

NIȚĂ TUDORACHI^{*)}, RODICA LIPSA"Petru Poni" Institute of Macromolecular Chemistry
Grigore Ghica Voda Alley, No 41A, Iasi, 700487, Romania

Comparative study on starch modification with lactic acid and poly(lactic acid)

Summary — In the present study, we report on starch modification with L-lactic acid or poly(L-lactic acid) (PLA) with low molecular weight ($M_n \approx 3000$), with potential uses in biomedical area. Molecular weights of copolymers obtained from starch and lactic acid were higher than that of copolymer obtained from starch and PLA. Unmodified starch showed greater stability than the two copolymers. We can notice that starch modified with L-lactic acid shows higher solubility than starch modified with PLA, although the latter is soluble in most organic solvents used.

Key words: starch, L-lactic acid, poly(L-lactic acid), starch copolymers, thermal stability, solubility.

PORÓWNAWCZE BADANIA SKROBI MODYFIKOWANEJ ZA POMOCĄ KWASU MLEKOWEGO I POLI(KWASU MLEKOWEGO)

Streszczenie — Opisano metodę modyfikacji skrobi za pomocą kwasu mlekowego lub poli(kwasu mlekowego) (PLA) o stosunkowo małym ciężarze cząsteczkowym ($M_n \approx 3000$). Otrzymane kopolimery scharakteryzowano metodą IR (rys. 1). Ciężary cząsteczkowe wyznaczone metodą chromatografii żelowej są większe w przypadku kopolimerów z kwasem mlekowym niż kopolimerów z PLA (rys. 2, tabela 1). Stwierdzono, że stabilność termiczna skrobi niemodyfikowanej jest lepsza niż zsyntetyzowanych kopolimerów (rys. 3 i 4, tabela 2). Oceniono wpływ modyfikacji na rozpuszczalność w wodzie i różnych rozpuszczalnikach organicznych (tabela 3) i wykazano, że skrobia modyfikowana za pomocą kwasu mlekowego jest lepiej rozpuszczalna w wodzie niż niemodyfikowana oraz modyfikowana PLA.

Słowa kluczowe: skrobia, kwas mlekowy, poli(kwas mlekowy), kopolimery skrobi, stabilność termiczna, rozpuszczalność.

Starch is a non-expensive biopolymer available from annually renewable resource. It can be found in plants (rice, wheat, corn, potatoes) as a mixture of two polysaccharides: amylose, the nearly linear polymer consisting of α -(1,4)-anhydroglucose units, and amylopectin, a highly branched polymer of α -(1,4)-anhydroglucose units crosslinked through α -(1,6) linkages. Starch molecule has two types of important functional groups: OH group which is able to undergo substitution reactions and C-O-C linkage responsible for the molecular chain braking. The OH group has a nucleophilic character and by reaction with different reagents it is possible to obtain a series of compounds of modified properties. Chemical and physical properties of starch have been widely investigated due to its ease to be converted into a thermoplastic and then be used in different applications. In order to compete with non-degradable plastics, grafting or blending starch with a synthetic hydrophobic polymer is a suitable route to improve its properties. Systems consisting of polyethylene-ethylene/acrylic acid copolymer-starch differing in starch content (20–47 wt. %) [1], were prepared by extrusion to be used for package

manufacturing. Graft copolymerization of starch with vinyl monomers (acrylonitrile, acrylamide, methacrylamide, acrylic acid, methacrylic acid) was examined, and the effect of monomers and initiators concentration, time and temperature on grafting percentage and grafting efficiency were studied [2-8]. It is preferred over physical blending, since chemical linkages provide direct linkage between starch and synthetic polymers.

Esters of starch that can be processed as thermoplastic materials were prepared by substitution reactions of starch with alkenylsuccinic anhydrides. The effects of starch concentration, starch/anhydride ratio, pH, temperature and reaction time on the esterification efficiency were determined [9]. Biodegradable, high moisture-resistant crosslinked starch was synthesized with adipic acid and acetic acid anhydride [10]. Long chain esters of starch with degrees of substitution ranging from 0 to 3 have hydrophobic properties; they could be used as substitutes for oil based plastic materials [11]. By gelatinization of native starch with formic acid followed by treatment with fatty acid chlorides, the hydrophobicity and the mechanical resistance of starch esters increased with fatty chloride chain length [12]. The synthesis of aliphatic poly-

