMA), i*n particular an alloy of nickel and titanium (Nitinol) which has been applied in medical practice [5]**.** Research into the medical applications of such materials has been conducted for several years. Implants made of the alloy have been applied in bone surgery as self-locking materials to bond bones (in oral and maxilofacial surgery, spine surgery). However, there are numerous drawbacks associated with the use of such metal products, which are typical of such implants, such as: corrosion, frequent induction of inflammations and difficult removal after complete bone adhesion [1, 2].

In numerous areas SMAs have been rapidly replaced by polymers due to the latter's lower production costs, generally better shape stability, a wider range of shape change, a possibility of precise adjustment of shape recovery temperature in a wide temperature range, a relatively high shape change rate and easy production of complicated shapes in routine processes of thermoplastic processing, such as extrusion moulding or injection moulding [1, 2, 6].

First reports on shape memory polymers appeared in the 1950's, when Charlesby discovered that polyethylene cross-linked by ionising radiation restores the "remembered" shape when stimulated by a thermal stimulus [7]. So far, a number of types of various synthetic shape memory materials have been invented. Initially, due to lack of proper biocompatibility, medical applications of such polymers were restricted to devices which were not implanted into the human body [1, 2, 6].

Biocompatibility of polymers applied *in vivo*

Synthetic materials, which are foreign matter in a human body, can be applied *in vivo* only if they meet the fundamental criterion of biocompatibility. This means that they have to remain non-toxic throughout the period of contact with tissues, that they cannot induce inflammation or allergy, have any negative effect on blood and tissue cells or be carcinogenic or mutagenic. When conducting research into biocompatible memory shape materials, one must bear in mind that it is impossible or extremely difficult in a full-scale process to completely get rid of certain compounds which are found in a finished product: non-reacted monomers, initiators, solvents, by-products, plastifiers. Traces of such low-molecule compounds are released from the implant polymer to the human body and have a toxic effect on it as well as induce inflammation at the implant site [3, 8]. Therefore, toxic components should be avoided when designing the synthesis method and the composition of such materials.

Williams [8], defines the notion of biocompatibility and stresses that the property should relate to the final implant whose interaction with the human body in performing a specific task should produce desired effects, with an acceptable response from the host [8]. It is therefore important that the new material, regarded as biocompatible at the initial stages, should not change its structure when being processed and sterilised [2, 8, 9].

Biocompatibility is not only a result of the composition, but also of the dimensions and the shape of the biomaterial which induces cellular response *in vivo*. For instance, large fragments of materials may induce an inflammatory condition if their dimensions enable endocytosis by macrophages. It is not an easy task to design a biocompatible implant to be inserted in a live tissue and it requires selection of an appropriate method of processing and sterilisation, characteristics of the target tissue and proper adaptation of the mechanical properties of the implant to it. It is also extremely important to make the right choice of the type of material from which the implant is to be made and to select the right shape so that its mechanical properties are appropriate for its role at the implant site [9].

General characterisation of the shape memory effect

The shape memory effect, which combines the right morphology of a polymer and the right technological process, is associated with its final molecular structure. For a polymer to have this specific property, it has to have at least two molecular elements in its structure: netpoints and switching segments (Table 1).

Two categories of shape memory polymers are distinguished in terms of the nature of bonds which fix the original and temporary shape: thermoplastic and cross-linked.

Thermoplastic polymers are linear copolymers with rigid and flexible elements in their structure. Interactions between switching segments are responsible for fixing the original and temporary shape. The rigid elements usually form typical crystalline phases as a result of phase separation, for which the melting point (T_m) is associated with the highest value of the transition temperature (T_{perm}). They play the role of netpoints and stabilise the original shape. Flexible (elastic) elements of the chain are usually amorphous, sometimes crystalline. Their glass transition temperature (T_g), or the melting point as the second highest transition point (T_{trans}), stabilises the temporary shape and plays the role of switching segments**.** For most shape memory polymers applied in medicine, the shape memory effect is triggered by temperature. The original shape is conferred at the temperature which is close to T_m of

Table 1.

