Synthesis and Characterization of New Glycopolymers based on Monosaccharides and Maleic Anhydride

I. Glucose derivatives

ANA-MARIA PANA[1]*, LUCIAN-MIRCEA RUSNAC[1], GEZA BANDUR[1], EUGEN SISU[2], VALENTIN BADEA[1], MIHAELA SILION[3]

[1] Politehnica University of Timişoara, the Faculty of Industrial Chemistry and Environmental Engineering, 2 P-ţa Victoriei, 300006, Timişoara, Romania

[2] The Chemistry Institute of Romanian Academy, Timişoara, 24 Mihai Viteazul Bvd., 300223, Timişoara, Romania

[3] "Petru Poni" Institute of Macromolecular Chemistry, 41A Aleea Gr. Ghica Voda, 700487, Iasi, Romania

Polymers become more important in everyday life. Although extremely useful in their life cycle, polymers become long-term pollutants. Worldwide, along the increased research in the environmental field, one can obviously observe a keen interest into new biodegradable and biocompatible plastic materials. This paper presents the synthesis and characterization of a new class of biodegradable copolymers based on carbohydrates. An oligomer was synthesized by the polycondensation of 3-benzyl-5,6-(bis(maleyloxy))-1,2-isopropylideneglucofuranose with propane-1,3-diol in the presence of p-toluenesulfonic acid and then it was copolymerized with hydroxypropyl (meth)acrylate, using benzoyl peroxide as initiator.
The oligomer was characterized by FTIR, NMR spectroscopy and HPLC-MS, and the copolymers were analyzed using FTIR and thermogravimetry.

Keywords: glucose, glycopolymer, maleic anhydride

As the fossil raw materials become extinct and the interest in the environment increases one can understand the worldwide tendencies in replacing them with renewable materials [1].

The most important class of renewable organic compounds in terms of volume are the carbohydrates, which account for 75% of the 200 billion tons of biomass produced annually worldwide [2]. Therefore carbohydrates offer the ideal conditions for industrial development to substitute products of fossil origin.

Although carbohydrates are abundant, their molecules contain hydroxyl groups with different selectivity when it comes to electrophilic acylation. A useful solution would be successive steps of OH blocking/deblocking in order to pursue the desired acylation. The esters thus obtained are reasonable biodegradable, biocompatible, digestible, water soluble, resistant to different pH and temperatures as well as to strong saline media, characteristics that would explain the growing interest in this kind of materials [2].

Due to the diverse applications of glycopolymers and to the recent developments in the field of polymerization (which allow the design of controlled structured macromolecules), the research in the field carbohydrate based polymers has widespread worldwide. The term glycopolymer has a broad meaning, referring to both natural and artificial polymers as well as to synthetically modified natural polymers. Glycopolymers can be classified into three groups (fig. 1): polymers having the carbohydrate attached to the side chains, polymers having the carbohydrate in the main polymer chain and crosslinked polymers where the saccharides are included into the hydrocarbon matrix.

Until now, polymers containing the carbohydrate into the side chain were synthesized [3]; these are the derivatives of monosaccharide (glucose, galactose, mannose, xylose) acrylates and methacrylates [4] as well as disaccharides (lactose) and polysaccharides (i.e. inulin) [5], with protected or unprotected OH groups. The syntheses of these polymers were carried out by radical polymerization. There are also known methods of ionic and (metathesis) ring opening polymerization [6-8].

This paper presents the synthesis of a new glucose based oligomer, the saccharide skeleton being included into the polymer chain (type b, according to fig.1). D-glucose was chemically modified according to scheme 1. The resulting

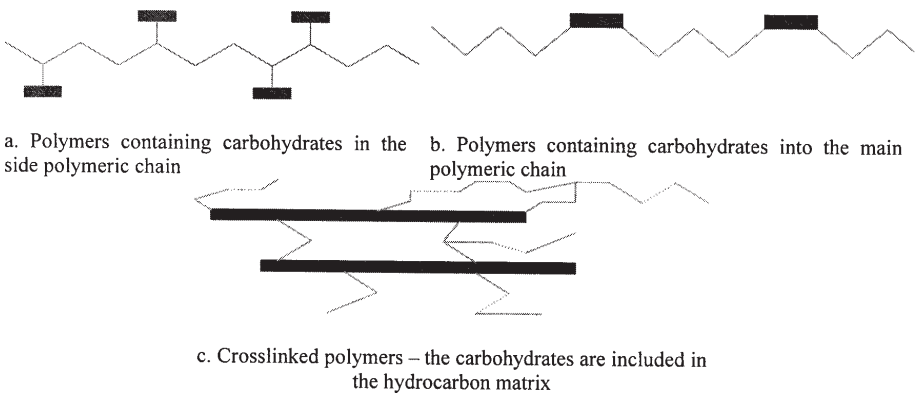
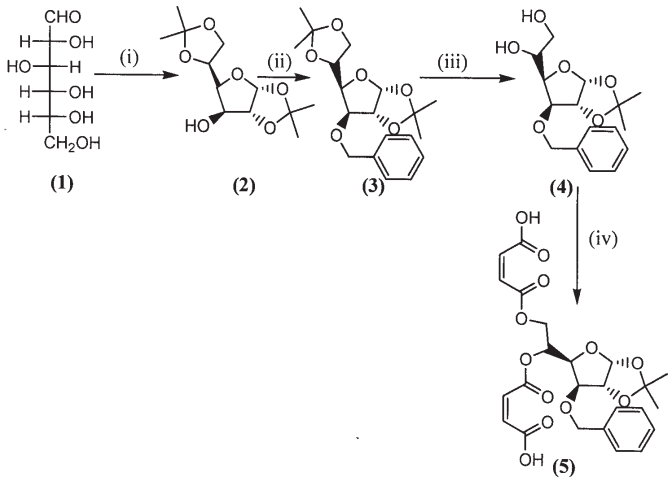


