

# BLEND OF POLY(L-LACTIDE) AND POLY(L-LACTIDE-CO-TRIMETHYLENE CARBONATE) AS PROMISING MATERIALS FOR BONE AND CARTILAGE TISSUE ENGINEERING

JAKUB MARCHEWKA\*, JADWIGA LASKA

AGH UNIVERSITY OF SCIENCE AND TECHNOLOGY,  
FACULTY OF MATERIALS SCIENCE AND CERAMICS,  
DEPARTMENT OF BIOMATERIALS AND COMPOSITES,  
MICKIEWICZA 30, 30-059 KRAKÓW, POLAND

\*E-MAIL: JMAR@AGH.EDU.PL

## Abstract

The aim of this work was to evaluate the properties of polymer blends of poly(L-lactide) and poly(L-lactide-co-trimethylene carbonate) 15/85 and to select two compositions to be used to prepare the materials for bone and cartilage tissue engineering. PLLA and PLLATMC as the polymers with significantly different mechanical properties could be used to prepare a wide range of polymer blends. They were investigated by ultimate tensile strength and Young modulus measurements. Considering similar mechanical properties to these types of human tissues PLLA:PLLATMC 80:20 and 30:70 blends have been chosen as appropriate materials for bone and cartilage engineering, respectively. The materials were examined by thermal analysis (thermogravimetry and differential scanning calorimetry), ATR-FTIR spectroscopy and surface analysis (roughness and contact angle measurements). Miscibility of two polymers was discussed. High thermal stability of the blends allow to process them by fused deposition modelling which is one of the most promising methods for the manufacturing of computationally designed scaffolds. Based on the results of thermal analysis at least partial miscibility of PLLA and PLLATMC in the examined blends is indicated. Detailed interpretation of ATR-FTIR spectra let to distinguish the polymers despite their structural similarities. Surface properties of the materials depend on the preparation method and on their form.

**Keywords:** poly(L-lactide); poly(L-lactide-co-trimethylene carbonate); polymer blends; mechanical properties; biomaterials

[Engineering of Biomaterials 145 (2018) 8-15]

## Introduction

Most of the materials for bone and cartilage regeneration are prepared on the base of natural and synthetic polymers [1]. Natural polymers like collagen [2-3], fibrin [4-5], chitosan [6-7], alginates [8-9] and hyaluronates [10-11] are used in the form of hydrogels as the carriers of growth factors and cells. The advantage of applying natural polymers is a simple homogeneous distribution of cells, medicines and other bioactive substances. Synthetic polymers including polylactide, polyglycolide and their copolymers [12-14] are applied in the form of fibres or three-dimensional structures as scaffolds for cell growth.

Preparation of a polymer blend as two- or multi-component physical mixture of homopolymers, copolymers or both of them is one of the basic method used for production of new materials. Polymers could be modified by addition of small amounts of other components to achieve desired properties, or they could be mixed in various ratios to produce blends with properties significantly different from these of the individual components [15-16]. Homogeneity of new materials is an important issue so polymer miscibility should be analyzed in detail [17-18]. Biodegradable polymer blends are often used to prepare materials for tissue regeneration with precisely adjusted properties [19].

The most commonly used polymers for bone and cartilage regeneration are polylactide blends [20] including blends with polycaprolactone [21-22], polyglycolic acid or poly(lactic-co-glycolic acid) [23-24], poly(ethylene glycol) [25-26], etc. Blends of polylactide and poly(trimethylene carbonate) [27-28] dedicated for biomedical applications [29-30] are only described by few authors. The aim of this research was to evaluate the properties of the new poly(L-lactide) and poly(L-lactide-co-trimethylene carbonate) blends with potential application in bone and cartilage tissue engineering.

## Materials and Methods

### Materials

Semi-crystalline poly(L-lactide) sold under the trade name BIOCOP® PLLA Sn free (PLLA) and amorphous poly(L-lactide-co-trimethylene carbonate) 15/85 sold under the trade name BIOCOP® PLLATMC 15/85 (PLLATMC) were purchased from BioMatPol, Poland. They were medical-grade polymers synthesized with non-toxic compounds. Chemical structure of the polymers is presented in FIG. 1. TABLE 1 summarizes their basic properties according to the manufacturer. Dichloromethane (≥99.5%) was purchased from Avantor Performance Materials, Poland.

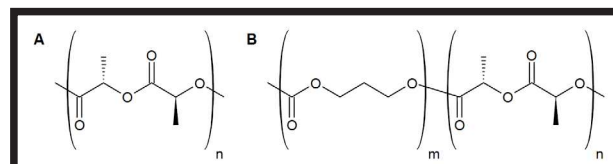


FIG. 1. Chemical structure of PLLA (A) and PLLATMC (B).

TABLE 1. Basic properties of PLLA and PLLATMC.

polymer	PLLA	PLLATMC
number average molar mass $M_n$ [g/mol]	160000	60000
dispersion coefficient D	2.1	2.0

Poly(L-lactide) (PLLA) and poly(L-lactide-co-trimethylene carbonate) 15/85 (PLLATMC) blends were prepared by polymer solution casting. For this, an appropriate amount of each polymer for a total of 4.0 g was added to 40 mL of dichloromethane. The polymers were combined in the following ratios: 100:0, 90:10, 80:20, 70:30, 60:40, 50:50, 40:60, 30:70, 20:80, 10:90, 0:100. The mixtures were stirred at room temperature until homogeneous solution was obtained. Then, resulting solutions were carefully poured on Petri dishes (10 cm in diameter) and left overnight to dry at room temperature. Prepared films were peeled off and two different sides, air-facing and plate-facing, were marked.

## Methods

Ultimate tensile strength and Young's modulus were determined using Zwick 1435 (Zwick Roell, Germany) universal testing machine. 75 mm x 10 mm foils placed in the steel clamps with a distance of 50 mm were analyzed at an extension rate of 5 mm/s until the fracture occurred. Five measurements were conducted for each sample.