Basic structural elements of shape memory polymers

Molecular structure of shape memory polymers	
NETPOINTS	SWITCHING SEGMENTS
determine the permanent shape	responsible for fixing the temporary shape
Nature of bonds: -chemical (covalent bonds) -physical (intermolecular interactions)	Nature of reversible bonds: -chemical (covalent bods) -physical (intermolecular interactions) They can also be formed as a result of temporary aggregation of side chains.

rigid segments, usually as a result of conventional technological processes, such as extrusion moulding or injection moulding. The original shape is remembered after the material has been cooled down to the temperature below T_m, as a result of physical intermolecular interactions between rigid segments. In order to achieve the shape memory effect, the molecular network has to be temporarily maintained in the strained state under the conditions which correspond to the material's potential application; subsequently it can be deformed and conferred a temporary shape at a temperature above the glass transition temperature T_g or softening temperature T_m of the chain elastic phase. This requires the presence of strained chain segments which are under external stress, but secured against return to the original shape. This is achieved by introducing reversible netpoints to the polymer chain as switching segments. The process is accompanied by increased order of the elastic phase of the chain, i.e. decrease in entropy. Return from the temporary to permanent shape is achieved after heating the system above T_g or T_m for elastic segment, which is lower than T_m for rigid segments. In that case, the stimulus results in thermally induced cleavage of additional transverse bonds, whereby the system can return-by relaxation-to the original state with a higher entropy value. The principle of thermally induced shape memory effect is illustrated in Fig. 1.

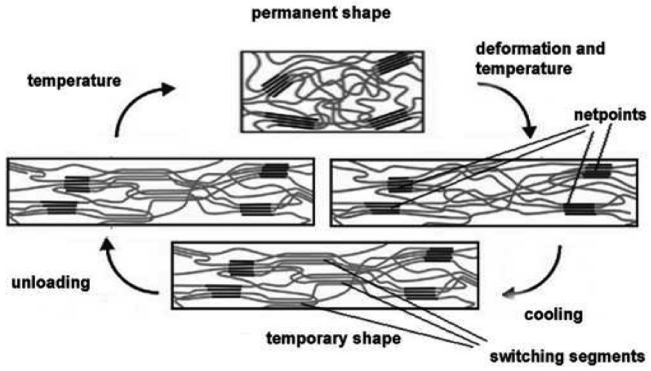


Fig. 1. Molecular mechanism of thermally induced shape memory effect

Rigid segment in cross-linked SMP are formed by creation of cross-linking covalent bonds connecting elastic segments (bonds formed by radiation or by chemical cross-linking). If transverse bonds are formed by functional groups which can undergo reversible photoreactions, the technology of shape memory polymers could be expanded by making use of light as a stimulus. Other types of stimuli, such as electric current or magnetic field, may be used for heating the material indirectly [1, 2, 4]. If such additional transverse bonds are based on physical interactions between molecules, it is possible to distinguish between temperatures of transition T_{trans}, which may be either the temperature of glass transition T_g or melting point T_m [4]. In polymers for which $T_{trans}=T_m$ the original shape recovery rate is higher [1].

In mechanical tests with shape memory polymers, the following parameters are usually determined [1, 2, 4]:

- straining rate Rf – it denotes the ability of a polymer to attain and maintain the state of mechanical strain ε_m, which causes the material to assume a temporary shape ε_u;
- shape recovery rate Rr – it denotes the polymer's ability to return to the previous shape ε_p after being strained ε_m;
- switching temperature $T_{switch} = T_{trans}$.

Biodegradable shape memory polymers

The 1990's and the first years of the 21st century began an era of degradable shape memory materials. Such versatile materials have been found to be especially useful in short-term low-invasive tissue surgery; their application allows for elimination of an additional surgery aimed at implant removal, which is the case with metal implants [1, 2, 10]. A shape memory implant of a temporary shape could be placed inside the body, requiring only a minimum surgery (a shape with a minimum cross-section, with no need of a large operation field). After a pre-defined period (seconds, minutes) or responding to an external stimulus, it would assume (by expansion) the permanent shape, meeting the therapeutic requirements [1, 2, 4]. After a period needed to heal the lesion (from 1 to several months), the material would be resorbed, which would prevent long-term cellular response and other delayed undesired interactions between the body and the implant [11].