Fig.1. Classification of glycopolymers

* email: ana.chis@chim.upt.ro; Tel.: +40256404225

product, 3-benzyl-5,6-(bis(maleyloxy))-1,2-isopropylidene-glucofuranose, a diacid, was then polycondensed with propane-1,3-diol, using p-toluenesulfonic acid as catalyst. The oligomer thus obtained was copolymerized with hydroxypropyl acrylate (HPA) and hydroxypropyl methacrylate (HPMA).



Scheme 1. The reactions involved in obtaining 3-benzyl-5,6-(bis(maleyloxy))-1,2-isopropylidene-glucofuranose; i) acetone, H_2SO_4, 0°-r.t., 5h; ii) BnBr, NaH, DMF, MeOH; iii) CH_3COOH, 80%, 45 min, 70-75°C; iv) MAh, TEA, 20 h, 60°C

Experimental part

Materials

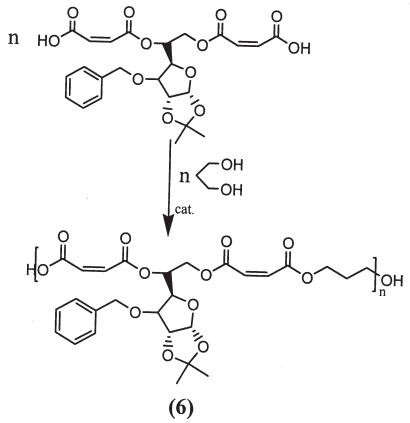
D-(+)-glucose, purity >98%, benzyl bromide, purity >98% (BnBr), maleic anhydride, purity >99% (MAh), triethylamine, purity >99% (TEA), glacial acetic acid, purity >99%, propane-1,3-diol, purity >98%, p-toluenesulfonic acid monohydrate, purity >99%, 2-hydroxypropyl acrylate (HPA) and 2-hydroxypropyl methacrylate were purchased from Merck and were used without further purification. Acetone (ChimoPar Bucureşti), DMF (Merck), methanol (Chimopar Bucureşti), hexane (Merck), ethyl acetate (Merck), toluene (Chimopar Bucureşti) and methylene chloride (Chimopar Bucureşti) were purified according to literature [9].

D-glucose (1) was acetonated according to a literature protocol [10]. The diacetoneglucose (2) derivative was then benzylated using benzyl bromide (BnBr), in the presence of NaH as catalyst, in DMF. The catalyst excess was neutralized by adding an excess of MeOH [11]. 3-benzyl-1,2:5,6-diisopropylideneglucofuranose (3) was then subjected to a selective OH deblocking using 80% acetic acid as catalyst, at a temperature of 70-75°C. After purification via silica gel chromatographic column (Hexane:AcOEt = 1:1, v/v), 3-benzyl-1,2-isopropyl-ideneglucofuranose (4) was acylated using maleic anhydride (MAh) [12, 13].

Synthesis of 3-benzyl-5,6-(bis(maleyloxy))-1,2-isopropylidene-glucofuranose

1.8254 g (0.00588 mol) of (4) are dissolved in 10 mL N,N-dimethylformamide (DMF), whereupon 3.5 g (0.035 mol) of maleic anhydride and 0.25 mL (0.726 g, 0.00175 mol) triethylamine (TEA) are added. This mixture is vigorously stirred while being heated to 60°C. After 24h, 20 mL of distilled water is added while gradually cooling the mixture. The desired product, is extracted into methylene chloride, then washed with distilled water and dried over Na_2SO_4 (η = 60%). 3-benzyl-5,6-(bis (maleyloxy))-1,2-isopropylideneglucofuranose (5) was characterized using FTIR and TLC (Rf = 0.1, AcOEt:MeOH = 2:1, v/v).

Product (5) was polycondensed with propane-1,3-diol according to scheme 2.



Scheme 2. Polycondensation of 3-benzyl-5,6-(bis(maleyloxy))-1,2-isopropylidneglucofuranose with propane-1,3-diol

Synthesis of the oligomer by polycondensation of 3-benzyl-5,6-(bis(maleyloxy))-1,2-isopropylidene-glucofuranose with propane-1,3-diol

The polycondensation in solution was carried out as follows: 1.7 g (0.003359 mol) of (5) were dissolved into 20 mL toluene to which 0.25 mL (0.003359 mol) propane-1,3-diol were previously added. The catalyst, p-toluenesulfonic acid, was added (0.2 % wt. of the reactants) and then the vigorous stirring began. The mixture was heated to 90-95°C and maintained for 28 h until the acidity indices showed the end of the reaction. During the reaction time, the oligomer formed was precipitated and deposited at the bottom of the flask. Product (6), the oligomer, insoluble into toluene, was isolated by dissolving into chloroform, yield 75% [14].

