БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ

ИНСТИТУТ ПО ПОЛИМЕРИ

НАЦИОНАЛЕН ЦЕНТЪР ЗА НОВИ МАТЕРИАЛИ

МОДУЛ 2: НОВИ МАТЕРИАЛИ ЗА МЕДИЦИНАТА И ФАРМАЦИЯТА

ТРЕТА ПОСТЕРНА СЕСИЯ:

“МЛАДИТЕ УЧЕНИ В СВЕТА НА ПОЛИМЕРИТЕ”

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М. Симеонов, Е. Василева, А. Апостолов, Д. Рабаджиева, С. Тепавичарова; *Желатинови капсули и утаяване на калциеви фосфати в тяхно присъствие*; Химиически факултет – Софийски университет “Св. Климент Охридски” & Институт по обща и неорганична химия – БАН.

БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ
ИНСТИТУТ ПО ПОЛИМЕРИ

Synthesis and characterization of polyoxyethylated calix[8]arenes

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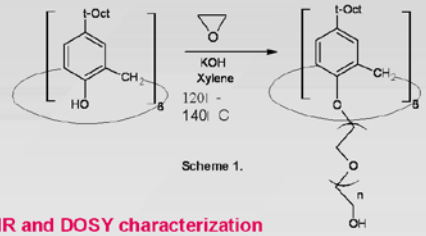
Introduction

Due to their macrocyclic structure and ability to form inclusion complexes with various substances, the calix[n]arenes are considered promising materials with versatile potential applications in different areas of biochemistry and pharmacy.

However, the calix[n]arenes are insoluble in water, that considerably limits their practical application. A series of products based on p-tert-octylcalix[8]arene with different degree of polyoxyethylation have been synthesized by anionic polymerization of ethylene oxide (Scheme.1). The resulting products are amphiphilic star-shaped macromolecules, consisting of a hydrophobic calix[n]arene core and eight arms of hydrophilic poly(ethylene oxide) chains. In aqueous media these compounds yield a variety of self-assembled structures and lyotropic liquid-crystalline systems. That broadens significantly the field of their applications. The communication presents synthesis of a series of amphiphilic p-tert-octylcalix[8]arenes and a preliminary study of their aqueous solution properties.



Scheme 1.

Abbreviation	Theoretical degree of polymerization of the PEO moieties	Degree of polymerization of the PEO moieties determined from ^{1}H NMR data in $CDCl_3$
1OEC –III	19	14
1OEC-IV	22	17
1OEC-V	42	41
1OEC-VI	57	52
1OEC-VII	100	96

^{1}H NMR and DOSY characterization

Diffusion Ordered NMR Spectroscopy (DOSY) exploits the differences in translational diffusion coefficients of various species present in a mixture, thus allowing discrimination between components with different sizes.

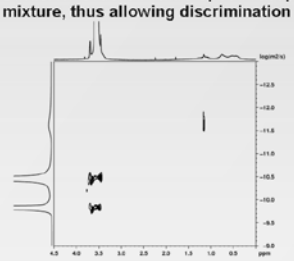


Figure 2a: DOSY spectrum of OEC-VII in D_2O.

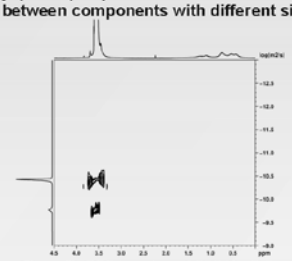


Figure 2b: DOSY spectrum of OEC-V in D_2O.

DOSY was used for determination of the diffusion coefficients and size of aggregates formed in aqueous solutions of the polyoxyethylated p-tert-octyl-calix[8]arenes, containing 19, 22, 42 and 100 oxyethylene units.

The systems with 19 and 100 polyoxyethylene units form two types of aggregates, with apparent hydrodynamic diameter d_h of 20 nm and 190 nm (Figure 2a).

The systems with 22 and 42 polyoxyethylene units display only one component in their DOSY spectra corresponding to particles with relatively small sizes with d_h of about 20 nm (Figure 2b).

CMC Determination

The non-polar dye 1,6-diphenyl-1,3,5-hexatriene (DPH), was used for determination of the Critical Micellization Concentration (cmc) of the polyoxyethylated calix[n]arenes. The absorbance of DPH in hydrophobic environment shows a characteristic maximum at 356 nm. The cmc values were estimated from the break of the intensity vs. concentration curves as shown in Figure 3a-3c. Figure 3d shows the molar mass dependence of cmc.

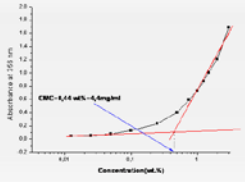


Figure 3a. Absorption intensity at 356 nm and CMC determination of 1OEC-IV

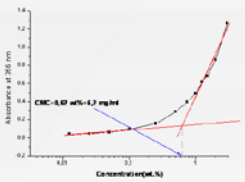


Figure 3b. Absorption intensity at 356 nm and CMC determination of 1OEC-VI

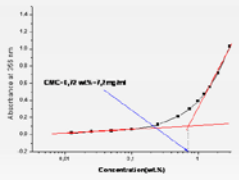


Figure 3c. Absorption intensity at 356 nm and CMC determination of 1OEC-VII

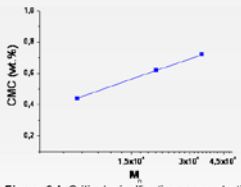


Figure 3d. Critical micellization concentration versus molar mass

Light scattering study

Some parameters characterizing the self-assembled structures formed by selected polyoxyethylated p-tert-octyl-calix[8]arenes were obtained by dynamic and static light scattering. The concentration ranges were invariably above the cmc whereas the temperature was kept constant (25°C). Figure 4a shows the particle size distribution for the aqueous solution of 1OEC-III (19 oxyethylene units), which is in excellent agreement with the data from DOSY (Figure 2a). Figure 4b shows the angular dependence of the relaxation rate from which diffusion coefficients and hydrodynamic radii were obtained. The particles that 1OEC-III forms in water are relatively small in size (about 8 nm) with a molar mass as determined via Debye plot corresponding to roughly 20 macromolecules per particle (Figure 4c).