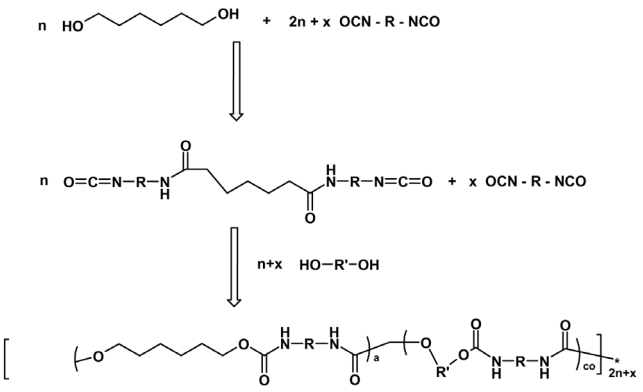
Biocompatible shape memory polymers can in most cases successfully replace previously used implants made of metal alloys. They can be used to make surgical devices, such as: self-expanding stents, self-locking staples, surgical pins [3, 12].

The biodegradable SMP's invented so far have in their polymer chains the basic elements made of aliphatic polyesters, such as: polyglycolide (PGA), poly-ε-caprolactone (PCL), poly-L-lactide (PLLA). This is mainly because polyesters have been in use in medicine for many years: their biocompatibility and biodegradability is well documented [1].

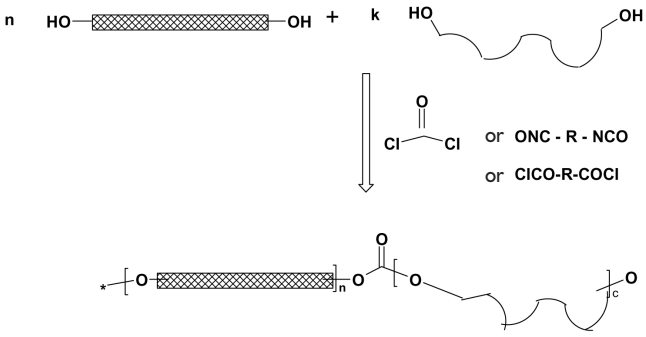
It is an advantage of SMP's with flexible segments, which contain poly-ε-caprolactone (PCL), that it is possible to achieve a T_{trans} of a synthesised polymer close to the human body temperature (37-40°C) by selecting the appropriate molecular weight of the designed polymer, the component which forms the rigid segments, and the flexible phase to rigid phase ratio [1, 2, 13].

Many various strategies have been demonstrated so far aimed at synthesis of biodegradable SMP [1, 4]. The typical shape memory degradable polymers for medical applications, which have been described in the literature, are segmented polyurethanes obtained in two-stage synthesis [10]. The first stage involves synthesis of macrodiol from cyclic diesters or lactones (oligolactide, oligocaprolactone, oligolactide-co-glycolide with terminal hydroxyl groups); subsequently, a prepolymer with terminal isocyanate groups is obtained in a reaction of macrodiol with diisocyanates. The second stage of the synthesis the prepolymer reacts with the chain elongation factor (scheme 1).

The synthesis produces polyurethanes whose chains include both rigid and elastic segments. Depending on the chemical structure, length and deployment of those segments in a molecule, materials of various properties are obtained, with various T_{trans}. Other bifunctional coupling compounds are used instead of diisocyanates, such as di-acid chlorides, phosgene (scheme 2) [1,10].



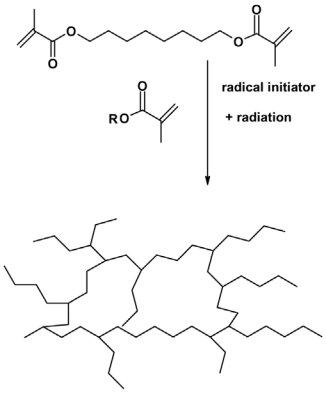
Scheme 1. Synthesis of thermoplastics block urethanes



Scheme 2. Synthesis of thermoplastics linear copolymers

One of the first shape memory degradable polymers was one synthesised by Lendlein and co-workers, a polyurethane made up of PCL with terminal hydroxyl groups and oligo(p-dioxanone) (ODX) coupled with isocyanate. What is important with regard to the application of the material, its T_{trans} is close to the temperature of a human body. An attempt at using the material in self-locking suture has been successful [13].