Thermogravimetry (TG/DTG) in the temperature range of 25 to 600°C were performed with Netzsch STA 449 F3 Jupiter (Netzsch, Germany). 10 mg samples were analyzed at a heating rate of 10°C/min in an inert atmosphere of 99.999% nitrogen with a flow rate of 40 mL/min. Differential scanning calorimetry (DSC) analysis in the temperature range of -50 to 200°C were conducted with Mettler Toledo DSC 1 (Mettler Toledo, Switzerland). 5 mg samples were analyzed at a heating rate of 10°C/min in an inert atmosphere of 99.999% nitrogen with a flow rate of 30 mL/min.

Attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectra were collected at room temperature in a range from 4000 to 400 cm<sup>-1</sup> after 256 scans at 2 cm<sup>-1</sup> resolution using Vertex V70 (Bruker, USA) with ZnSe crystal.

Two different sides of the films were examined and photographed under an Olympus BX41 (Olympus, Japan) light microscope at magnification of 100 x.

Both sides of the films were characterized by surface roughness and contact angle analysis. Surface roughness measurements were conducted with Hommel Tester T1000 (Jenoptik, Germany). Water contact angle measurements were performed with Kruss DSA10 MK2 drop shape analyzer (Kruss, Germany) using goniometer method and UHQ water (0.23 ± 0.05 µl volume of the drop). Each parameter was calculated as an average of ten measurements.

## Results and Discussions

Poly(L-lactide) is a relatively hard and brittle material whereas poly(L-lactide-co-trimethylene carbonate) is an elastomer. Mixing them can lead to blends with different mechanical properties. Whole range of the compositions has been investigated to obtain blends with mechanical properties similar to bone or cartilage tissue. Young's modulus and tensile strength of the blends are presented in FIG. 2, and compared with bone and cartilage tissue properties in TABLE 2. As composition of 80 wt.% of PLLA and 20 wt.% of PLLATMC showed Young's modulus similar to bone tissue, and composition of 30 wt.% of PLLA and 70 wt.% of PLLATMC was similar to cartilage tissue, further research was performed using these two compositions. It should be pointed out that both of them withstand higher loads than the discussed natural tissues.

### Mechanical properties measurements

Dependence of ultimate tensile strength and Young's modulus on blends composition are presented in FIG. 2. These parameters were significantly different for PLLA and PLLATMC, so a vast range of the materials with intermediate properties as blends of these polymers could be prepared. PLLA was a semi-crystalline rigid and brittle polymer. Measured ultimate tensile strength was 47.12 ± 0.98 MPa and Young's modulus was 2485 ± 153 MPa. PLLATMC was an amorphous ductile polymer. Ultimate tensile strength was 0.31 ± 0.02 MPa and Young's modulus was 0.64 ± 0.14 MPa, so it was two and four order of magnitude lower, respectively, in comparison with PLLA.

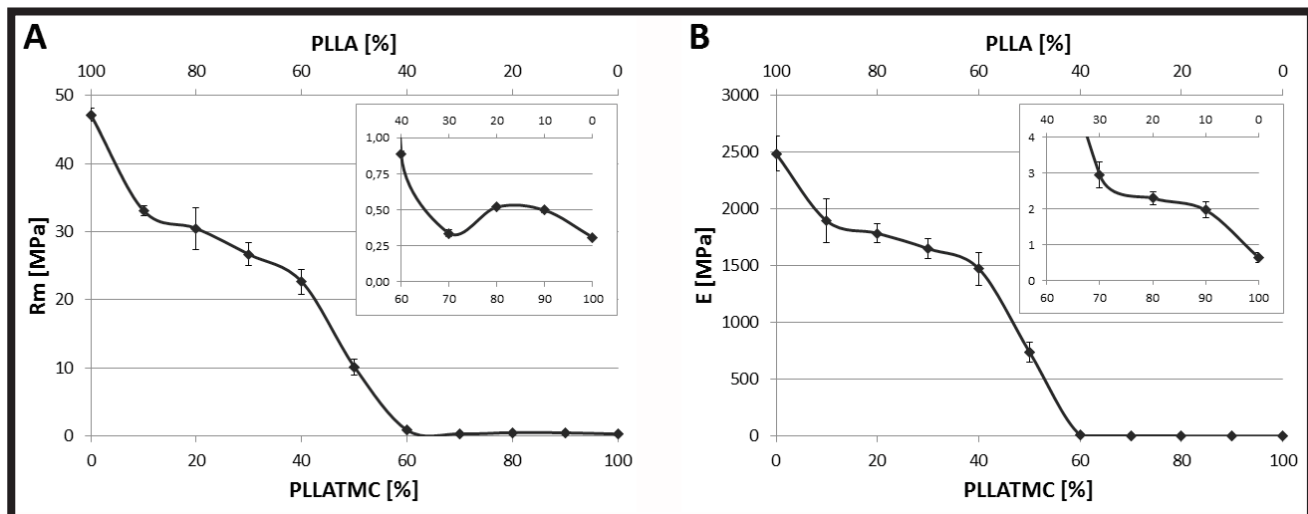


FIG. 2. Dependence of ultimate tensile strength Rm (graph A) and Young's modulus E (graph B) on blend composition.

TABLE 2. Mechanical properties of the selected blends of PLLA/PLLATMC and human bone and cartilage.

	PLLA:PLLATMC 80:20	Bone (wet) [Yamada]	PLLA:PLLATMC 30:70	Cartilage [Yamada]
Tensile strength [MPa]	30.49 ± 3.06	14.0	0.34 ± 0.02	0.29
Young's modulus [MPa]	1786 ± 81	1830	2.95 ± 0.36	2.5

PLLA and PLLATMC blends with a various ratios of both components were analyzed to select two compositions with mechanical properties appropriate to prepare materials for bone and cartilage tissue engineering. Two ranges of the mechanical properties could be seen in FIG. 2. In the first one (PLLA:PLLATMC from 90:10 to 60:40) ultimate tensile strength and Young's modulus were similar to PLLA and changed linearly with blend composition according to the following equations (where  $X$  is the content of PLLATMC [%] and  $R$  is the correlation coefficient):

$$Rm = -0.3508 \cdot X + 36.997 \quad (R^2 = 0.9910)$$

$$E = -13.969 \cdot X + 2050 \quad (R^2 = 0.9876)$$

They could be used to define a composition and to prepare a material with desired properties. In the second range (PLLA:PLLATMC from 40:60 to 10:90) both parameters were similar to PLLATMC but, contrary to the first one, a linear changes were not observed.