Synthesis of the copolymers via free radical bulk polymerization

The oligomer was copolymerized with hydroxypropyl acrylate (HPA) and hydroxypropyl methacrylate (HPMA) in weight ratios of 1:1, 1:2, 1:3 and 1:4 (oligomer : acrylate or methacrylate) – benzoyl peroxide was the initiator. The copolymerization was carried out according to the following procedure: the oligomer was dissolved in a certain amount of HPA or HPMA, at 40°C. Then benzoyl peroxide is added (1% wt.) and stirred vigorously. This homogenous mixture was then placed into preheated glass tubes. Gradually the temperature was increased with 10 degrees per hour until 110°C. The copolymers thus obtained are thermorigid.

Characterization of the products obtained

All syntheses were monitored using thin layer chromatography (TLC) performed on silica gel plates, Merk, DC-Autofolien Kiesegel 60 F 254, using different eluants. The FTIR spectra were recorded on a Jasco FT/IR-410 spectrometer. The IR analyses were done using KBr tablets for solid samples and between KBr glasses for the liquid ones; the ATR Diamant device was used for recording the copolymers spectra. The NMR spectra were recorded on Bruker Avance DRX 400 spectrometer in $CDCl_3$ using tetramethylsilane as reference.

Mass spectrometry results were obtained using an Agilent 6500 Series Accurate-Mass Quadrupole Time-of-Flight (Q-TOF) LC/MS. The sample was separated on a Zorbax SB-C18 (4.6 x 150 mm, 5 μm) reverse phase column.

The mobile phase consisted of water (solvent A) and methanol (solvent B) filtered and degassed under vacuum before use. The gradient program was 95% solvent B followed by ramping up to 100% solvent B at 5 min and then maintaining for 10min. The total run time was 20 min. The flow rate was 0.5 mL/min; the detector UV-VIS DAD was monitored at 210 nm. The LC System was directly connected to the electrospray ion source. The Q-TOF MS conditions were set as follows: electrospray ionisation (positive ion mode), drying gas (N_2) flow rate 5.0 L/min; drying gas temperature 325°C; nebuliser pressure 5 psig, capillary voltage 4000 V; fragmentation voltage 200 V; the full-scan mass spectra of the investigated compounds were acquired in the range *m/z* 50–3000. Data were collected and processed using MassHunter Workstation software.

The thermogravimetric analyses were performed using Netzsch TG 209, in nitrogen atmosphere and dynamic conditions. The data were collected and processed using a Proteus Analysis data system, from Netzsch.

Results and discussions

Figure 2 presents the IR spectra of diacetoneglucofuranose (2), 3-benzyl-1,2:5,6-diisopropylideneglucofuranose (3), 3-benzyl-1,2-isopropyl-ideneglucofuranose (4) and 3-benzyl-5,6-(bis(maleyloxy))-1,2-isopropylideneglucofuranose (5).

By comparing the IR spectra of diacetoneglucose (2) and benzyldiacetoneglucose (3) one can observe that the large intense signal from about 3400 cm^{-1} corresponding to the hydroxyl group has disappeared in case of product (3). The spectrum of (3) shows the aromatic bands at about 3000-3100 cm^{-1} belonging to the benzyl protective group. The spectrum of (4) presents a broad signal at 3400-3500 cm^{-1} corresponding to the associated OH bonds, characteristic for the freed hydroxyls in the 5th and 6th positions from the glucofuranose ring; the signals at about 3000-3100 cm^{-1} are still present which confirms that (4) has not lost its benzyl group by deblocking.

The IR spectrum of (5) confirms the formation of the ester: C=O ester bands at about 1730 cm^{-1}; the wide characteristic band from 3500 cm^{-1} expresses the carboxylic OH; the intense signal at about 1650 cm^{-1} is characteristic to the C=C bonds. The polycondensation was also confirmed via FTIR. Fig. 3 comparatively shows the changes between the spectra of the reactant and the product: the large and intense alcoholic signal at about 3400 cm^{-1} confirms the structure of the oligomer, together with the esteric C=O from 1730 cm^{-1} and C=C groups from the maleic anhydride skeleton.