Lendlein and co-workers also examined memory shape materials produced by photo-crosslinking. The general strategy of such a synthesis involves introducing functional groups into the skeleton of the degraded polyester chain, which can cross-link the material when treated with UV radiation (scheme 3).



Scheme 3. Synthesis of photocrosslinked shape memory polymers

The synthesis conducted by Lendlein's research group [14] involved obtaining an oligodiol made up of polyesters of aliphatic hydroxyacids. The prepolymer is subsequently subjected to transesterification with acrylic esters. Poly-ε-caprolactone dimethacrylate transformed into an SMP network after photo-crosslinking. The process produced a material with very good shape memory properties, with no aromatic or urethane groups which, however, hydrodegrades very slowly and which is not thermoplastic, the property greatly hindering its further processing. Another such material was poly-(L-lactide-co-glycolide) dimethacrylate, which is brittle and with limited usability due to a relatively high T_{trans} (between 48 and 66°C). Changes of T_g in the polymer were effected by differentiating the chemical structure of the prepolymer, obtained initially in a lactone ring opening copolymerisation in the presence of penthaerythritol. It was also made possible to regulate the hydrolytic degradation rate by changing the content of easily hydrolysed ester bonds. Such amorphous branched polymers, called multifunctional polymer lattice, are very interesting due to their transparency, which makes them usable in ophthalmology [1, 14].

Nagata and co-workers [15] also conducted research into biodegradable shape memory polymer lattice, obtained by photo-crosslinking of PCL-based oligodiol with 4,4(adipodioxy)dicinammic acid (CAC) as a chain-elongation factor, and a multiblock biodegradable copolymer of poly-ε-caprolactone oligodiol and poly(ethylene glycol) (PEG) with CAC, synthesised by photo-crosslinking. Biodegradability and the shape memory effect was examined for both polymers. It was found that the shape memory is affected not only by the composition and microstructure of the co-polymer chain, but also by the photo-crosslinking duration [1, 15, 16]. PCL/PEG co-polymers demonstrate numerous combinations of properties, such as hydrophility, permeability, degradability. The biodegradation rate was found to increase proportionally to the PEG content in a co-polymer due to reduced extent of crosslinking [1].

Other researchers [16] have also obtained a shape memory polymer of a similar structure, consisting of poly(ε-caprolactone) (PCL) with the coumarine group attached to it. The photosensitive material was subjected to quick reversible photo-crosslinking by being irradiated with 280/254 nm waves. What is important, the system did not require a photoinitiator, which is a highly toxic compound. Cross-linked UV films demonstrated a good shape memory effect; they returned to their original shape immediately and they demonstrated elastic properties above the T_m of PCL segments. It was found in *in vitro* degradation studies that – as expected – the presence of side coumarin groups and the polymer cross-linking significantly slows down the degradation reaction.

An interesting PCL-based polymer has been described by L. Xue and co-workers [17]. Thanks to using an oligotriol produced by an enzymatic ε-caprolactone ring-opening polymerisation with glycerol, they obtained tri-arm polyurethanes with T_{trans} 36-39°C.

A PCL-based SMP has been examined by a team led by Zhu [18], who obtained radiation-induced cross-linked polymer blends of PLC and polymethyl vinyl siloxanone (PMVS) with the shape recovery rate higher than 95% and T_{trans} 48-56°C. The amount of crystalline fraction in polymer depends on the radiation dose and the polymer cross-linking extent [18,19].

It turned out that the greatest disadvantage of PCL-based SMP's is their lack of good mechanical properties after returning to the permanent shape, required for medical applications (very low modulus of rigidity, too slow biodegradation of such materials) [1].

Wang and co-workers [20] synthesised SMP from a polyactide oligomer with terminal hydroxyl groups and determined its mechanical properties and the shape memory effect. They noticed that PLA-diol-based polyurethanes demonstrated a better shape memory effect with small strain and a shorter shape recovery time following a thermal stimulus, than those obtained from oligocaprolactone. Unfortunately, the temperature of glass transition T_g of polilactidyl segments (ca. 60°C) is much higher than the temperature of denaturation of human proteins, which makes the polymers unusable in biomedicine. Controlling the content of caprolactone units in statistical copolymers with lactide results in achieving desired level of T_g, and a change of proportion of lactidyl units changes the degradation rate to a different value than that recorded for PLC-based polyurethanes [1].