Mechanical properties of the human tissues were described in detail by Yamada (1970) [31]. In that review an average ultimate tensile strength for bone (wet) and cartilage were specified as 14.0 MPa and 0.29 MPa, respectively, and an average Young's modulus as 1830 MPa and 2.5 MPa, respectively. Two compositions of polymer blends, namely PLLA:PLLATMC 80:20 and 30:70, have been chosen as blends appropriate to prepare materials for bone and for cartilage tissue engineering, respectively. For 80:20 blend Young's modulus was similar to human bone tissue and ultimate tensile strength was almost two times higher whereas for 30:70 blend both parameters were slightly higher in comparison to cartilage tissue. The results are summarized in TABLE 2.

### Thermal analysis

Thermal properties of the investigated blends are important from the point of view of their processing, filament fabrication, and 3D printing. TG and DTG curves of polymers (PLLA and PLLATMC) and polymer blends (PLLA:PLLATMC 80:20 and 30:70) are given in FIG. 3 and FIG. 4, respectively. Typical effects of decomposition of both polymers were observed. At measurement conditions degradation process started about 260°C and ended about 360°C. Based on the shape of curves parameters (onset, midpoint, endset, mass change) were determined and collected in TABLE 3. High thermal stability of both components as well as their blends in the temperature range of 20 to 260°C allows for their processing at about 200°C (fused deposition modelling).

DSC curves of PLLA and PLLATMC are shown in FIG. 5. PLLA as a semi-crystalline polymer had a melting peak with maximum at 177°C and enthalpy change of -42.82 J/g. According to Pyda et al. (2004) [32] enthalpy of crystallization for 100% crystalline PLLA is  $91 \pm 3$  J/g, and based on this value a degree of crystallinity for the sample was estimated as 47%. Glass transition at 46°C was also observed. For PLLATMC as an amorphous polymer the only observable effect was glass transition at -7°C. DSC curves of the blends presented in FIG. 6 revealed three effects. The first glass transition (at -4°C and at -11°C for 80:20 and 30:70 blends, respectively) can be associated with a presence of PLLATMC. The second glass transition (at 49°C both) and melting peak (at 180°C and at 177°C, respectively) were related to the presence of PLLA. All of observed thermal effects are described in TABLE 4.

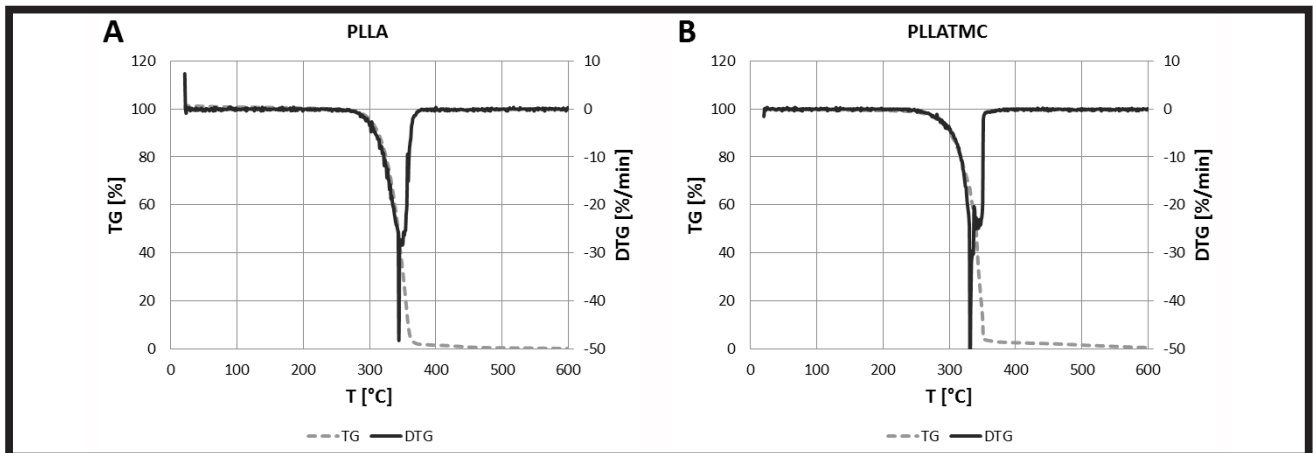


FIG. 3. TG and DTG curves of PLLA (graph A) and PLLATMC (graph B).

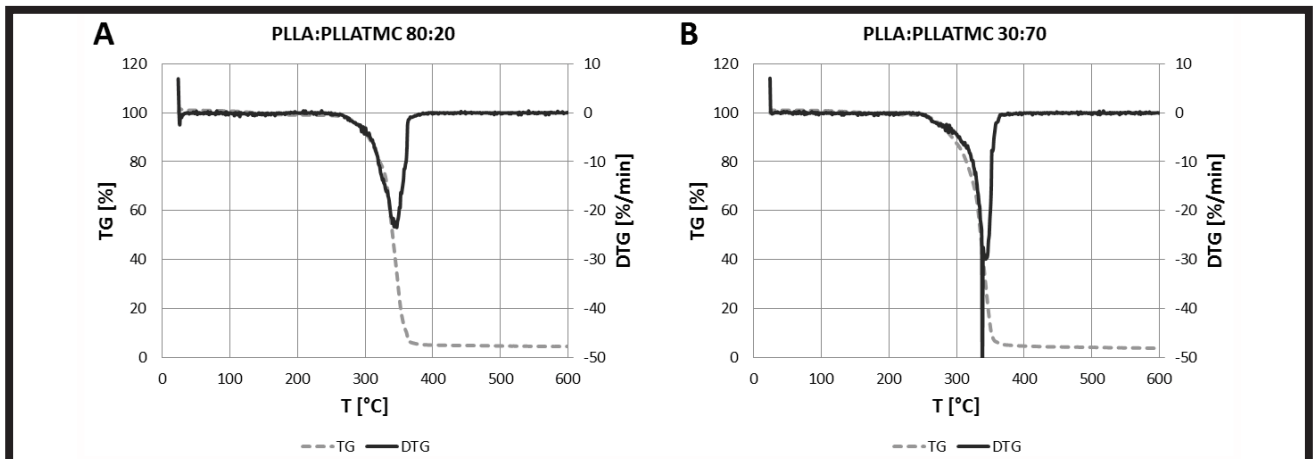


FIG. 4. TG and DTG curves of PLLA:PLLATMC 80:20 (graph A) and PLLA:PLLATMC 30:70 (graph B).