^{*)} Author for correspondence; e-mail: ntudor@icmpp.ro

ester-grafted polysaccharides (starch) can be done by *in-situ* polymerization of a cyclic ester monomer (ϵ -caprolactone) in the presence of starch and an organometallic catalyst initiator, wherein the ring-opening polymerization is conducted *via* bulk polymerization of the ester monomer, preferably in the absence of solvents [13]. The grafting reactions were characterized by very short reaction times of the order of a few minutes to achieve complete conversion of monomer. Biodegradable compositions, particularly these using poly(ϵ -caprolactone)-grafted starch are suitable for use in a number of applications including biodegradable moldings, sheets, films or foam structures and are processed by any of the melt processing methods employed in the plastics industry.

Biodegradable polyesters and copolyesters derived from α -hydroxy acids, lactones and lactides such as: poly(glycolic acid) (PGA), poly(lactic acid) (PLA), poly(malic acid) (PMA), poly(ϵ -caprolactone) (PCL) [14–20], were used in biomedical applications as bioabsorbable bone plates and other surgical fixation devices, surgical sutures and carriers for controlled release of drugs. PLA were most frequently studied in orthopedic applications as they are biodegradable, nontoxic, nonimmunogenic and showed high tensile strength. To improve some of their mechanical properties, PLA were blended with more flexible polymers such as PCL.

There has been also a growing interest in the synthesis and use of block copolymers consisting of PLA, PGA or PCL blocks associated with one or more hydrophilic chains to obtain drug delivery systems [21].

Poly(lactic-*co*-glycolic acid) oligomers (PLGA) of faster biodegradation in comparison with their high molecular weight polymers, suitable for short term drug delivery applications, were synthesized [22]. Thermoplastic blends of corn starch with some biodegradable synthetic polymers *i.e.*: PCL, PLA or cellulose acetate have also potential to be used in biomedical applications [23]. Starch and PLA were melt blended in the presence of methylene diphenyl diisocyanate (MDI) [24]. The blend with 45 wt. % of wheat starch and 0.5 wt. % of MDI gave the highest tensile strength of about 68 MPa and 5.1 % elongation in comparison with pure PLA (62.7 MPa tensile strength and 6.5 % elongation). Also storage modulus and water absorption increased significantly with starch content.

In our paper we present data regarding the synthesis and characterization of some copolymers obtained by grafting corn starch with lactic acid or with poly(lactic acid) using manganese acetate as a catalyst in polycondensation reactions.

EXPERIMENTAL

Materials

Corn starch (Amidex S.A. Tg. Secuiesc, Romania), with 24–28 % of amylose content ($M_n = 2.0 \cdot 10^4$ –

$1.4 \cdot 10^5$) and 72–76 % of amylopectine content ($M_n = 8.6 \cdot 10^5$ – $4.6 \cdot 10^6$), humidity 2.0 %, acidity 2.0 (determined using 0.01 NaOH solution), proteins and lipids 1.0 %, ash 0.25 %.

L(+)-lactic acid (Fluka, Switzerland), 90 wt. % aqueous solution of density 1.20 g/mL were used as received.

Manganese acetate, dimethylformamide (both anal. grade, Fluka, Switzerland), methanol, acetone (both lab. grade, S. C. Petrom S.A., Ploiesti, Romania) and toluene (lab. grade, S. C. Arpechim S.A., Pitesti, Romania) were used without further purifications.

Syntheses

Poly(lactic acid)

PLA of low molecular weight was prepared by polycondensation of L-lactic acid in the presence of manganese acetate (0.40 wt. %) as a catalyst. The temperature of the reaction was maintained at 104–110 °C (2.5 h), 140–150 °C (3 h) and 175–180 °C (1 h). The reaction took place under nitrogen pressure and secondary reaction products (water, lactide) were removed when we used an equipment of distillation. The reaction product presented raised viscosity and the yield of reaction was about 76 %.