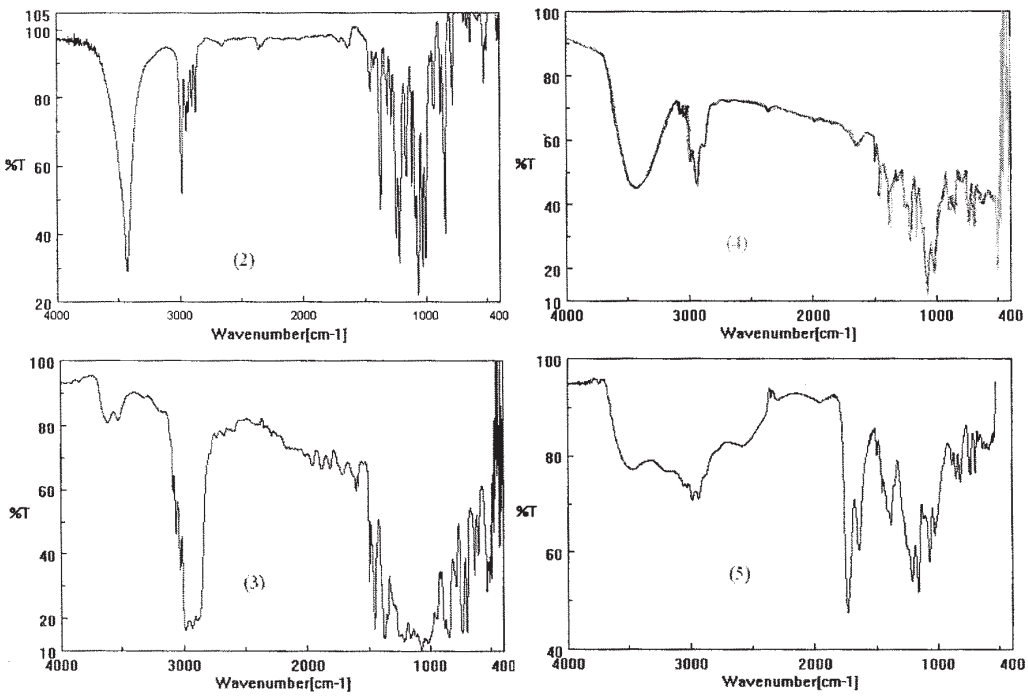


Fig 2. FTIR spectra of the intermediaries presented in scheme 1

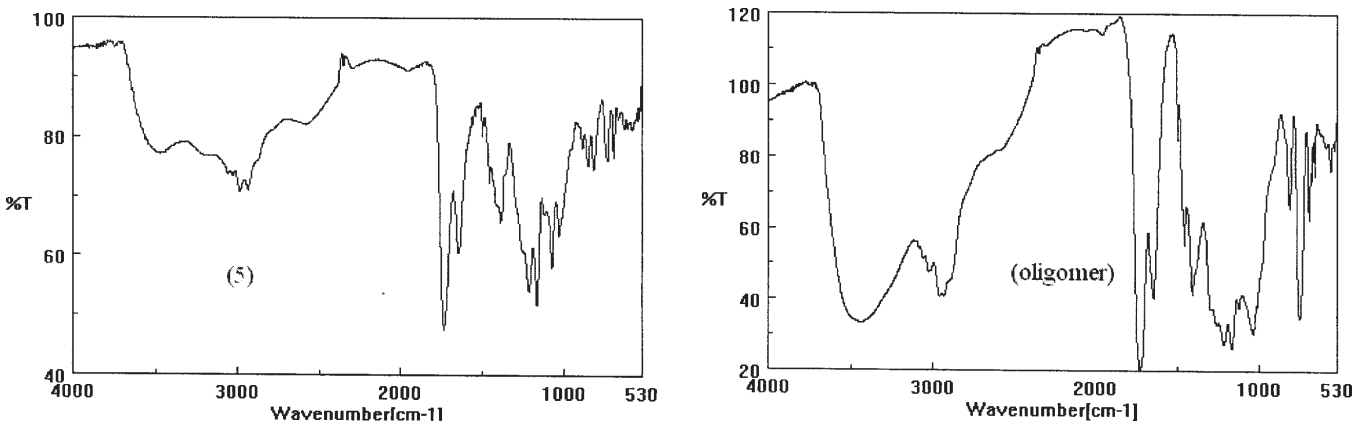


Fig 3. FTIR spectra of 3-benzyl-5,6-(bis(maleyloxy))-1,2-isopropylideneglucofuranose and the oligomer

The polycondensation was also monitored using the acidity indices. Figure 4 shows the profile of the acidity indices in time.

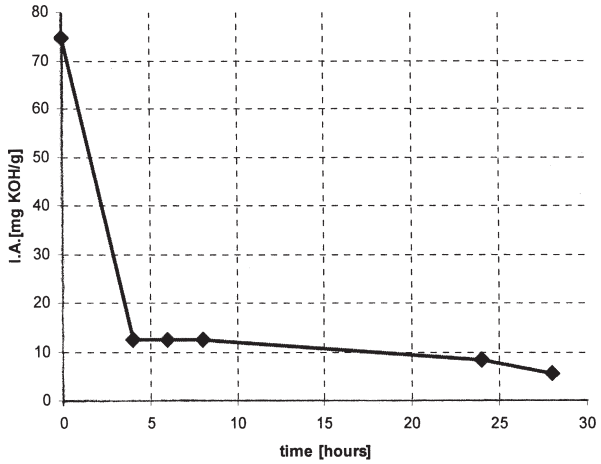


Fig .4. Variation of acidity indices in time for the polycondensation

The isolated oligomer is soluble in chloroform. The NMR analyses were performed in order to confirm its structure.

The ^{1}H NMR spectra shows the characteristic signals for H-C=C-H at 6.26, 6.37, 6.85 ppm, the carboxylic O-H at 11 ppm (singlet), the glucofuranose skeleton: 1.32-1.36 ppm for isopropylidene (singlet), 4.35-5.47 ppm for furan C-H, the aromatic C-H at about 7.17-7.76 ppm (multiplet). The methylene groups from the diol are placed at 1.91 ppm (multiplet), 2.85 ppm and respectively at 3.67 ppm.

The ^{13}C NMR spectrum of the oligomer shows signals at 169.5, respectively 165.5 ppm belonging to the carboxylic C=O. At about 135 and 140 ppm are found the signals for C=C and between 128 and 129 the C-H aromatic bonds, belonging to the benzyl protective group. The glucofuranose skeleton is confirmed by signals at 62-71 ppm, while the CH_3 from the isopropylidene is expressed by signals at about 28 ppm. The methylenes from propane-1,3-diol show signals at 31 ppm, 58 and 62 ppm.