TABLE 3. Results of TG/DTG measurements for decomposition of the samples.

PLLA:PLLATMC	100:0	80:20	30:70	0:100
onset [°C]	323	320	318	327
midpoint [°C]	342	339	335	340
endset [°C]	362	358	352	352
mass change [%]	-98.2	-94.7	-94.8	-97.0

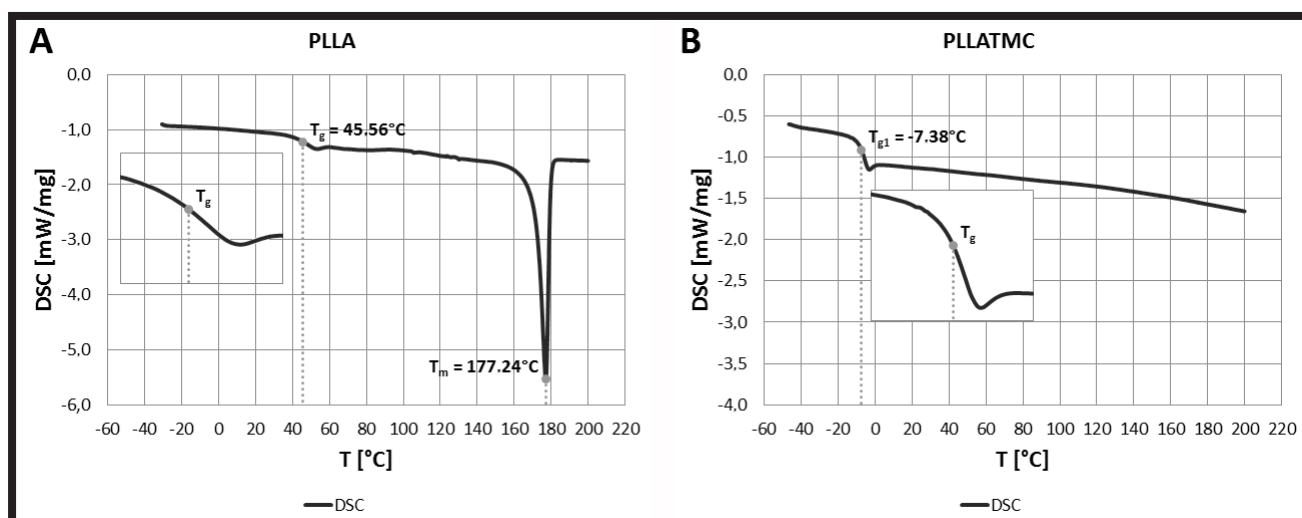


FIG. 5. DSC curves of PLLA (graph A) and PLLATMC (graph B) in the temperature range of -50 to 200°C.

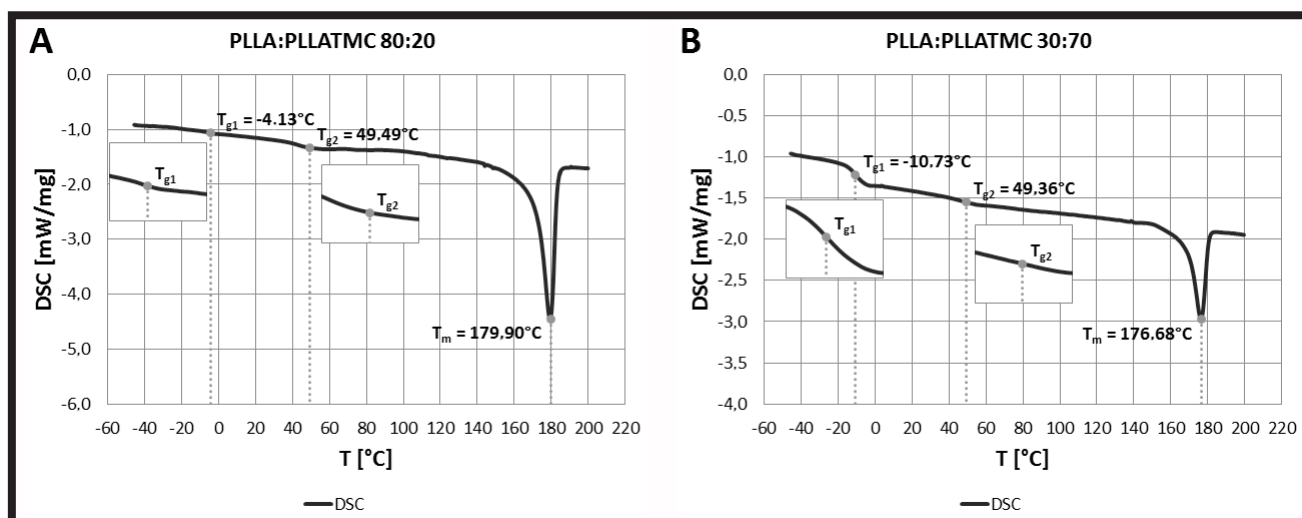


FIG. 6. DSC curves of PLLA:PLLATMC 80:20 blend (graph A) and PLLA:PLLATMC 30:70 blend (graph B) in the temperature range of -50 to 200°C.

TABLE 4. Results of DSC measurements of the samples.