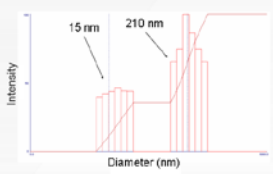


Figure 4a. Particle size distribution of aqueous solution of 1OEC-III. C = 11 mg/ml

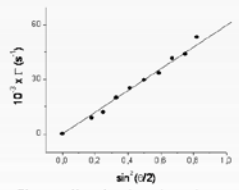


Figure 4b. Angular dependence of the relaxation rate for 1OEC-IV in water at 25°C.

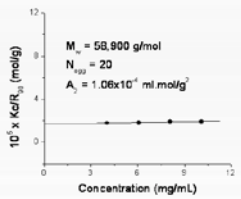


Figure 4c. Debye plot for 1OEC-IV in water at 25°C.

Conclusion

The uniqueness of the novel materials is in their stable hydrophobic core and hydrophilic arms – a combination of properties that open possibilities for further synthetic routes and wider practical applications.

Acknowledgment: The support by the NSF of Bulgaria (Grants: DRNF 02/13(2009) and DCVPO 02/2 (2009)) is highly acknowledged.

БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ
ИНСТИТУТ ПО ПОЛИМЕРИ

MALEINATED PP/MWNT COMPOSITES – RHEOLOGY, STRUCTURE, THERMAL AND MECHANICAL PROPERTIES

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INTRODUCTION

Polypropylene nanocomposites containing multiwall carbon nanotubes (MWCNTs), from 0wt% to 1 wt%, were prepared by dilution of a masterbatch (20% MWCNTs in PP) with isotactic polypropylene (iPP) applying extrusion processing with and without using maleic anhydride (MA) compatibiliser. The nanocomposites were investigated by oscillatory rheological tests. The viscometric methods were applied for control and characterization of the nanodispersion structure. The morphology of the composites was analyzed using scanning electron microscopy. The thermal stability was studied by TG and DTG analysis. Both nanotubes and maleic anhydride enhance the thermal stability of the compositions. The tensile strength, tensile modulus and elongation of the composites were determined by mechanical testing. The tensile strength and tensile modulus are positively influenced by the MWCNT content, this effect being lower for the maleinated compositions, while the MWCNT and MA content aggravates the elongation properties in a similar manner.

MATERIALS AND METHODS

Nanocomposites were produced by direct melt compounding in Brabender DSE 35/17D twin screw extruder according to a two step process. The masterbatch was diluted to different carbon nanotube concentrations in the range of 0.05 to 1 wt% with neat iPP at melt temperature of 200°C and a screw speed of 30 rpm. MA-PP was added into the nanocomposites in the concentration range from 2.5 to 7.5 wt% at the second stage. The rheological measurements were carried out by means of a cone-plate Rheotron Brabender rotational viscometer (oscillatory mode) at 200°C melt temperature for each concentration. The morphology of the samples is studied by scanning electron microscopy (SEM). The samples were treated by two methods – preliminary melting at 200°C and etching according to a special procedure. The thermal gravimetric analysis (TGA) was performed in air at 10°C/min from 20°C to 900°C with sample weight 100 mg. The tensile experiments were carried out with the "Tiratest 2300" universal testing machine.

RESULTS AND DISCUSSION

RHEOLOGICAL CHARACTERIZATION AND STRUCTURE OF MALEINATED iPP/MWCNT COMPOSITES

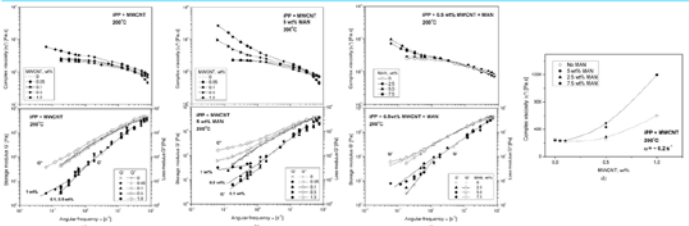

Figure 1. Dependence of complex viscosity [η*], storage and loss moduli G' and G'' on angular frequency ω for the systems: a) iPP + MWCNT; b) iPP + MWCNT + 5 % MA; c) iPP + 0.5% MWCNT + MA (2.5, 5, 7.5%); d) complex viscosity [η*] against weight fraction of nanotubes; T = 200°C.

The viscosity function changes showing non-linear increasing after nanotube concentration above 0.1 wt% indicating the interactions of the nanotube and this effect is more pronounced for the maleinated iPP/MWCNT composites. The effect of maleic anhydride addition leads to higher values of the rheological parameters (with about 1 order for 1 wt% of MWCNTs). The effect of MA concentration shows that the parameter values for the MA amount of 5 and 7.5 wt% are rather close and hence 5 wt% of MA was chosen as the optimal one for further investigations.

Figure 2(a,b) compares SEM micrographs of 0.5 wt% PP/MWCNT composite after melting at 200 °C (a) and after etching (b). Figure 2(a) shows a good dispersion of nanotubes in the iPP matrix, while in Figure 2b there are small aggregates and single tubes dispersed uniformly in the matrix. This effect is more pronounced with varying the MA content from 2.5 to 7.5 wt% (Figure 2(e,f,g)), where more single nanotubes are observed in the matrix. Figure 2(c,d) present single nanotubes embedded into the etched polypropylene matrix. The length of the nanotube is around 10 μm and this is in correspondence with the data for the masterbatch. The diameter is bigger than 10-15 nm which is indicative that the nanotube is covered with the layer of the masterbatch polypropylene.

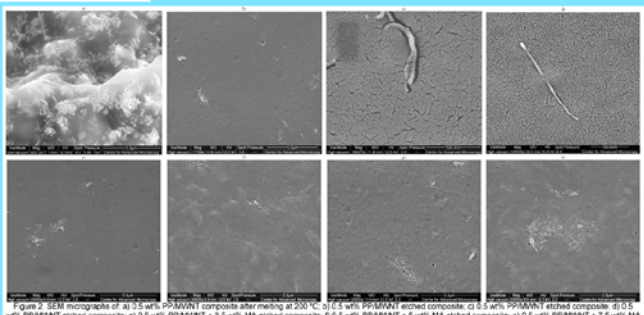

Figure 2. SEM micrographs of: a) 0.5 wt% PP/MWNT composite after melting at 200 °C; b) 0.5 wt% PP/MWNT etched composite; c) 0.5 wt% PP/MWNT etched composite; d) 0.5 wt% PP/MWNT etched composite; e) 0.5 wt% PP/MWNT + 2.5 wt% MA etched composite; f) 0.5 wt% PP/MWNT + 5 wt% MA etched composite; g) 0.5 wt% PP/MWNT + 7.5 wt% MA etched composite; h) 0.5 wt% PP/MWNT + 5 wt% MA etched composite.