The HPLC- ESI-MS analysis was performed in order to determine the molar weight of the oligomer synthesized by polycondensation. The oligomer was dissolved in methanol to obtain a concentration of 100 µg/mL and 5 µL was injected into the HPLC device. The blank chromatogram (not shown) showed no peaks in the HPLC beside the solvent front. The retention time for the oligomer was 2.622 min for a gradient of 95:5 MeOH:H_2O (v/v). The full scan MS spectrum of the methanolic oligomer solution is shown in fig. 7. The most abundant ion corresponds to $[M+Na]^+$ single charge sodium adduct at *m/z* 605 (where M is the molecular weight for the oligomer structure when n = 1). Furthermore, other ions of *m/z* 547 ($[M-2H_2O+H]^+$) and 564 ($[M-H_2O]^+$) are also detectable. These ions probably arise from in-source by dehydrations and losses of one or two molecules of water of the oligomer unit for n = 1. The peaks at *m/z* 1169 ($[2M-H_2O+Na]^+$) and *m/z* 1111 ($[2(M-2H_2O)+H]^+$) correspond to a single charged sodium and proton adducts of the dimer, formed by

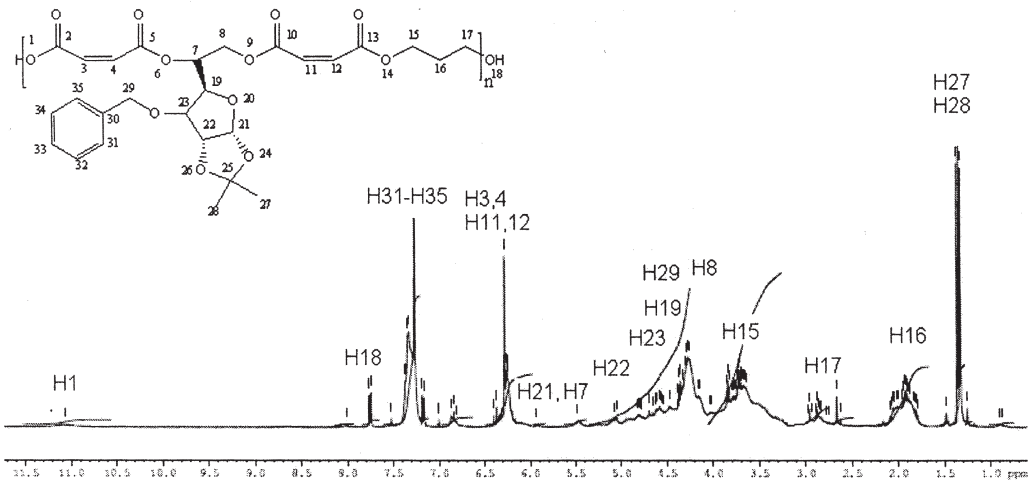


Fig . 5. The ^{1}H NMR for the oligomer [$CDCl_3$, δ (ppm)]

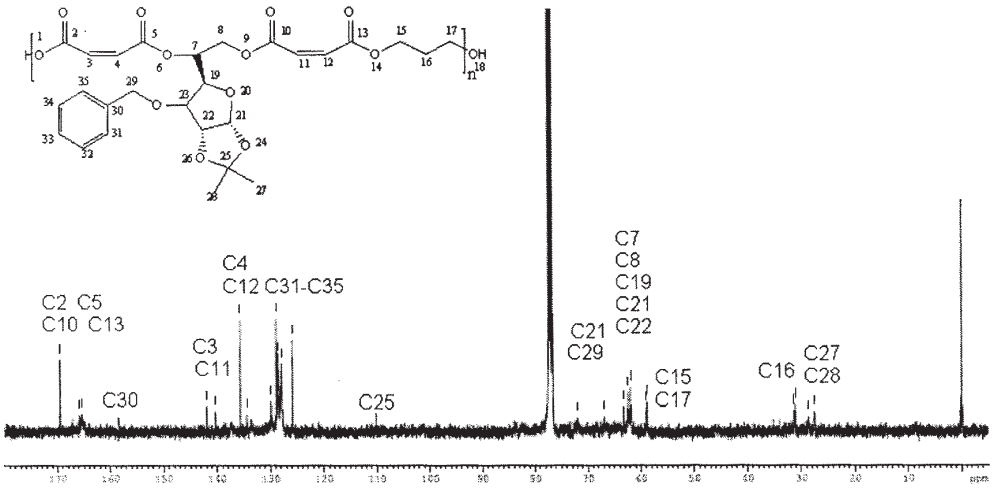


Fig.6. The ^{13}C NMR spectrum of the oligomer [$CDCl_3$, δ (ppm)]