Copolymer 1

The modification reaction of starch was carried out by dissolving it in L-lactic acid (90 wt. % aqueous solution). The molar ratio starch/L-lactic acid was 1/5.4 and as a catalyst manganese acetate was used in amount 0.8 wt. % in relation to the initial components. We assumed the molecular weight of the glycosidic unit was $M=162$. A reaction vessel was equipped with a stirrer, reflux condenser, thermometer, heating mantle, dosage system of the components and valve for nitrogen. Starch (0.06 moles; 9.72 g) was introduced into the reaction vessel containing 0.32 moles (29.16 g) of L-lactic acid in stirring aqueous solution. After complete dissolving of starch, the adequate quantity of catalyst in 2 mL of distilled water was introduced. The temperature was raised to 85–90 °C, the reaction took place under N_2 stream and reflux for 9 hours. Then, heating was stopped and stirring was continued, when temperature reached 40–45 °C. The obtained reaction product was next precipitated in acetone (8–10 °C) and washed with dioxane for unreacted starch removal. The obtained copolymer was filtered, vacuum dried for 72 hours at 50 °C, then was ground. We obtained a white color product, the yield of reaction was 21 %. The yield depends greatly on the solvent used for precipitation. Among the solvents or mixtures of solvents tested acetone proved to be more efficient. In the same conditions we synthesized another copolymer (copolymer 1A), but the reaction time was only 5 hours. The yield of reaction in this case was 27 %.

Copolymer 2

Starch modification with PLA of low molecular weight was carried out by grafting reaction in solution using solvent mixtures. The molar ratio starch/PAL was 20/1. Starch (3.3 g) was dispersed in 20 mL of DMF/water or DMF/methanol mixture (1/1) under stirring at 60 °C, while separately 3.3 g of PLA ($M_n=3140$) was dissolved in 10 mL of DMF/toluene (2/1 mixture). After mixing of the two solutions, the aqueous solution of catalyst of manganese acetate ($(\text{CH}_3\text{COO})_2\text{Mn}\cdot 4\text{H}_2\text{O}$ (0.8 % in relation to initial components) was added. The reaction took place in two stages: in the first stage the mixture was maintained for 8.5 hours at 85–90 °C with reflux, then the temperature was raised for 3 hours at 110 °C and developed with solvents and secondary products removal (about 18 mL). After cooling at laboratory temperature, the reaction mixture was precipitated with 200–250 mL of acetone and a white color precipitate was obtained. After decantation and centrifugation at 5000 rpm. the product was washed with water, dried under vacuum at 50–60 °C for 72 hours, then it was ground. The yield of reaction was 54 %.

Method of testing

IR spectra were recorded using a Specord M80 spectrophotometer (Germany). The samples were homogenized and pressed on KBr pellets.

The molecular weight of starch modified with L-lactic acid was determined by gel permeation chromatograph (GPC) technique at ambient temperature. The system was equipped with an adjustable flow capacity and constant rate pump LC 1120 type and an evaporative mass detector PL-EMD 950 type. It was fitted out also with columns PL-gel 5 μm MIXED-D and PL-gel 5 μm MIXED-C packed with polystyrene/divinylbenzene copolymer. PL-polymer, polystyrene standards (580–316 500) were employed. Dimethylformamide was used as a mobile phase at a flow rate of 0.7 mL/min.

Thermogravimetric analyses (TG and DTG) were carried out using a derivatograph Q-1500 D (MOM Budapest, Hungary) at the following conditions: the weight of the sample 50 mg, the heating rate 10 deg/min, the maximum heating limit 700 °C, reference material $\alpha\text{-Al}_2\text{O}_3$.

The solubility of starch and of starch modified with L-lactic acid and PLA of low molecular weight was determined in different organic solvents at room temperature. Solutions of 1 wt. % concentration were prepared by stirring of the samples on a magnetic stirrer for 2–3 hours, then were filtered on qualitative paper and weighed. Samples that contained after filtration and drying more than 60 % of the initial quantity were considered as insoluble, between 2–60 % as partial soluble, and less than 2 % as soluble.

RESULTS AND DISCUSSION

Starch was modified by grafting with L-lactic acid or PLA to obtain copolymer 1 and copolymer 2, respectively. PLA of low molecular weight was synthesized by melt polycondensation of L-lactic acid. Starch functionalization was applied to modify its hydrophilic character and improve solubility in water and several organic solvents. The synthesized copolymers were used in the form of chemical and physical conjugates with some drugs as ampicilline or acetylsalicylic acid [25]. IR spectra of unmodified starch and synthesized copolymers are presented in Fig. 1.