A team led by Min [21] examined biodegradable polylactyde-co-poly(glycolid-co-caprolactone), a copolymer synthesised from prepolymers: diol obtained from lactic acid (PLLA) and poly(glycolid-co-caprolactone)diol (PGC) in the presence of diisocyanate. The

mechanical properties of the resultant macrodiol can be adjusted by changing the lengths of segments and proportion of co-monomers in macrodiols. The SMP's produced in the process had Rf and Rr of over 90% and T_{trans} ca. 45°C and degraded rapidly (loss of mechanical properties within 1-2 months) .

Research was also conducted of a biodegradable polymer, poly (3-hydroxybutyrate)-co-(3-hydroxyvalerate), obtained by biotechnological methods with the use of microbes; however, a high value of T_{trans} (over 45°C) of the material obtained so far is a restricting factor for its application in medicine [1, 21].

It has turned out that many PCLU (polyurethanes composed mainly of poly(ε-caprolactone)) polymers do not have sufficient mechanical strength required for most applications. Such materials include segmented polyurethanes which contain an elastic polyactide (PLA)-based segment and a rigid one which consists of 1,6 hexamethylene diisocyanate and 1,4 butandiol (HDI-BDO). The temperature of glass transition of the polymer may be regulated within the range from 33 to 53°C, by changing M_n of the PLA oligomer and the rigid/elastic phase ratio. This enables adapting T_{trans} to the range of human body temperatures. As compared to PCLU, the materials demonstrate a better shape memory effect in small strains and are quicker to response to a thermal stimulus [22].

A risk of toxic effect of shape memory polymers should be minimised by selecting such monomers whose homo- and copolymers are known materials with confirmed biocompatibility [2]. Otherwise it may be difficult to achieve appropriate biocompatibility of the synthesised materials.

It was found that certain polyurethane polymer materials may be highly thrombogenic. Lack of biocompatibility was also observed after olefin elements, e.g. a polyethylene chain, were introduced to the polymer structure. Using implants covered with polyurethane foam resulted in toluenediamine (TDA) detection in patients' urine. TDA is a substance whose carcinogenicity has been confirmed in animal tests. Moreover, many known shape memory polyurethane polymers contain aromatic structures which, as might be expected, are not fully biocompatible and may be carcinogenic [3]. Degradation of segment polyurethanes is frequently very slow, which makes it complicated to use such materials in production of short-term implants [1].

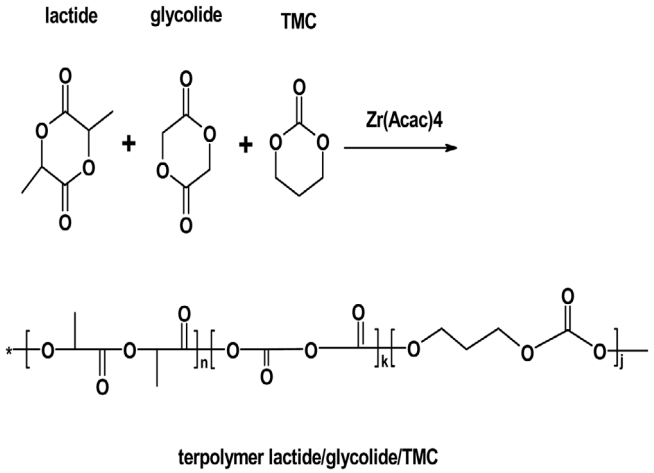
Another method of obtaining shape memory materials which ensure rather full biocompatibility and bioresorbability is ring-opening polymerisation or co-polymerisation of lactides (glycolide, lactide), lactones (ε-caprolactone) and cyclic carbonates (trimethylenecarbonate) [23]. The process of copolymersation must be conducted in such a way as to produce a block, segment-structured chain polymer, similar to segment polyesterurethanes [10].

Owing to their compatibility with human tissues (clinically confirmed), biosorption and non-toxic degradation products, the materials have been used for years to produce medical products such as sutures, implants, and in drug release systems, as microspheres, nanospheres, polymer matrixes, microcapsules and drug-polymer conjugates. The degradation products of those polymers are non-toxic [24÷27].