PLLA:PLLATMC		100:0	80:20	30:70	0:100
glass transition I	T [°C]	-	-4.13	-10.73	-7.38
	$\Delta C_p$ [J/(g·K)]	-	0.030	0.430	0.531
glass transition II	T [°C]	45.56	49.49	49.36	-
	$\Delta C_p$ [J/(g·K)]	0.297	0.210	0.150	-
melting	T [°C]	177.24	179.90	176.68	-
	$\Delta H$ [J/g]	-42.82	-43.28	-15.14	-

Glass transition temperature is a very useful factor to assess miscibility of polymers. Full miscibility of the components of polymer blend is recognized by a single glass transition temperature. It can be calculated according to the Fox equation where  $T_{g1}$  and  $T_{g2}$  are glass transition temperatures of pure polymers, and  $w_1$  and  $w_2$  are weight fractions of the components in the blend:

$$\frac{1}{T} = \frac{W_1}{T_{g1}} + \frac{W_2}{T_{g2}}$$

In the case of full miscibility of PLLA and PLLATMC single glass transition temperatures at 33.35°C and 6.56°C should be observed for 80:20 and 30:70 blends, respectively. Detection of two values of glass transition temperature for polymer blends can be an evidence for phase separation of the components. However, the  $T_g$  values observed for the blends are different from these obtained for pure polymers. They also vary depending on weight ratio of the components. Glass transition assigned to PLLA was 49°C for both blends, while pure PLLA exhibited glass transition at 45°C. Higher  $T_g$  in the blends suggests that PLLA in its amorphous phase is packed more tightly than in pure polymer and needs more energy to increase the interchain distances. Glass transition of PLLATMC in 80:20 and 30:70 blends was observed at -4°C and -10°C, respectively, comparing to -7°C in pure polymer. It shows that PLLATMC as elastic copolymer is much more sensitive to the addition of rigid PLLA. It seems that relatively small amounts of PLLA (in our studies 30%) in the blend help the PLLATMC to achieve the elastic state, while excess of PLLA makes it more difficult. Most probably the distribution of polymer molecules and the interchain interactions play a significant role in glass transition. In the case of our studied system both components possess lactide units in their molecules that should induce better miscibility. However, high content of PLLA causes stronger interactions with PLLATMC molecules hindering their movements. This is why the  $T_g$  of PLLATMC in 80:20 blend is higher than in pure polymer. On the other hand, low content of PLLA interacting with lactide units of PLLATMC helps in creation of crystalline rigid segments in elastomer and microphase separation.

No crystalline phase (melting) is observed in pure PLLATMC, however it is expected in thermoplastic copolymers like the investigated one.

Glass transition width as a difference between endset and onset temperatures is the other parameter used to evaluate the miscibility of polymer blend components. It is described to be about 6°C for pure homopolymers, about 10°C for fully miscible polymers and over 32°C for immiscible polymers. Width of glass transition assigned to PLLA was 8°C for pure, 13°C for 80:20 blend and 15°C for 30:70 blend and assigned to PLLATMC was 4.5°C, 2.5°C and 10°C, respectively. These values could indicate at least a partial miscibility of PLLA and PLLATMC in 80:20 and 30:70 blends, which is in agreement with the discussion on  $T_g$  changes.

#### ATR-FTIR analysis

ATR-FTIR spectra of the samples are presented in FIG. 7 and detailed interpretation is summarized in TABLE 5. The chemical structure of PLLATMC as a 15/85 copolymer consists of carbonate moieties but contains also some amount of the same units as PLLA. Comparing the spectrum of PLLATMC to the spectrum of PLLA the most recognizable are peaks attributed with  $-\text{CH}_2-$  rocking in an aliphatic chain of carbonate moiety at 925  $\text{cm}^{-1}$  and 787  $\text{cm}^{-1}$ . The most intense peaks in each spectrum were attributed to C=O stretching (at about 1735-1750  $\text{cm}^{-1}$ ), C-O asymmetric stretching (1230-1265  $\text{cm}^{-1}$  and 1180-1195  $\text{cm}^{-1}$ ) and C-O-C symmetric stretching (1075  $\text{cm}^{-1}$  and 1025-1040  $\text{cm}^{-1}$ ). Apart of the peak at about 1075  $\text{cm}^{-1}$  characteristic absorption varied with the change of PLLA:PLLATMC ratio. For example for C=O stretching it decreased from 1747  $\text{cm}^{-1}$  to 1736  $\text{cm}^{-1}$  for 100:0 and 0:100 samples, respectively.

#### Surface characterization

Microscopic images of two different sides of the films are given in FIG. 8. Using polymer solution casting air-facing and plate-facing surfaces are formed as a result of solvent evaporation. Diverse morphology between them was clearly visible in the pictures. The most characteristic was air-facing side of 30:70 sample with noticeable inhomogeneity.