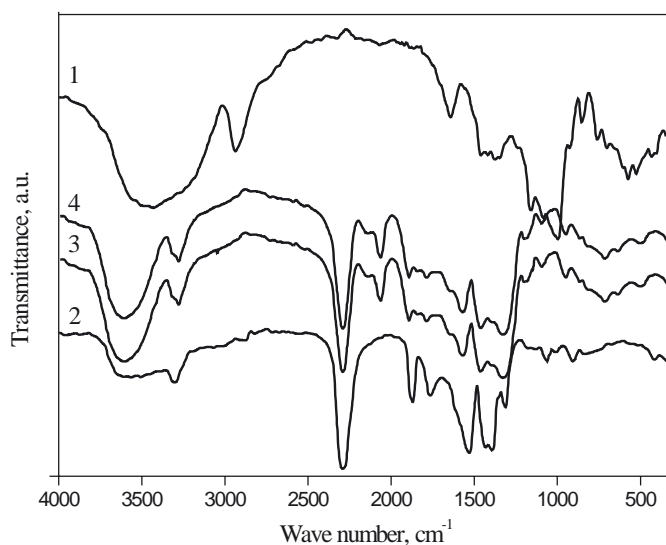


Fig. 1. IR spectra: 1 — starch, 2 — PLA, 3 — starch/lactic acid, 4 — starch/PLA

In the case of copolymers starch/L-lactic acid (copolymer 1) and starch/PLA (copolymer 2) the presence of some very wide absorption bands at 3400 cm^{-1} is observed, characteristic to OH group and to water absorbed (bands specific to starch) and for PLA this band has a more reduced frequency. The ester group at 1730 cm^{-1} present in the synthesized copolymers confirms the condensation reaction of lactic acid or PLA with starch. The presence of PLA as homopolymer in the synthesized product is excluded, as it is soluble in acetone and was removed by precipitation. In copolymer starch/L-lactic acid, the intensity of this band is more pronounced than in copolymer starch/PLA. This difference may be caused by different ratio starch/lactic acid in the initial mixture (lactic acid excess in the first case) that leads to the formation of more ester groups. Between $1550\text{--}1610\text{ cm}^{-1}$ the presence of some intense bands characteristic for the COO^- group were recorded. For starch most illustrative bands were recorded at $960\text{--}1190\text{ cm}^{-1}$ on account of the vibration of C-O linkage that existed in the glycosidic ring C-O-C and in the C-OH groups. These