Poly(L-lactide) (PLLA) is a material with confirmed shape memory properties. However, the permanent shape recovery rate is low and the T_{trans} is too high for it to be used in the human body, which has been mentioned earlier.

Copolymerisation is a method which may lower its glass transition temperature and, consequently, its T_{trans}. Nowadays biodegradable, completely resorbable shape memory polyester materials are obtained by copolymerisation of trimethelenecarbonate (TMC), lactide, glycolide in the presence of initiators – low-toxic compounds of zirconium or zinc (diagram 4).

Terpolymers obtained from those monomers are bioresorbable copolyesters which demonstrate shape memory properties at temperatures close to that of the human body. Copolymerisation at the right



Scheme 4. The ROP copolymerization of cyclic monomers

conditions and with the right initiators produces a multiblock, segment chain polymer. The chain microstructure in such aliphatic co-polyesters depends on the intensity of intermolecular transesterification, which may be regulated by the temperature of the polymerisation process and by selecting the right initiator. A process with the right initiator and the synthesis method (one-step or two-step block polymerisation, terpolymerisation of lactide, glycolide monomers and TMC oligomer) yields polymers with various chain structures (completely amorphous or largely crystalline) [10, 28÷33].

The shape memory effect can also be achieved in such copolymers as poly(L-lactide-co-glycolide) (PLGA), poly(lactide-co-p-dioxanone) (PLDON) and poly(lactide-co-ε-caprolactone) (PCLA) obtained by ring-opening copolymerisation in the presence of tin octanate as an initiator, with the proper number of lactidyl units in the copolymer chain.

Of the examined polymers, PLGA demonstrated the highest strength and the highest Rr and Rf values [34]. PCLA copolymers, obtained by ring-opening copolymerisation at various percentage of monomers, have been examined by Lu and co-workers [35]. The materials demonstrated the T_{trans} values within the range close to that typical of the human body. They noticed that increasing e-caprolactone content is accompanied by linear increase in the material's tensile strength.

There are increasing numbers of reports in the literature on new SMP materials with potential for biomedical applications, such as: poly(glycol-glycerol-sebacate) PGGS terpolymer, whose temperature of the permanent shape recovery (T_{trans} = 37.5°C) is close to the human body temperature and Rr = 99.5% [36], or blends of polylactide (PLA) and biodegradable polyamide elastomers (PAE) [37].

Unfortunately, data on full biocompatibility or safe sterilisation methods for an increasing group of SMP materials proposed for biomedical applications are still incomplete. The willingness to use a shape memory material in contemporary medicine entails the necessary biocompatibility tests with specific cell lines, similar to those which will surround an implant in a short-term or lon- term in vivo application [37]. Not many reports have been published so far of *in vitro* studies of shape memory polymers and their effect on cell cultures and in vivo studies with animals [38,39]. It is also necessary to perform an analysis and evaluation of biocompatibility of new polymers following sterilisation as the process may bring about changes of physical and chemical properties of the polymer [39].