EFFECT OF MWCNT CONCENTRATION AND MALEIC ANHYDRIDE ADDITIVE ON THERMAL PROPERTIES

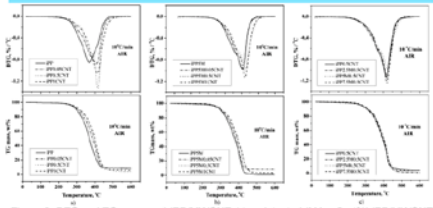

Figure 3. DTG and TG curves: a) iPP/MWCNT; b) maleinated (MA = 5 wt%) iPP/MWCNT; c) iPP system with 0.5 wt% MWCNT and 2.5, 5 and 7.5 wt% MA

No	Sample	Sample index	$T_{0.1}$ (°C)	$T_{0.5}$ (°C)	T_p (°C)
1	iPP	iPP	300	370	370
2	iPP+ 5%MA	iPP5M	305	380	405
3	iPP+0.05%MWCNT	iPP0.05CNT	307	388	410
4	iPP+ 5%MA+0.05%MWCNT	iPP5M0.05CNT	310	390	405
5	iPP+0.1%MWCNT	iPP0.1CNT	307	388	405
6	iPP+ 5%MA+0.1%MWCNT	iPP5M0.1CNT	308	390	410
7	iPP+0.5%MWCNT	iPP0.5CNT	310	395	418
8	iPP+ 2.5%MA+0.5%MWCNT	iPP2.5M0.5CNT	310	390	415
9	iPP+ 5%MA+0.5%MWCNT	iPP5M0.5CNT	311	395	420
10	iPP+ 7.5%MA+0.5%MWCNT	iPP7.5M0.5CNT	310	397	420
11	iPP+1%MWCNT	iPP1CNT	312	400	418
12	iPP+ 5%MA+1%MWCNT	iPP5M1CNT	311	395	420

Table 1. Sample designation and TGA decomposition temperature at 10% ($T_{0.1}$) and 50% ($T_{0.5}$) weight loss and DTG peak temperature (T_p) in air (rate 10°C/min)

The MWCNT content enhances the thermal stability of the studied nanocompositions. The highest effect is observed for concentration as low as 0.05 wt% MWCNT (40°C higher degradation peak). The further contribution of increasing the nanotube content is less pronounced and reaches 50°C for 1 wt%. The addition of maleic anhydride improves the thermal resistance of neat iPP. Both MA and MWCNT separately increase the thermal stability but no synergism is observed due to their combined incorporation in the nanocomposites. The different MA content exerts the same effect on thermal stability.

EFFECT OF MWCNT CONCENTRATION AND MALEIC ANHYDRIDE ADDITIVE ON MECHANICAL PROPERTIES

The tensile strength of the MWCNT composites is improved with about 11 % compared to the neat polymer. The addition of maleic anhydride reduces this enhancement to about 5%. The nanotube content exerts the highest effect on the tensile modulus – about 28 %. The MA effect on the tensile modulus is less pronounced but similar to that of nanotubes. The addition of MA leads to 25 % lower elongation values compared to these of the neat polymer. The elongation of both maleinated and non-maleinated samples is further decreased to with about 50 % with the growth of MWCNT concentration to 1 wt%.

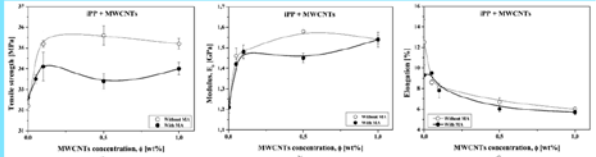

Figure 4. Mechanical parameters of maleinated and non-maleinated iPP nanocomposites vs. MWCNT concentration: a) tensile strength; b) tensile modulus; c) elongation.

ACKNOWLEDGMENT

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БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ
ИНСТИТУТ ПО ПОЛИМЕРИ

Design and Preliminary Biological Evaluation of Furan-Containing Aminophosphonate and Poly(oxyethylene aminophosphonate)s

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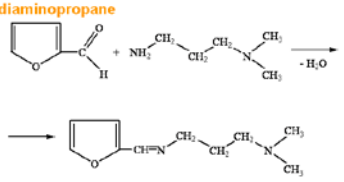
Introduction

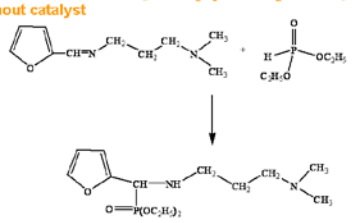
Aminophosphonic acid derivatives constitute a valuable class of biologically active compounds with a great potential for medical and pharmaceutical applications. The pharmacological importance and utility of the aminophosphonic acid derivatives have stimulated extensive studies on various aspects of their chemistry, stereochemistry and biological properties. Aminophosphonate derivatives bearing furan ring – an aminophosphonate and two poly(aminophosphonate)s, have been synthesized. The aminophosphonate N,N-dimethyl-[N'-methyl(diethoxyphosphonyl)-(2-furyl)]-1,3-diaminopropane was obtained in the presence of $NaOC_2H_5$ and CdI_2 as catalysts, as well as without catalyst. The addition of the poly(oxyethylene H-phosphonate)s to the Schiff base proceeded under catalytic amount of CdI_2 and in the absence of catalyst. The aminophosphonate and poly(aminophosphonate)s have been tested for cytotoxicity against four human leukemic cell lines. It has been found that the poly(aminophosphonate)s exert higher cytotoxic effects, then their low molecular analogue. The aminophosphonate has been evaluated for *in vitro* antitumor activity to several cell lines, derived from human epithelial tumors and was observed that the compound exhibits significant cytotoxicity to the malignant breast cancer and adenocarcinoma cells. The *in vitro* safety testing of the compound revealed absence of cytotoxicity and the *in vivo* testing has shown weak to moderate clastogenicity.