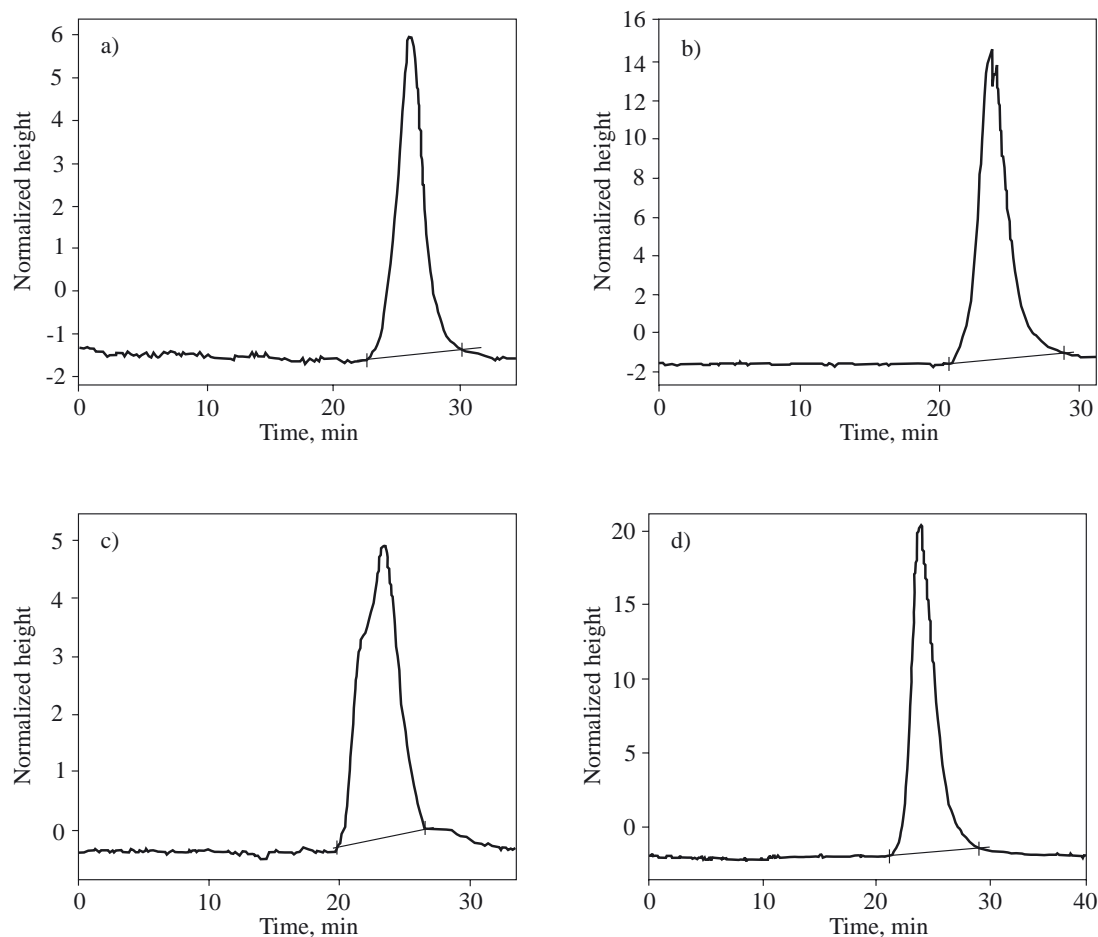


Fig. 2. GPC curves of the synthesized: a) PLA, b) copolymer 1, c) copolymer 1A, d) copolymer 2

bands were also found in the synthesized copolymers, demonstrating the presence of the glycosidic linkage. In the IR spectrum of the unmodified starch the presence of an absorption band at 1650 cm^{-1} was observed, characteristic to the OH group from the absorbed water, band that was not observed in the synthesized copolymers.

Table 1. Molecular weights of polymers, determined by GPC

Sample	Solvent	\bar{M}_n	\bar{M}_w/\bar{M}_n
poly(lactic acid)	DMF	3140	1.2
copolymer 1	DMF	6909	1.2
copolymer 1A	DMF	10 176	1.3
copolymer 2	DMF	6088	1.2

The molecular weights of polymers obtained determined by GPC are presented in Table 1, and the corresponding chromatograms in Figure 2. From the data presented in Table 1 we observe that the molecular weights of the copolymers obtained from starch and lactic acid (copolymers 1 and 1A) are higher than that of copolymer 2 obtained from starch and PLA. The polycondensation reaction of starch with PLA took place at a higher temperature than in the first case, thus promoting starch

hydrolysis and lowering its molecular weight. Generally, the degree of polydispersity (\bar{M}_w/\bar{M}_n) was relatively low with values 1.2–1.3. The chromatograms recorded for the synthesized copolymers presented unimodal distributions of the molecular weights.

Table 2. Thermal behavior of starch, PLA and copolymers

Sample	T _{10%} , °C	T _{50%} , °C	W ₂₂₀₋₄₂₀ ^{*)} , %	E _a , J/mol	Reaction order	W ₄₂₀ ^{**) %}
starch	210	290	70	274	3.0	80
poly(lactic acid)	138	214	92 ^{a)}	76.80	1.2	95
copolymer 1	176	261	74	58.60	1.0	100
copolymer 2	104	241	67	118.29	1.4	100

^{*)} W₂₂₀₋₄₂₀ — weight loss is recorded at 220–420 °C.

^{**)} W₄₂₀ — weight losses at 420 °C.

^{a)} weight loss recorded at 105–288 °C.

Data concerning the thermal behavior of the unmodified starch and of the synthesized copolymers are presented in Figure 3 and Table 2.