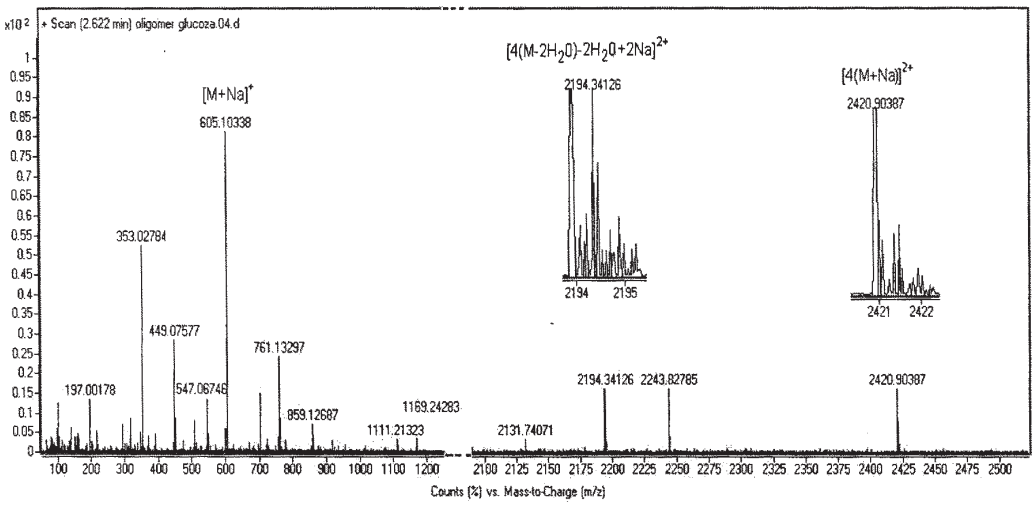


Fig.7. The full MS spectra of the oligomer (methanol solution)

Table 1
SOLUBILITY CHARACTERISTICS OF THE OLIGOMER

Reactive solvent	Butyl acrylate	Methyl Methacrylate	Styrene	Hydroxypropyl Acrylate	Hydroxypropyl Methacrylate
Solubility	None	Very poor	None	Good	Very good

successive dehydrations. The peak at *m/z* 2194 corresponds to ($[4(M-2H_2O)-2H_2O+2Na]^{2+}$) double charge sodium adduct, while a peaks at *m/z* 2243 corresponds only to the single charge adduct ($[4(M-H_2O)-2H_2O+Na]^{+}$). Finally, the double charged ions corresponding to the molecular weight of the oligomer are shown at *m/z* 2420 ($[4M+Na]^{2+}$), which directly confirmed the oligomer n = 8 formation. The actual molecular weight of the oligomer is 4656 Da, so the structure of the oligomer has 8 mer units connected to one another.

The structure of the oligomer being confirmed the following analyses characteristic to the oligomer were performed. The solubility of the oligomer into different reactive solvents was tested (table 1).

Based on the solubility characteristics of the oligomer described by table 1, copolymers of the oligomer with hydroxypropyl acrylate (HPA) and hydroxypropyl methacrylate (HPMA) in different mass ratios were obtained (table 2). The polymerization initiator was benzoyl peroxide.

Table 2
THE COPOLYMERS SYNTHESIZED

copolymer	copolymer	Mass ratio Oligomer: reactive solvent
O_HPA1	O_HPMA1	1:1
O_HPA2	O_HPMA2	1:2
O_HPA3	O_HPMA3	1:3
O_HPA4	O_HPMA4	1:4

The FTIR spectra of the copolymers confirm the structure of the crosslinked polymers formed (fig.8). The O-H from the HPA structure has a broad peak at about 3400 cm^{-1}. The signals at 3000-3100 cm^{-1} express the C-H aromatic bond, from the benzyl protective group, while the signals from 2800-3000 cm^{-1} are specific to methylene and methyl groups from the copolymer skeleton. The C=O esteric bond is expressed by signals at 1730 cm^{-1}, while the C-O esteric bond is placed at 1180 cm^{-1}. The copolymers with HPMA showed similar FTIR spectra.

These copolymers were analyzed by thermogravimetry, in nitrogen atmosphere, at temperatures ranging between 20 and 500°C. The copolymers obtained have good thermal stabilities. Figure 9 shows the thermograms for the copolymers with HPMA at a heating rate of 5 K/min.

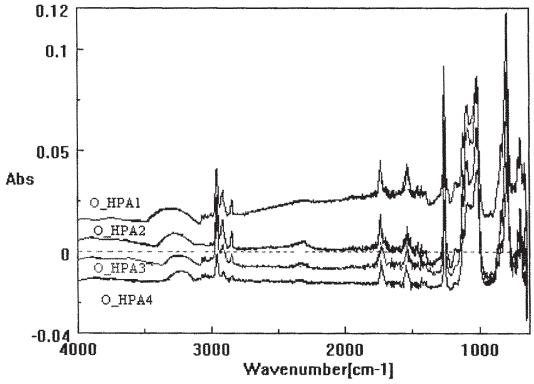


Fig.8. The FTIR spectra of the copolymers

The thermoplastic homopolymers are more stable at higher temperatures than the oligomer. The degradation of the copolymers takes place in two steps: the first at 310÷360°C which corresponds to the decomposition of the oligomeric chain and the second at 370÷410°C and corresponds to the degradation of the acrylic chains. The thermograms (TG) and their first derivatives (DTG) for the hydroxypropyl methacrylate homopolymer (PHPMA) and respectively for the oligomer and HPMA copolymer (mass ratio 1:1) show that there are two inflexion temperatures for the copolymers (324.6 and respectively 387.8°C) while for the homopolymer only one (387.3°C) (fig. 10) [15].

The weight losses for the oligomer, homopolymers and copolymers on different heating intervals are presented in tables 3 and 4.