Synthetic Route

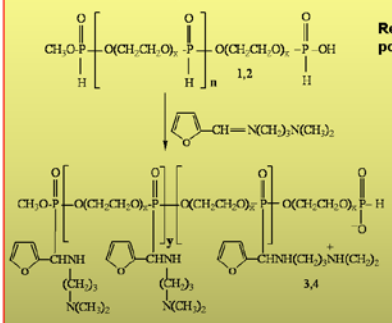
1) Synthesis of Schiff base N,N-Dimethyl-N'-furfurylidene-1,3-diaminopropane



2) Synthesis of N,N-dimethyl-[N'-methyl(diethoxyphosphonyl)-(2-furyl)]-1,3-diaminopropane through addition of diethyl phosphite to the the Schiff base using $NaOC_2H_5$ and CdI_2 as catalysts, as well as without catalyst



3) Addition of Poly(oxyethylene H- phosphonate) to the Schiff base proceeded under catalytic amount of CdI_2 and in the absence of catalyst



3 - x = 4 (PEG 200)
4 - x = 13 (PEG 600)

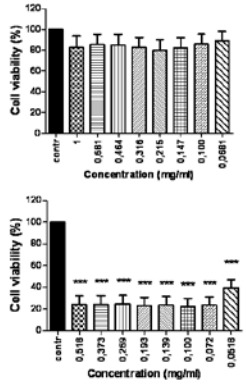
Reaction conditions for the preparation of poly(oxyethylene aminophosphonate)s

Schiff base, mol	POEPH, mol	Catalyst, mol	Reaction temperature,°C	Reaction time, h	Yield, %
0.017	0.017 *	-	65	15	90
0.022	0.022 *	CdI_2 (2.8×10^{-4})	50	3	92
0.062	0.062 **	CdI_2 (1.2×10^{-4})	50	3	91

* - POEPH – poly(oxyethylene H-phosphonate) based on PEG-200;
** - POEPH – poly(oxyethylene H-phosphonate) based on PEG-600;

Antitumor Activity and Safety Testing

Fig. 1 Cytotoxicity of a N,N-dimethyl-[N'-methyl(diethoxyphosphonyl)-(2-furyl)]-1,3-diaminopropane (A) and sodium dodecyl sulphate (B); 3T3 NRU test



The data from the safety *in vitro* experiments showed absence of cytotoxicity at all concentrations used, in contrast to the effect of the positive control substance (sodium dodecyl sulfate).

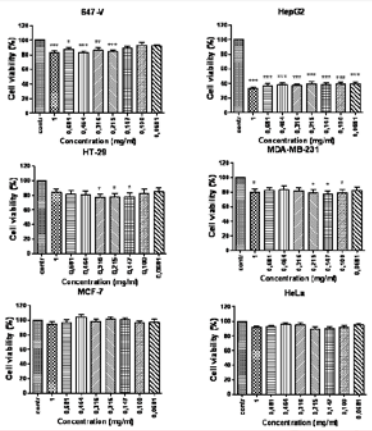


Fig. 2. *in vitro* antitumor activity of N,N-dimethyl-[N'-methyl(diethoxyphosphonyl)-(2-furyl)]-1,3-diaminopropane

The tested furan-containing aminophosphonate exhibited very high antitumor activity *in vitro* ($p<0.001$) to the CL derived from human hepatocellular carcinoma (HepG2) in a wide concentration range (from 1 mg/ml to 0.0681 mg/ml and a dilution factor of $6\sqrt{10} = 1.47$). A similar effect has been observed after application of the test substance on cell cultures from human bladder carcinoma CL 647-V. Significantly lower antiproliferative activity of the aminophosphonate was observed on cells from the cell lines HT-29 и MDA-MB-231 ($p<0.05$). The test substance had no antitumor *in vitro* activity towards the MCF-7 and HeLa CLs derived from ductal carcinoma of the breast and from cervical carcinoma, respectively (Fig. 2)

Conclusions

Aminophosphonate derivatives bearing furan ring – an aminophosphonate and two poly(aminophosphonate)s, have been synthesized.

Poly(oxyethylene aminophosphonate)s were obtained via additional polymer analogous reaction between poly(oxyethylene H-phosphonate)s and N,N-Dimethyl-N'-furfurylidene-1,3-diaminopropane (Schiff base).They were tested for cytotoxicity in a panel of human tumor cell lines, representative for some clinical important types of neoplastic diseases. These polymers are interesting as polymer drug carriers and as polymers with own bioactivity.

The furan-containing aminophosphonate N,N-dimethyl-[N'-methyl(diethoxyphosphonyl)-(2-furyl)]-1,3-diaminopropane could be a good candidate for the development of new anticancer drug for treatment of hepatocellular carcinoma.

This investigation has been financially supported by Bulgarian National Science Fund: Contracts: DTK 02/34(2009); DCVP 02/2 (2009) National Centre for New Materials UNION