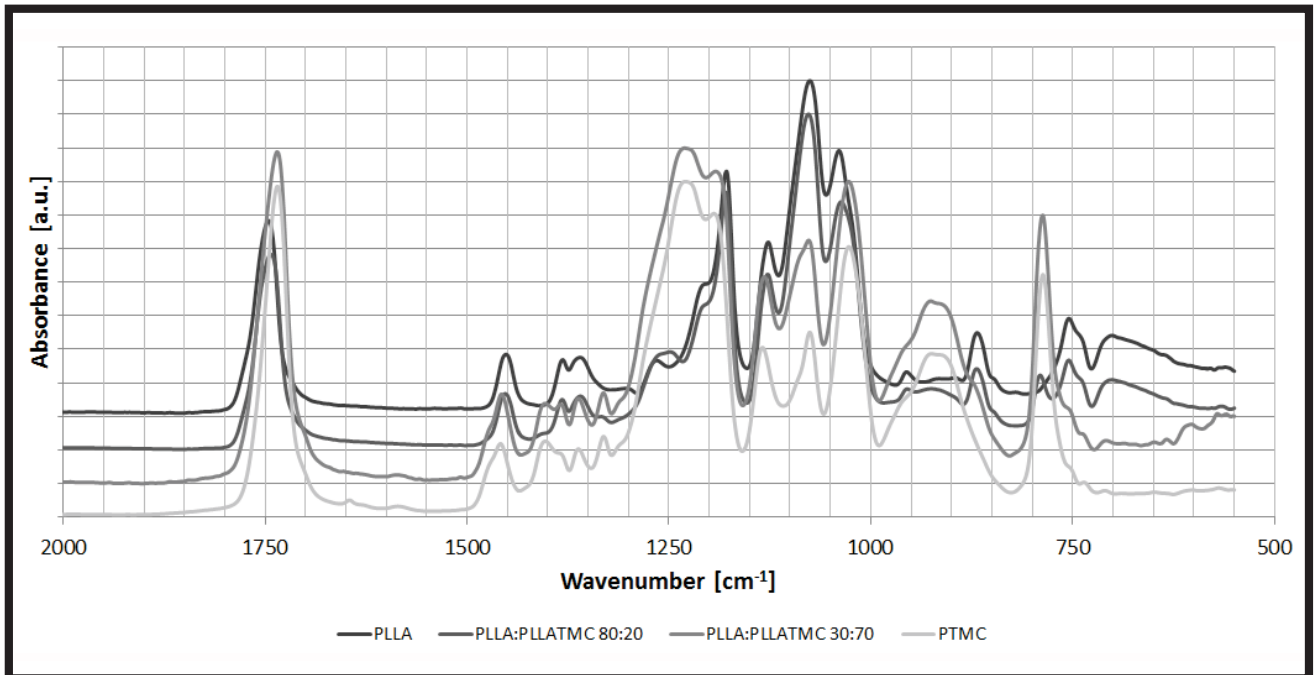
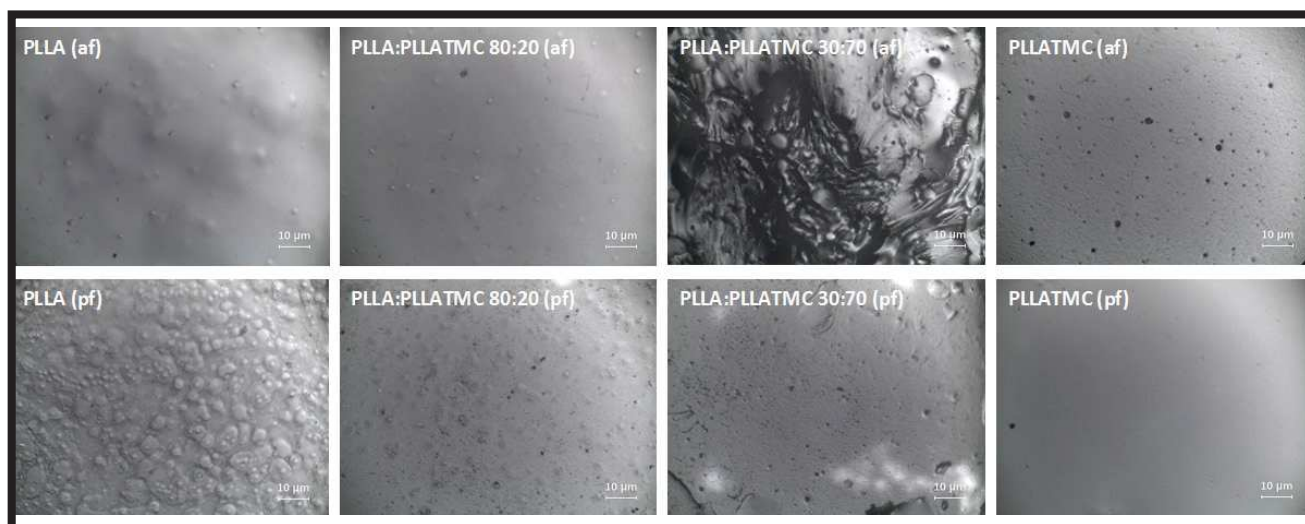


FIG. 7. ATR-FTIR spectra of PLLA, PLLATMC and PLLA:PLLATMC blends (80:20 and 30:70).



**TABLE 5. Detailed interpretation of ATR-FTIR spectra of the samples (abbreviations: vs - very strong, s - strong, m - medium, w - weak, sh - shoulder, nv - not visible).**

Type of vibration	Characteristic absorption [cm <sup>-1</sup> ] and intensity			
	PLLA	PLLA:PLLATMC		PLLATMC
		80:20	30:70	
C-H symmetric stretching (O-CHR- moiety)	2997 w	2997 w	2974 w	2974 w
C-H symmetric stretching (C-CH <sub>3</sub> moiety)	2943 w	2943 w	nv	2921 w
C=O stretching	1747 s	1744 s	1736 vs	1736 vs
CH <sub>3</sub> scissoring	1453 m	1453 m	1456 m	1458 m
CH <sub>3</sub> rocking	1382 m	1382 m	1403 m	1403 m
CH <sub>3</sub> rocking	1361 m	1359 m	1362 m	1362 m
-CH <sub>2</sub> - rocking	nv	nv	1330 m	1330 m
C-O asymmetric stretching (O-C=O moiety)	1265 m	1249 m	1230 vs	1230 vs
C-O asymmetric stretching (O-CH <sub>2</sub> - moiety)	1179 s	1179 s	1193 s sh	1194 s sh
C-C stretching	1127 s sh	1128 m	1132 m	1134 m
C-O-C symmetric stretching	1075 vs	1077 vs	1076 s	1075 m
C-O-C symmetric stretching	1039 s sh	1037 s sh	1028 s	1028 s
-CH <sub>2</sub> - rocking (O-CH <sub>2</sub> - moiety)	nv	nv	926 m	925 m
C-O stretching (O-CH(CH <sub>3</sub> ) moiety)	868 m	869 m	nv	nv
-CH <sub>2</sub> - rocking (-(CH <sub>2</sub> ) <sub>n</sub> - moiety)	nv	790 m	787 s	787 s
-CH <sub>2</sub> - rocking (-(CH <sub>2</sub> ) <sub>n</sub> - moiety)	754 m	754 m	nv	nv