It was ascertained that the unmodified starch presented better thermal stability than the two copolymers, while PLA showed the lowest thermal stability, especially in the temperature interval where the weight

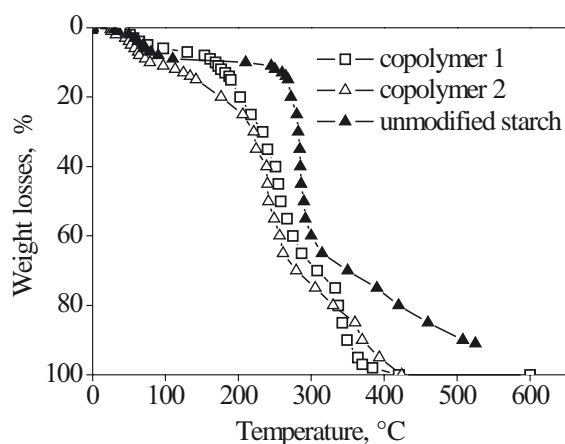


Fig. 3. Dependence of weight losses on temperature as a result of thermal oxidative decomposition

losses were 50 %. The reduced thermal stability in the case of starch grafted with L-lactic acid or PLA could be explained by the hydrolysis reactions that took place and led to breaking the glycosidic linkages of starch and lowered the molecular weight. The copolymer modified with L-lactic acid showed better thermal stability up to 340–350 °C. Actually this was observed also in the case of molecular weights determined by GPC for the two copolymers. Copolymer 1 presented higher molecular weight. By thermal oxidative decomposition of the copolymers and of a starch, we noticed the existence of 2–3 thermal decomposition processes with different rates of weight losses. In each case we noticed the presence of a main process where weight loss took place with a maximum rate. Activation energies (E_a) of decomposition reactions and the reaction order were determined in each case for the main decomposition process, using Siwaminthan and Modhavan, Coats and Redfern methods [26, 27]. The general equations used were:

$$\frac{d\alpha}{dT} = A \exp\left(\frac{-E_a}{RT}\right) [\alpha^m (1-\alpha)^n] \cdot [-\ln(1-\alpha)^p] \quad (1)$$

$$\frac{\log[1-(1-\alpha)^{1-n}]}{(1-n) \cdot T^2} = \log\left(\frac{AR}{\beta E_a}\right) - 2.303 \left(\frac{E_a}{RT}\right) \quad (2)$$

where: α — conversion degree (ratio of the weight loss at time "t" and at the end of the process), A — pre-exponential factor, T — temperature, E_a — activation energy of decomposition, R — gas constant, n — reaction order, m , p — exponents of the conversion function, β — heating rate.

The values of the two parameters (E_a and n) were lower for the copolymers in comparison with the unmodified starch (Table 2).

In Figure 4 we present the variation of the activation energy as a function of the conversion of thermal decomposition reactions. In all cases, we noticed a sudden falling-down of the activation energy to a conversion of 0.20, except PLA where this parameter was not significantly modified (it remained almost constant during the whole process). At a conversion higher than 0.2, the va-

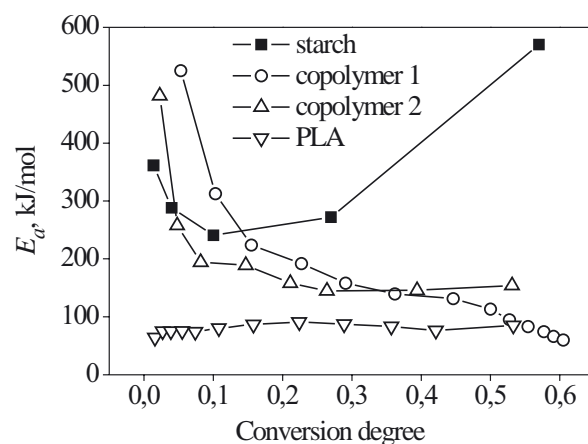


Fig. 4. Dependence of activation energy on conversion degree during thermal decomposition reaction

riation of the activation energy lowered with a much reduced rate, while in the case of starch we could notice a rapid growth of the activation energy, due to different thermal stability.

Table 3. Solubility of copolymers in organic solvents

Solvent	Solvent solubility parameter (cal/cm ³) ^{1/2}	Solubility ^{a)}			
		starch	copolymer 1	copolymer 2	PLA
Water	23.4	ps	s	i	i
Dimethylsulfoxide	14.5	ps	s	s	s
Dimethylformamide	12.1	i	s	ps	s
Acetone	11.9	i	i	i	s
Ethyl ether	10.6	i	i	ps	ps
Methylene chloride	9.7	i	ps	i	ps
Chloroform	9.3	i	ps	i	ps
Toluene	8.9	i	ps	i	ps
Dioxane	7.9	ps	i	ps	s

^{a)} s — soluble; ps — partially soluble; i — insoluble.