THERMALLY SENSITIVE PEPTIDE-BASED HYBRID COPOLYMERS FOR DNA COMPLEXATION

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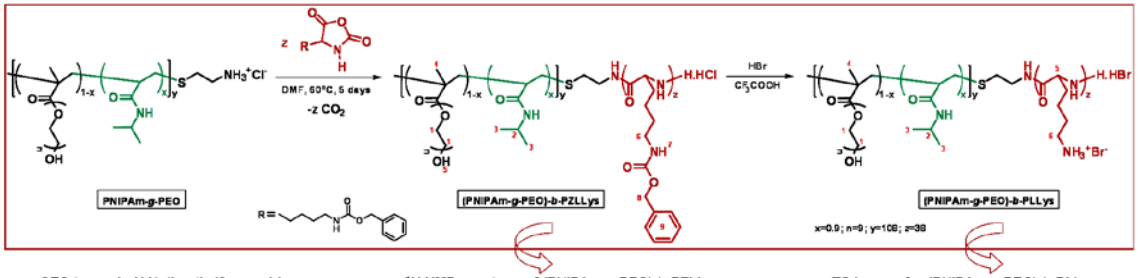
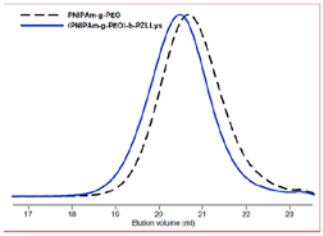
COMBINING BIOPOLYMER ELEMENTS WITH SYNTHETIC POLYMERS INTO A SINGLE MACROMOLECULAR HYBRID CONJUGATE IS AN INTERESTING STRATEGY FOR SYNERGETICALLY MERGING THE PROPERTIES OF THE INDIVIDUAL COMPONENTS AND OVERCOMING SOME OF THEIR LIMITATIONS. PEPTIDE-BASED HYBRID COPOLYMERS FIND APPLICATIONS IN VARIOUS FIELDS INCLUDING TISSUE ENGINEERING AND SMART DRUG OR GENE DELIVERY SYSTEMS.

HEREIN WE PRESENT THE CONTROLLED SYNTHESIS OF PEPTIDE-BASED THERMALLY SENSITIVE HYBRID COPOLYMERS THAT ARE ABLE TO CONDENSE DNA INTO STABLE NANOSIZED AGGREGATES (POLYPLEXES)

I Controlled ammonium-mediated ring-opening polymerization of Z-L-lysine *N*-carboxyanhydride (ZLLys-NCA)

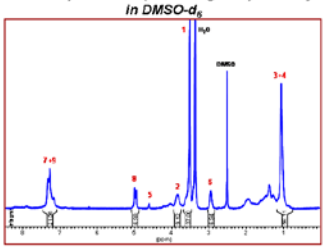


SEC traces in N,N-dimethylformamide



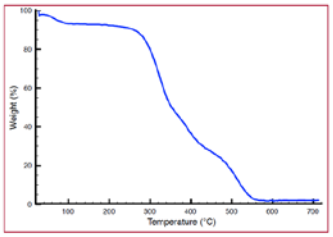
✓ The formation of block copolymer architecture with monomodal molar-mass distribution was demonstrated.

^{1}H NMR spectrum of (PNIPAm-g-PEO)-b-PZLLys in DMSO-d_6



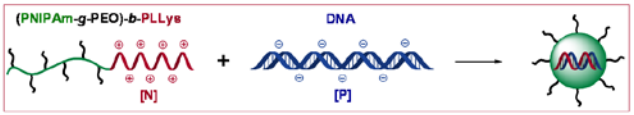
✓ The experimental degree of peptide polymerization was calculated (z=38).

TGA curve for (PNIPAm-g-PEO)-b-PLLys

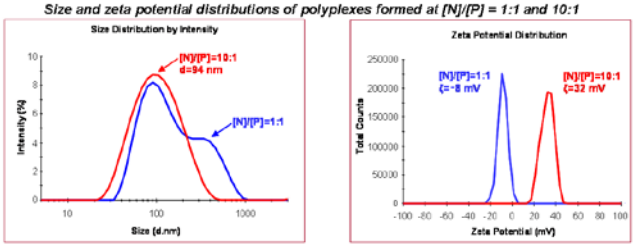


✓ A three-stage mechanism of thermo-oxidative destruction was observed.

II DNA complexation – formation of stable polyelectrolyte complexes (polyplexes)

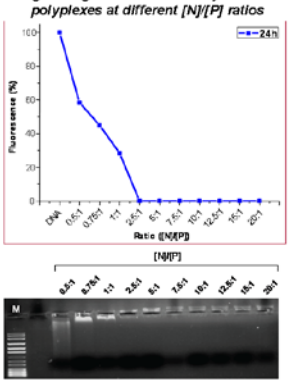


Size and zeta potential distributions of polyplexes formed at [N]/[P] = 1:1 and 10:1



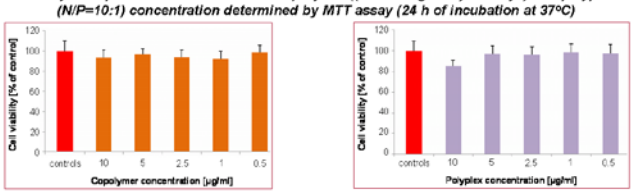
✓ Stable (more than 8 months) nanosized (d~90 nm) polyplexes with positive surface charge (ζ=32 mV) were formed at [N]/[P]=10:1.

Ethidium bromide displacement and agarose gel retardation assays of the polyplexes at different [N]/[P] ratios



✓ The ability of the hybrid copolymer to condense DNA was evaluated.

Viability of HepG2 cells as a function of copolymer ((PNIPAm-g-PEO)-b-PLLys) and polyplex (N/P=10:1) concentration determined by MTT assay (24 h of incubation at 37°C)



CONCLUSIONS

- Hybrid copolymers with thermally sensitive and polypeptide segments were synthesized and characterized.
- Optimal conditions for DNA condensation into stable nanosized complexes (polyplexes) were found.
- There is no apparent cytotoxic effect of the hybrid copolymer and the polyplex on HepG2 cells.
- Overall results indicate that the polyplexes can be further evaluated for potential biomedical applications.

The financial support from the Bulgarian National Science Fund (project *DO 02-247/2008*) and from the Science Research Center at the Burgas Prof. Assen Zlatarov University (project *NIH-207*) is gratefully acknowledged. We thank Dr. M. Apostolova and Ms. R. Kozarova for the ethidium bromide displacement, gel-retardation and cytotoxicity assays.

БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ
ИНСТИТУТ ПО ПОЛИМЕРИ

Analytical Characterization of Nanosized System as Cisplatin Carrier

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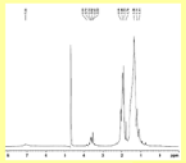
Abstract: A core-shell type star-shaped polymer was thoroughly characterized and evaluated as nanocarrier of cisplatin. The macromolecule is built up of hyperbranched hydrophobic polystyrene core and hydrophilic shell of polyacrylic acid arms. This carrier was characterized applying both conventional and Diffusion Ordered NMR Spectroscopy (DOSY), IR-spectroscopy and analytical centrifugation. The macromolecules were loaded with cisplatin via ligand exchange reaction between carboxylate and chloride ligands. The loaded polymer particles were visualized by AFM. Drug loading and release were followed by AAS and ICP-AES. The conjugates were less toxic than cisplatin, displayed sustained drug release and revealed potential as antitumor therapeutic system.