**FIG. 8. Microscopic images of the air-facing (af) and plate-facing (pf) sides of the films.**

**TABLE 6. Roughness parameters (Ra - arithmetical mean height, Rt - total height of profile, Rz - maximum height of profile) of air-facing and plate-facing sides of the films.**

PLLA:PLLATMC		100:0	80:20	30:70	0:100
Ra [ $\mu\text{m}$ ]	air-facing	$0.72 \pm 0.10$	$0.36 \pm 0.06$	$11.31 \pm 1.41$	$1.36 \pm 0.27$
	plate-facing	$0.55 \pm 0.05$	$0.28 \pm 0.07$	$10.52 \pm 1.05$	$1.64 \pm 0.36$
Rt [ $\mu\text{m}$ ]	air-facing	$6.22 \pm 1.23$	$2.34 \pm 0.50$	$95.88 \pm 12.54$	$15.31 \pm 2.75$
	plate-facing	$4.31 \pm 0.70$	$2.41 \pm 0.54$	$87.67 \pm 9.33$	$17.79 \pm 3.19$
Rz [ $\mu\text{m}$ ]	air-facing	$3.91 \pm 0.65$	$1.69 \pm 0.31$	$62.02 \pm 5.85$	$7.85 \pm 1.26$
	plate-facing	$3.25 \pm 0.29$	$1.66 \pm 0.23$	$55.31 \pm 5.22$	$10.24 \pm 1.54$

**TABLE 7. Water contact angle of air-facing and plate-facing sides of the films.**

PLLA:PLLATMC		100:0	80:20	30:70	0:100
contact angle [ $^{\circ}$ ]	air-facing	$82.7 \pm 1.4$	$81.5 \pm 0.5$	$75.4 \pm 2.0$	$103.9 \pm 1.4$
	plate-facing	$73.3 \pm 1.8$	$74.8 \pm 1.1$	$74.7 \pm 1.4$	$104.1 \pm 1.7$

The results of surface roughness and water contact angle analysis are shown in TABLE 6 and TABLE 7, respectively. Roughness parameters of air-facing side were higher than plate-facing side for films of PLLA and two PLLA:PLLATMC blends in contrast to PLLATMC. The differences between both sides were a result of the gradient formed by solvent evaporation during preparation of the films. For 30:70 PLLA:PLLATMC film roughness parameters were one order of magnitude higher compared to the others. This could be a result of the lower miscibility of both components in this polymer blend. For PLLA and 80:20 sample water contact angle of air-facing sides was higher than these of plate-facing sides, while for PLLATMC and 30:70 sample it was similar. The measurements were affected by differences in surface roughness of the samples, and contact angles were the lowest for 30:70 sample with the highest roughness.

## Conclusions

Biodegradable polymers like poly(L-lactide) and poly(L-lactide-co-trimethylene carbonate) 15/85 with significantly different mechanical properties are an appropriate materials to prepare a wide range of polymer blends for various applications. 80:20 and 30:70 weight ratios of PLLA to PLLATMC were chosen to develop materials for bone and cartilage tissue engineering, respectively. Importantly, a linear relationship between mechanical properties (ultimate tensile strength, Young's modulus) and composition for PLLA:PLLATMC ratios from 90:10 to 60:40 was observed. Thermal processing of the materials is possible in the temperature range from above 180°C when they melt up to 260°C when decomposition starts. The changes in glass transition temperatures of blends comparing to pure polymers suggest partial miscibility of the components. PLLA and PLLATMC in spite of structural similarity are discriminated by ATR-FTIR spectroscopy so the method could be used to investigate polymer blends. Depending on the preparation method surface properties of the materials (roughness and water contact angle) are different.

Fused deposition modelling (FDM) as one of the most promising method is proposed to be used to produce bone and cartilage scaffolds with a structure precisely described by a computer-designed model. Developed PLLA:PLLATMC 80:20 and 30:70 blends after processing to the form of a filament could be used in FDM 3D printers.

## Acknowledgements

*This research was financed by the statutory research No 11.11.160.182 of Faculty of Materials Science and Ceramics, AGH University of Science and Technology, Krakow, Poland.*