Starch solubility in organic solvents in comparison with starch modified with L-lactic acid or PLA is presented in Table 3. Tests were made using solvents of different values of the parameter of solubility, the products were dissolved under stirring at laboratory temperature. The study did not aim to determine the degree of solubility at higher temperatures, as we intended to use the synthesized products as matrices for drug delivery systems.

From the data presented in the Table 3 we notice an improvement in the solubility of copolymers in comparison with starch, especially when solvents of higher values of the parameters of solubility than 10 (cal/cm³)^{1/2} were used. Also, we can notice that starch modified with L-lactic acid presents higher solubility than starch modified with PLA, although this is soluble in most organic solvents used. The development of the reaction and choice of components influence the characteristics of the

resulted copolymer and consequently its solubility in organic solvents. As by this grafting reaction starch becomes soluble in several organic solvents and water, it can be used as a carrier for chemical or physical conjugation with some active substances that will be subsequently delivered by a sustained or controlled mechanism.

REFERENCES

1. Figiel A., Zięba T., Leszczyński W.: *Polimery* 2004, **49**, 547.
2. Gao J., Jingao Y., Wang W., Chang L., Tian R.: *J. Appl. Polym. Sci.* 1998, **68**, 1965.
3. Athawale V. D., Lele V.: *Starch* 1998, **50**, 426.
4. Athawale V. D., Rathi S. C., Lele V.: *Europ. Polym. J.* 1998, **34**, 159.
5. Park I. H., Song S. Y., Song B. K.: *Angew. Makromol. Chem.* 1999, **267**, 20.
6. Hebeish A., Beliakova M. K., Bayazeed A.: *J. Appl. Polym. Sci.* 1998, **68**, 1709.
7. Athawale V. D., Rathi S. C.: *Reactive & Functional Polymers* 1997, **34**, 11.
8. Brzozowski Z. K., Noniewicz K.: *Polimery* 1994, **39**, 82.
9. Jeon Y. S., Viswanathan A., Gross R. A.: *Starch* 1999, **51**, 90.
10. Pat. USA. 5 629 416 (1997).
11. Aburto J., Thieband S., Alric I., Borredon E., Bikiaris D., Prinós J., Panayiotou C.: *Carbohydrate Polymers* 1997, **34**, 101.
12. Aburto J., Hamaili H., Alric I., Borredon E., Gaset A.: "Biopolymer Science: Food and Non Food Applications", September 28—30, 1998, Montpellier (France).
13. Pat. USA 5 540 929 (1996).
14. Duda A., Penczek S.: *Polimery* 2003, **48**, 16.
15. Libiszowski J., Kowalski A., Biela T., Duda A.: *Polimery* 2004, **49**, 690.
16. Andreopoulos A. G., Hatzi E. C., Doxastakis M.: *J. Mater. Sci.: Mater. Med.* 1999, **10**, 29.
17. Andreopoulos A. G., Hatzi E. C., Doxastakis M.: *J. Mater. Sci.: Mater. Med.* 2000, **11**, 393.
18. Hyon S. H.: *Polymer Preprints* 1996, **37**, 125.
19. Nam Y. S., Lee K. H., Park T. G.: *Polym. Prepr.* 1998, **39**, 216.
20. Cai Q., Bei J., Wang S.: *Polym. Adv. Technol.* 2002, **13**, 105.
21. Yasukawa T., Kimura H., Tabata Y., Ogura Y.: *Advanced Drug Delivery Reviews*, 2001, **52**, 25.
22. Wang N., Wu X. S., Upton H. L., Donahue E., Siddiqui A.: *Proc. Amer. Chem. Soc. Div. PMSE* 1997, **76**, 13.
23. Mano J. F., Koniarova D., Reis R. L.: *J. Mater. Sci.: Mater. Med.* 2003, **14**, 127.
24. Wang H., Sun X., Seib P.: *J. Appl. Polym. Sci.* 2002, **84**, 1257.
25. Tudorachi N., Lipsa R.: *Rev. Roum. Chim.* 2005, **50**, 175.
26. Siwaminthan V., Modhavan N. S.: *J. Anal. Appl. Pyrolysis* 1981, **3**, 131.
27. Coats A. W., Redfern J. R.: *Nature* 1964, **68**, 201.

Received 19 V 2005.