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Literature

1. Ratna D., Karger-Kocsis J.: J. Mater. **Sci., 2008, 43, 254.**
2. Lendlein A., Kelch S.: Angew. Chem. Int. Ed., 2002, 41: 2034.
3. El Fenirnat F., Laroche G., Fiset M., Mantovani D.: Adv. Eng. Mater., 2002, 4, No. 3, 91.
4. Behl M., Lendlein A.: Mater. Today, 2007, 10 (4), 20.
5. Casteman L.S., Motzkin S.M., Alicandri F.P., Banavit V.L., Johnson A.A., J. Biomed. Mat. Res., 1976, 10, 695.
6. Barot G., Rao I. J.: Z. Angew. Math. Phys., 2006, 57:652.
7. Charlesby A.: Atomic Radiation and Polymers., Pergamon Press, Oxford, 1960, 198.
8. Williams D.F Definitions in biomaterials. Proceedings of a Consensus Conference of the European Society for Biomaterials. Chester, England, March 3-5 Elsevier Amsterdam, 1986, 4.
9. Lisa Pruitt, Jevan Furmanski, Polymeric Biomaterials for Load-bearing Medical Devices, JOM, 2009, September, 61 (9).
10. Zini E., Scandola M., Dobrzynski P., Kasperczyk J., Bero M.: Biomacromolecules, 2007, 8, 3661-3667.
11. Vert M.: Polym. Sci. 2007, 32, 755-761.
12. Venkatraman S.S. et al.: Biomaterials. 2006, 27, 1573–1578.
13. **Lendlein A., Langer R.: Science, 2002, 296, 1673.**
14. Lendlein A., Zotzmann J., Feng Y., Alteheld A., Kelch S.: Biomacromolecules 2009, 10, 975.
15. Nagata M., Kitazima I.: Colloid Polym. Sci., 2006, 284, 380
16. Nagata M., Yamamoto Y.: J. Polym. **Sci., Part A: Polym. Chem., 2009, 47,** 2422.
17. Xue L., Dai S., Li Z.: Macromolecules. 2009, 42, 964.
18. Zhu G., Xu Q., Yan R Q, H, Liang G.: Radiat. Phys. Chem., 2005, 74, 42
19. Zhu G., Xu S., Wang J., Zhang L.: Radiat. Phys. Chem., 2006, 75, 443
20. Kim Y.B, Chung Ch.W., Kim H.W., Rhee Y.: Macrom. Rapid Comm., 2005, 26, 1070.
21. Min C., Cui W., Bei J., Wang S. ,Polym. AdV. Technol. 2005, 16, 608.
22. Wang W. et al.: Eur. **Polym. J. 2006, 42, 1240.**
23. Ikada Y., w: C.C. Chu, von Franhofer ed. **Wound Close Biomaterial and** Devices. CRC Press Boca Raton, FL US, 1992, pp.317-346.
24. Grijpma D.W, Zoondervan G.J. Pennings A.J.: Polym. Bull., 1991, 25, 327.
25. Vert M., Christel P., Chabot F., Larey J., Bioresorbable plastic materials for bone surgery in: Hastings G.W., Ducheyne P., eds. Macromolecular Biomaterials. CRC Press, Boca Raton, Florida, USA:, 1984, str.119-142.
26. Hausberger A.G., DeLuca P.P.: J.Pharm. Biomed.Analysis., 1995, 13(6), 747.
27. Gupta P.K., Mehta R.C., Douglas R.H., Deluca P.P.: Pharm. **Res., 1992, 9(11),** 1502.
28. Gębarowska K., Kasperczyk J., Dobrzyński P., Scandola M., Zini E., Eng. of Biomat., 2007, 63-64, 48.
29. Smola A., Dobrzyński P., Pastusiak M., Sobota M., Kasperczyk J., Eng. of Biomat., 2009, 89-91, 82-87.
30. Bero M., Dobrzyński P., Kasperczyk J., Polymers in Medicine and Surgery IOM Communications Ltd. , Copyright The Institute of Materials, United Kingdom London (2000), p.389-396.
31. Dobrzyński P., Kasperczyk J., Janeczek H., Bero M.: Macromolecules. 2001, 34, 5090.
32. Dobrzyński P., Kasperczyk J., Janeczek H., Bero M.: Polymer, 2002, 43, 2595.
33. Dobrzyński P., Kasperczyk J.: J. J. Polym. **Sci., Part A: Polym. Chem., 2006,44** – 1, 98, 114.
34. Min Ch., Cui W., Bei J., Wang S.: Polym. Adv. Technol. 2007, 18, 299.
35. Lu X. L., Cai W., Gao Z. Y.: J. Appl. **Polym. Sci., 2008, 108, 1109.**
36. Liu L., Cai W.: Mater. **Lett. 2009, 63, 1656.**
37. Zhang W., Chen L., Zhang Y.: Polymer 2009, 50, 1311.
38. Neuss S., Blomenkamp I. , Stainforth R., Boltersdorf D., Jansen M., Butz N., Perez-Bouza A., Knuchel R.: Biomaterials 2009, 30, 1697.
39. Rickert D, Lendlein A, Schmidt AM, Kelch S, Roehlke W, Fuhrmann R, et al. Biomed. Mater. Res. B: Appl. Biomater., 2003, 67(2),722.

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