## References

- [1] Engelberg I., Kohn J.: Physico-mechanical properties of degradable polymers used in medical applications: a comparative study. *Biomaterials* 12(3) (1991) 292-304.
- [2] Chajra H., Rousseau C.F., Cortial D., Ronziere M.C., Herbage D., Mallein-Gerin F., Freyria A.M.: Collagen-based biomaterials and cartilage engineering. Application to osteochondral defects. *Bio-Medical Materials and Engineering* 18(1) (2008) S33-45.
- [3] Willers C., Chen J., Wood D., Xu J., Zheng M.H.: Autologous chondrocyte implantation with collagen bioscaffold for the treatment of osteochondral defects in rabbits. *Tissue Engineering* 11(7-8) (2005) 1056-1076.
- [4] Filardo G., Drobnic M., Perdisa F., Kon E., Hribernik M., Marcacci M.: Fibrin glue improves osteochondral scaffold fixation: study on the human cadaveric knee exposed to continuous passive motion. *Osteoarthritis Cartilage* 22(4) (2014) 557-565.
- [5] Konst Y.E., Benink R.J., Veldstra R., van der Krieke T.J., Helder M.N., van Royen B.J.: Treatment of severe osteochondral defects of the knee by combined autologous bone grafting and autologous chondrocyte implantation using fibrin gel. *Knee Surgery, Sports Traumatology, Arthroscopy* 20(11) (2012) 2263-2269.
- [6] Han F., Yang X., Zhao J., Zhao Y., Yuan X.: Photocrosslinked layered gelatin-chitosan hydrogel with graded compositions for osteochondral defect repair. *Journal of Materials Science: Materials in Medicine* 26(4) (2015) 160.
- [7] Malafaya P.B., Pedro A.J., Peterbauer A., Gabriel C., Redl H., Reis R.L.: Chitosan particles agglomerated scaffolds for cartilage and osteochondral tissue engineering approaches with adipose tissue derived stem cells. *Journal of Materials Science: Materials in Medicine* 16(12) (2005) 1077-1085.
- [8] Diduch D.R., Jordan L.C., Mierisch C.M., Balian G.: Marrow stromal cells embedded in alginate for repair of osteochondral defects. *Arthroscopy* 16(6) (2000) 571-577.
- [9] Sukegawa A., Iwasaki N., Kasahara Y., Onodera T., Igarashi T., Minami A.: Repair of rabbit osteochondral defects by an acellular technique with an ultrapurified alginate gel containing stromal cell-derived factor-1. *Tissue Engineering Part A* 18(9-10) (2012) 934-945.
- [10] Kim S.S., Kang M.S., Lee K.Y., Lee M.J., Wang L., Kim H.J.: Therapeutic Effects of Mesenchymal Stem Cells and Hyaluronic Acid Injection on Osteochondral Defects in Rabbits' knees. *Knee Surgery and Related Research* 24(3) (2012) 164-172.
- [11] Tytherleigh-Strong G., Hurtig M., Miniaci A.: Intra-articular hyaluronan following autogenous osteochondral grafting of the knee. *Arthroscopy* 21(8) (2005) 999-1005.
- [12] Nagura I., Fujioka H., Kokubu T., Makino T., Sumi Y., Kurosaka M.: Repair of osteochondral defects with a new porous synthetic polymer scaffold. *Journal of Bone and Joint Surgery* 89(2) (2007) 258-264.
- [13] Sherwood J.K., Riley S.L., Palazzolo R., Brown S.C., Monkhouse D.C., Coates M., Griffith L.G., Landeen L.K., Ratcliffe A.: A three-dimensional osteochondral composite scaffold for articular cartilage repair. *Biomaterials* 23(24) (2002) 4739-4751.
- [14] Xue D., Zheng Q., Zong C., Li Q., Li H., Qian S., Zhang B., Yu L., Pan Z.: Osteochondral repair using porous poly(lactide-co-glycolide)/nano-hydroxyapatite hybrid scaffolds with undifferentiated mesenchymal stem cells in a rat model. *Journal of Biomedical Materials Research Part A* 94(1) (2010) 259-270.
- [15] Isayev A.I.: *Encyclopedia of Polymer Blends*, vol. 1-5. Wiley-VCH (2013).
- [16] Utracki L.A.: *Polymer Blends Handbook*, vol. 1-2. Kluwer Academic Publishers (2002).
- [17] Coleman M.M., Painter P.C., Graf J.F.: *Specific Interactions and the Miscibility of Polymer Blends*. CRC Press (1995).
- [18] Thomas S., Grohens Y., Jyotishkumar P.: *Characterization of Polymer Blends: Miscibility, Morphology and Interfaces*. Wiley-VCH (2014).
- [19] Zhang X., Peng X., Zhang S.W.: *Synthetic biodegradable medical polymers: Polymer blends*. [in:] Zhang X.: *Science and Principles of Biodegradable and Bioresorbable Medical Polymers - Materials and Properties*. Woodhead Publishing (2016) 217-254.
- [20] Saini P., Arora M., Ravi Kumar M.N.V.: Poly(lactic acid) blends in biomedical applications. *Advanced Drug Delivery Reviews* 107 (2016) 47-59.
- [21] Navarro-Baena I., Sessini V., Dominici F., Torre L., Kenny J.M., Peponi L.: Design of biodegradable blends based on PLA and PCL: From morphological, thermal and mechanical studies to shape memory behaviour. *Polymer Degradation and Stability* 132 (2016) 97-108.
- [22] Esmaeilzadeh J., Hesarakhi S., Hadavi S.M.M., Esfandeh M., Ebrahimzadeh M.H.: Microstructure and mechanical properties of biodegradable poly (D/L) lactic acid/polycaprolactone blends processed from the solvent-evaporation technique. *Materials Science and Engineering C* 71 (2017) 807-819.
- [23] Thanki P.N., Dellacherie E., Six J.L.: Surface characteristics of PLA and PLGA films. *Applied Surface Science* 253 (2006) 2758-2764.
- [24] Pandey A., Pandey G.C., Aswath P.B.: Synthesis of polylactic acid-polyglycolic acid blends using microwave radiation. *Journal of the Mechanical Behavior of Biomedical Materials* 1(3) (2008) 227-233.
- [25] Gui Z., Xu Y., Gao Y., Lu C., Cheng S.: Novel polyethylene glycol-based polyester-toughened polylactide. *Materials Letters* 71 (2012) 63-65.
- [26] Pluta M., Piorkowska E.: Tough crystalline blends of polylactide with block copolymers of ethylene glycol and propylene glycol. *Polymer Testing* 46 (2015) 79-87.
- [27] Marquez Y., Franco L., Puiggali J.: Thermal degradation studies of poly(trimethylene carbonate) blends with either polylactide or polycaprolactone. *Thermochimica Acta* 550 (2012) 65-75.
- [28] Li H., Chang J., Qin Y., Wu Y., Yuan M., Zhang Y.: Poly(lactide-co-trimethylene carbonate) and Poly(lactide/Poly(trimethylene carbonate) Blown Films. *International Journal of Molecular Sciences* 15(2) (2014) 2608-2621.
- [29] Qin Y., Yuan M., Li L., Guo S., Yuan M., Li W., Xue J.: Use of polylactic acid/poly(trimethylene carbonate) blends membrane to prevent postoperative adhesions. *Journal of Biomedical Materials Research Part B: Applied Biomaterials* 79(2) (2006) 312-319.
- [30] Adamus A., Wach R.A., Olejnik A.K., Dzierzawska J., Rosiak J.M.: Degradation of nerve guidance channels based on a poly(L-lactic acid) poly(trimethylene carbonate) biomaterial. *Polymer Degradation and Stability* 97 (2012) 532-540.
- [31] Yamada H.: *Strength of biological materials*. The Williams & Wilkins Company (1970) 21, 80.
- [32] Pyda M., Bopp R.C., Wunderlich B.: Heat capacity of poly(lactic acid). *Journal of Chemical Thermodynamics* 36(9) (2004) 731-742.