Characterization of star polymers

The core-shell type polymers were obtained through acidic hydrolysis of the linear poly(*tert*-butyl acrylate) arms of the precursors to polyacids thus yielding polymers with branched hydrophobic interior and hydrophilic multifunctional shell from poly(acrylic acid) chains [1, 2]. They are assigned as $PS_{core}PA_{arm}$.



$$R_h = \frac{kT}{6\pi\eta D}$$

$PS_{core}PA_{arm}38$: $D = 1.32\times10^{-11}$ m²/s, R_h=12.9 nm

$PS_{core}PA_{arm}58$: $D = 1.23\times10^{-11}$ m²/s, R_h=14.0 nm

Figure 1. ^{1}H NMR spectrum (a) and the DOSY spectrum (b) of the $PS_{core}PA_{arm}58$ star polymer at 293 K and pH = 9.

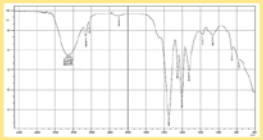


Figure 2. IR-spectrum of the $PS_{core}PA_{arm}58$ star polymer

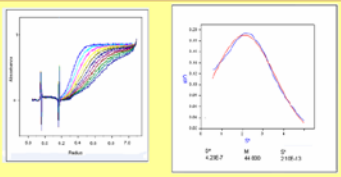


Figure 3. Data from analytical centrifugation experiment performed for $PS_{core}PA_{arm}43$. Method of data processing: Sedimentation Time Derivative, C = 2mg/ml; T = 20°C; ω = 20 000 rpm.

Loading of star polymers with cisplatin

The star copolymers were loaded with cisplatin by mixing of the aqueous copolymer solution with the drug followed by dialysis in order to remove the unbound cisplatin.

Figure 4. Schematic presentation of the possible ways of cisplatin binding to the star polymers.

Table 1. Data about the star copolymer loading with cisplatin in an aqueous solution at a drug concentration of 2 mg/ml, temperature 22 °C, pH 9 and incubation time 24 h.

Sample	Feeding molar ratio [carboxylate]:[cisplatin]	Loading efficiency %	Drug mass fraction in the loaded particles %
$PS_{core}PA_{arm}38$	3	80	45
$PS_{core}PA_{arm}58$	3	84	46

Spherical in shape particles were observed for the conjugates. Their diameters vary in the range from 17 nm to 23 nm.

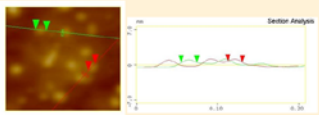


Figure. 5. AFM image of $PS_{core}PA_{arm}58$-Pt conjugate on mica surface.

Release of platinum(II) complexes in physiological saline

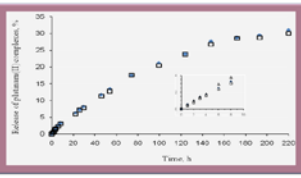


Figure 6. Release of Pt(II) complexes from cisplatin-loaded star copolymers in phosphate buffered saline (pH 7.4, 0.14 M NaCl) at 37 °C: (◆) $PS_{core}PA_{arm}58$-Pt and (□) $PS_{core}PA_{arm}38$-Pt.

Analytical methods for determination of Pt(II) conjugated to a polyacrylate chain or in presence of PBS and 0.14 M NaCl

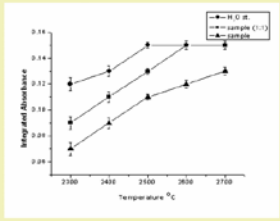


Figure 6. Atomization curves for Pt aqueous standards and for sample in phosphate buffered saline.

Table 2. Slopes of calibration curves for Pt – flame atomic absorption spectrometry

Metod	Flame atomic absorbtion spectrometry
b_0	0.0006±0.0001
$b_{s(1:1)}$	0.0003±0.0001
b_s	0.0002±0.0001

Table 3. Slopes of calibration curves for Pt – electrochemical atomic absorption spectrometry

Method	Electrothermical atomic absorbtion
b_0	0.76±0.03
$b_{s(1:1)}$	0.68±0.04
b_s	0.54±0.05

Table 4. Comparative results for concentration of Pt received via AAS and ICP-AES

Sample	Electrothermical atomic absorption spectrometry [mean±s]	Inductive coupled plasma atomic emission spectrometry [mean±s]
Sample 1	0.07±0.01	0.06±0.01
Sample 2	0.26±0.02	0.26±0.02
Sample 3	0.74±0.05	0.75±0.04

Table 5. Slopes of calibration curves for Pt for water standards and in the presence of polymer

Method	203. nm	214. nm
b_0	11.6±0.1	105±7
$b_{s(1:1)}$	11.5±0.1	103±8
b_s	11.8±0.1	106±8

Cytotoxicity

In order to evaluate whether cisplatin loaded into the designed nano-carriers exerts cytotoxic effects we carried out an in vitro cell viability study, using a panel of four human tumor cell lines, representative for some clinically important types of neoplastic disease. The immobilization of cisplatin in the polymeric nano-carriers results in a shift of the dose response curves to higher concentrations and respectively with an increase of the IC50 values. This could be ascribed to the fact that it is the free drug which interacts with DNA to trigger cell death, and hence the established lower cytotoxicity of loaded cisplatin is expected and is consistent with the sustained manner of drug release.

Table 6. IC50 values for the free cisplatin and its polymer conjugates.