For the first interval the weight loss is inessential, especially for the HPMA copolymers; in the case of HPA copolymers the loss is a bit higher but it does not exceed 2%. The tendency in weight loss is increasing along the increase of oligomer ratio; the pure oligomer has the biggest weight loss on the 20-300°C temperature interval. The difference of thermal stability between the HPA and the HPMA copolymers is negligible but it can be stated that the HPMA copolymers are more stable on the same temperature interval [16].

The significant weight loss is registered for the 20-400°C temperature interval; the maximum weight loss belongs to the HPMA copolymers. This fact can be explained by

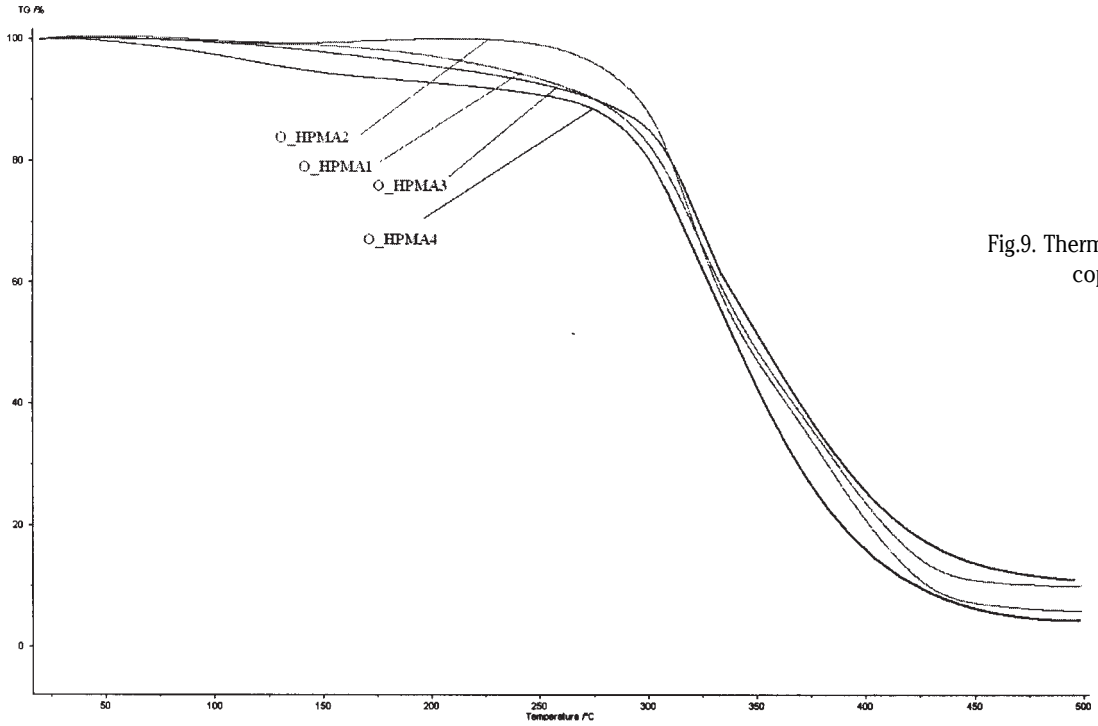


Fig.9. Thermograms of the HPMA copolymers

sample	Weight loss (%)				
	20 - 100°C	20 - 200°C	20 - 300°C	20 - 400°C	20 - 500°C
oligomer	0.74	2.63	24.93	60.88	98.6
PHPMA	1.02	4.21	10.74	79.79	99.7
O_HPMA1	0.18	2.65	16.9	76.04	99.7
O_HPMA2	0.18	0.22	11.77	79.05	99.1
O_HPMA3	0.16	3.61	15.3	78.7	99.3
O_HPMA4	0.15	7.12	19.12	80.46	99.8

Table 3
WEIGHT LOSSES FOR THE HPMA HOMOPOLYMER (PHPMA), THE OLIGOMER AND THE HPMA COPOLYMERS

sample	Weight loss (%)				
	20 - 100°C	20 - 200°C	20 - 300°C	20 - 400°C	20 - 500°C
oligomer	0.74	2.63	24.93	60.88	98.6
PHPA	1.74	2.88	6.46	57.38	98.97
O_HPA1	0.24	3.21	27.21	71.57	99.8
O_HPA2	1.58	8.66	26.5	72.62	97.3
O_HPA3	1.96	5.69	15.94	62.06	99.8
O_HPA4	1.32	3.81	11.1	72.76	98.7