Cell line	IC$_{50}$(μmol/l)					
	Cisplatin		$PS_{core}PA_{arm}58$-Pt		$PS_{core}PA_{arm}38$-Pt	
	72 h	96 h	72 h	96 h	72 h	96 h
MDA-MB-23[a]	9.2	4.8	> 200.0	107.2	> 200.0	145.2
K-562[b]	10.9	3.2	148.3	69.2	185.4	117.9
HL-60[c]	7.3	3.4	94.0	53.3	145.2	80.4
HUT-78[d]	4.1	2.03	49.7	20.9	71.2	28.4

[a]Breast cancer (ER-negative); [b]Chronic myeloid leukemia; [c]Acute promyelocyte leukemia; [d]T-cell lymphoma

Conclusions

A new core-shell nanocarrier with star geometry was designed as a delivery system of cisplatin. DOSY NMR spectroscopy and analytical centrifugation were used to determine important star polymer characteristics such as molecular mass, diffusion and sedimentation coefficient and hydrodynamic radius. A high drug payload was achieved and sustained release of the agent was observed. AAS and ICP-AES were used as reliable methods for quantitative determination of Pt(II) bound to the polymer or in presence of PBS saline. The complex analytical characterization of the nanosized cisplatin conjugate reveals it as a promising therapeutic system.

References:

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[2] Kowalczuk-Bleja, A., Sierocka, B., Muszyński, J., Trzebicka, B., Dworak, A., 2005. Core-shell polyacrylate and polystyrene-block-polyacrylate stars. Polymer, 46, 8555-8564.

Acknowledgements

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БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ
ИНСТИТУТ ПО ПОЛИМЕРИ

ШУМЕНСКИ УНИВЕРСИТЕТ
Епископ Константин Преславски

NEW SYNTHESIS OF FUNCTIONAL COPOLYMERS, CONTAINING STABLE TEMPO RADICALS

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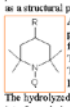
INTRODUCTION

The established antitumour and radiosensibilizing effects of the nitroxilic radicals, and also their low toxicity gives us the grounds to enlist them in their molecule of the citoxye groups [1]. The availability of the nitroxilic radicals in the molecule of the newly formed compounds disclose provide opportunites for solving many biomolecular and biopharmaceutical problems by using ESR method and also for making pharmaceutical applications [1-5]. As a stable TEMPO radicals (2,2,6,6-tetramethylpiperidine-1-oxyl) is widely used as a radical trap, and also as a structural probe for biological systems in conjugation, as a reagent in organic synthesis, and polymer chemistry [1,3,6-8].



Amino-, hydroxy-, and propargilamine derivatives of TEMPO are a great interest [4,5,9]. In our search for novel, low-toxic cell-penetrable and neuroprotective antioxidants [4]. The novel class of N-propargilamine nitroxides may have potential implication for the experimental therapies of Parkinson disease [5]. The structure of 4-amino-2,2,6,6-tetramethylpiperidine-1-oxyl (A-TEMPO) is examined in details [9].

The functional copolymers show a broad range of biological activities. The kind of poly(maleimide-co-2-ethylacrylic acid) show low toxicity and significant curative effects on Lewis Lung carcinoma and S180 [10].

The hydrolyzed form of the copolymers of divinyl ether with maleic anhydride (DIVEMA or Pyran) shows various biological activities such as interferon induction, antiviral and antitumor activity as well as immunostimulating effects [11]. Maeda reported in [12,13] of neocarzinostatin SMANCS/Lipiodol (S/L drugs) on the base of poly(styrene-co-maleic acid). Formulation based on S/L have shown to be effective both as a diagnostic tool and for therapeutic use in solid tumors. The free nitroxilic radicals 4-R-TEMPO show antitumor activity [1]. Their toxicity and effectiveness depend on the substituent R. In this work aim to obtain and characterize of new water soluble copolymers, as a macromolecular R-substituent in TEMPO.

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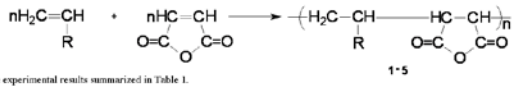
EXPERIMENTAL REZULTS AND DISCUSION:

Synthesis and modification of functional copolymers of Maleic anhydride

The alternating multifunctonal copolymers of maleic anhydride (MA) with electron donating comonomers: N-vinylpirrolidone (VP), acrylic acid (AA), vinyl buthyl ether (VBE), styrene (St) and vinyl acetate (VA) **1-5** were preparated by radical initiated copolymerization in solution at 60 °C:



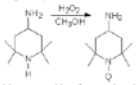
The experimental results summarized in Table 1.

Table.1. Copolymerization of electron donor monomers with Maleic anhydride in benzene at 60 or 70°C (C_{IN} =3,5 mol/l, AIBN-0,75 %)

Sample	M_1	M_2	Yield %	N %	Copolymer composition mol% m_1	m_2	[η] dl/g
1	VP	MA	82,8	8,84	49,8	50,2	0,68
2	AA	MA	77,1		50,0	50,0	0,30
3	VBE	MA	72,3		51,8	48,2	0,48
4	St	MA	89,7		50,0	50,0	0,69
5	VA	MA	82,0		49,8	50,2	0,62

Preparation of 4-amino-2,2,6,6-tetramethylpiperidine-1-oxyl (A-TEMPO).

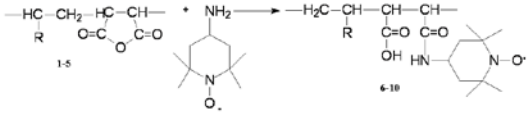
To the solution of 1,5g 4-amino-2,2,6,6-tetramethylpiperidine (A-TEMP) in 20ml methanole in flask was added 10ml 30% H_2O_2 at room temperature. On the reaction mixture was operated with ultrawave (40kHz) for about maximum time 30 min.



The reaction of oxidation was controlled with mobile system chloroforme-ethanole (4:1) and immovable phase silicagel. After that the solutioin was concentrated on the rotational vacuum-evaporator. Yield: 82,9% $C_9H_{17}N_2O$; %N=16,24; (Calc. 16,36%).