Table 4
WEIGHT LOSSES FOR THE HPA HOMOPOLYMER (PHPA), THE OLIGOMER AND THE HPA COPOLYMERS

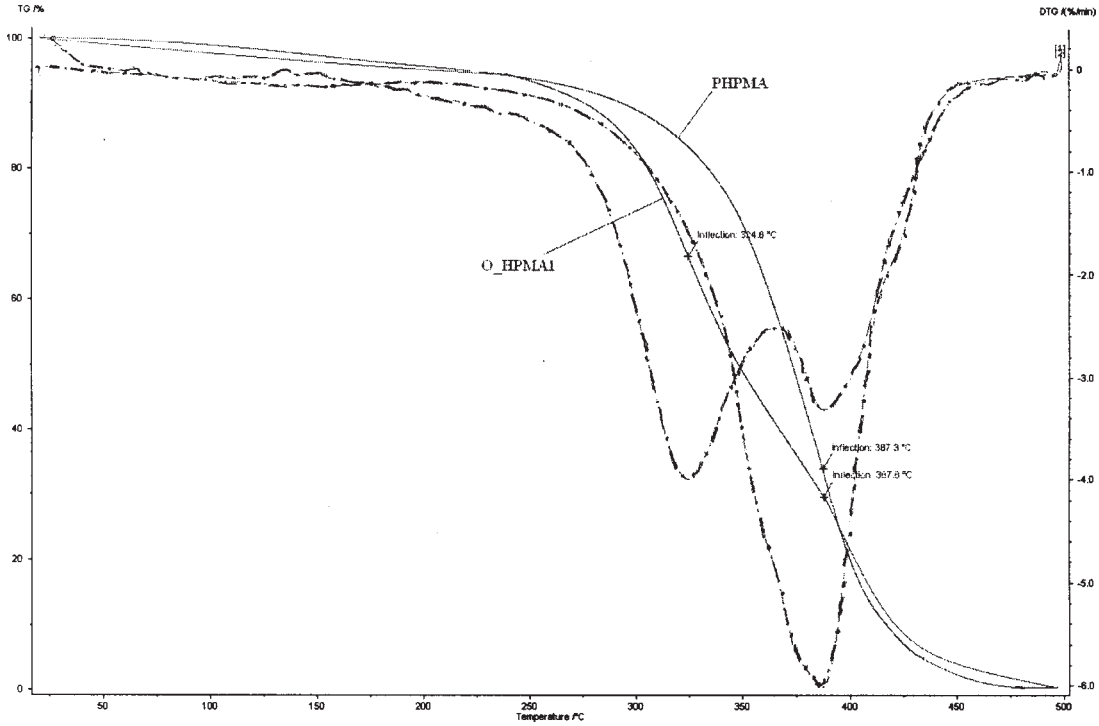


Fig. 10.The thermograms and their first derivative for the HPMA homopolymer and one copolymer (O_HPMA1)

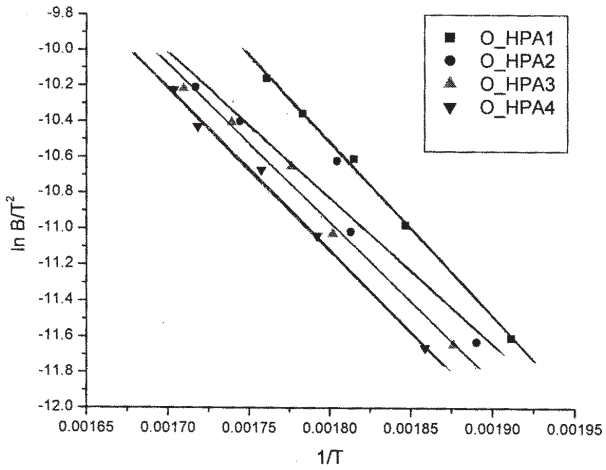


Fig. 11. Kissinger lines for the first step of degradation in the case of HPA copolymers

sample	Activation energy (kJ/mol)	
	First step	Second step
O_HPMA1	81.07	140.05
O_HPMA2	93.58	150.05
O_HPMA3	137.7	151.4
O_HPMA4	150.15	158.3

Table 5
ACTIVATION ENERGIES FOR BOTH STEPS OF THERMAL DEGRADATION FOR THE HPMA COPOLYMERS

sample	Activation energy (kJ/mol)	
	First step	Second step
O_HPA1	80.5	106.6
O_HPA2	97.32	157.94
O_HPA3	103.8	168.9
O_HPA4	110.7	170.3

Table 6
ACTIVATION ENERGIES FOR BOTH STEPS OF THERMAL DEGRADATION FOR THE HPA COPOLYMERS

the better oligomer solubility in HPMA (uniform oligomer dissolution between the molecules of reactive solvent).

So, the most stable copolymers are the ones with the smallest oligomer ratio; the best results were registered for the HPMA copolymers. The thermal stability of the copolymers is however inferior to that of the homopolymers in both cases.

Furthermore, the copolymers were subjected to a kinetic study of thermal degradation. The activation energy for the thermal degradation was evaluated using Kissinger method. The activation energy is determined using the slope of the linear dependence: $\ln(\beta/T_i^2) = f(1/T_i)$, where T_i is the inflexion temperature of the thermogram and β is the heating rate. The thermogravimetric analysis was conducted using different heating rates: 2.5; 5; 7.5; 10 and 12.5 K/min.

Figure 10 shows the Kissinger linear dependences for the first step of degradation in case of the HPA copolymers.

Tables 5 and 6 show the activation energies for the thermal degradation process of the HPA and HPMA copolymers.

The thermal degradation activation energy has similar values for the copolymers, but it slightly increases along the increase in HPMA and HPA content. The smallest value is registered in the case of HPA copolymer with a weight ratio of 1:1, for the first step of degradation, while for the second step of degradation, the smallest value is for the HPMA copolymer in the same weight ratio. The biggest value for the activation energy is registered for the HPA copolymer, in the second step of degradation for the biggest weight ratio used.

Conclusions

A new sugar based oligomer was synthesized. The oligomer structure was confirmed by IR and NMR spectroscopy and HPLC-MS analysis. The oligomer was copolymerized using HPA and HPMA and the thermoresistant copolymers obtained were characterized via FTIR and thermogravimetric analysis. The kinetic study for the degradation process allowed calculating the activation energies of the thermal decomposition process by applying Kissinger method.

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Manuscript received: 16.09.2009