Immobilization of 4-amino-2,2,6,6-tetramethylpiperidine-1-oxyl:

New functional copolymers, containing stable nitroxide radical were prepared by the polymeranalogous reactions of the copolymers 1-5 with A-TEMPO in DMF at 60 °C:



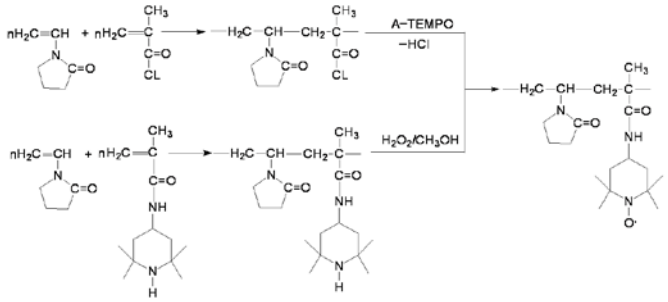
Where: **6**-poly(VP-co-MA/TEMPO); **7**-poly(AA-co-MA/TEMPO); **8**-poly(VBE-co-MA/TEMPO); **9**-poly(St-co-MA/TEMPO); **10**-poly(VA-co-MA/TEMPO)

The structure and composition of the obtained MA-copolymers **1-5** were determined by NMR and FT-IR spectroscopy. IR spectra of the MA-copolymers shows characteristic bands 1840 and 1778 cm^{-1}($\nu_{C=O}$) for MA units. For the modification TEMPO copolymers **6-10** the anhydride bands are completely displeaced and in IR spectra shows stretching bands about 1640-1680 cm^{-1} ($\nu_{C=O}$, Amide I), and 1712 cm^{-1} ($\nu_{C=O}$, COOH), also bands 1340 and 1190 cm^{-1} (N-O·).

Second method.

N-vinylpyrrolidone (VP) is an interesting monomer that has been used in the synthesis of functionalized copolymer with medico-biological properties [14,15].

In this work TEMPO-functionalized copolymers of N-vinylpyrrolidone was prepared through reactions between 4-amino-2,2,6,6-tetramethylpiperidine (A-TEMP) or A-TEMPO and carbonyl chloride group. All reactions presented in scheme:



The functional copolymer poly(N-vinylpyrrolidone-co-methacryloil chloride) were prepared out in solution (THF, DCE, Clf), presend AIBN as an initiator at 60°C.

The functional copolymer poly(N-vinylpyrrolidone-co-methacryloil chloride) were synthesized out in solution (THF, DCE, Clf), presend AIBN as an initiator at 60°C. The results in Table 2 show that the nature of solvent act on the copolymer composition and molecular mass of the copolymers.

Table 2. Copolymerization of VP (M_2) with MAC (M_1) in solvent M_1/M_2=50:50mol%,AIBN-0,75%, 60°C)

Solvent	Yield %	N_2 %	Compozition, mol% m_1	m_2	[η] dl/g
THF	82,8	6,24	48,4	51,6	0,54
DCE	82,3	6,37	49,5	50,5	0,50
Clf	79,7	7,61	58,1	41,9	0,47

The copolymerization VP with MAC were investigated at varying monomer feed composition M_1/M_2 from 80:20 mol% to 20:80 mol%, in THF. Experimental data presented in Fig.1.

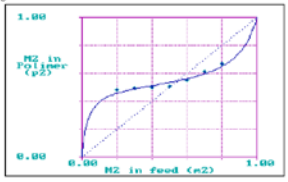


Fig. 1. Copolymer composition (F_2) as a function of monomer feed composition (M_2) for the copolymerization of N-vinylpyrrolidone (M_2) with methacryloil chloride (M_1) in THF

The monomer 2,2,6,6-tetramethylpiperidine-4-ylmethacrylamide (TMA) was prepared from solution of 4-amino-2,2,6,6-tetramethylpiperidine (A-TEMPO), methacryloilkhloride in toluene and triethylamine (TEA) under an nitrogen atmosphere with magnetic stirring. The monomer was isolated as a white crystals. Yield: 82%, $C_{13}H_{24}N_2O$, N=12,38% (calc. 12,49%).

New water soluble copolymers of N-vinylpyrrolidone was synthesized via copolymerization with 2,2,6,6-tetramethylpiperidine-4-ylmethacrylamide (TMA) using AIBN as an radical initiator in ethanole at 60°C.

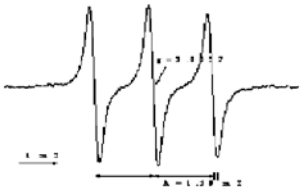


Fig.2. ESR spectrum of the poly(N-vinylpyrrolidone-co-2,2,6,6-tetramethylpiperidine-1-oxyl methacrylate) in ethanole

The structure of monomer and copolymer were determined by the FT-IR and ESR spectroscopy. For the modification MA-copolymers the anhydride bands (1778 and 1840cm^{-1}) are completely displeced. The tipical triplet signals in the ESR spectra (Fig.2) also band about 1340 and 1190cm^{-1} (stretching N-O·) in FT-IR spectra of the obtained copolymers is a proof for stable TEMPO radicals in the macromolecule.

БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ
ИНСТИТУТ ПО ПОЛИМЕРИ

Poly(oxyethylene aminophosphonate)s as polymer drug carriers

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Institute of Polymers, Bulgarian Academy of Sciences, Sofia 1113, Bulgaria

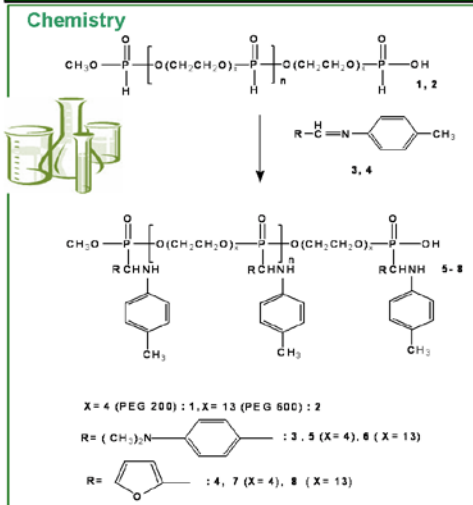
INTRODUCTION

The development of new effective polymeric systems for the treatment of different diseases, including cancer, diabetes, ischemia, severe combined immunodeficiency, neurodegenerative, offers enormous possibilities to the advanced pharmaceutical technology [1-5]. The polymer-drug conjugates have much potential to improve the therapy of variety human pathologies, solving major problems in medicine, such as the toxic effects of the drugs and the duration of drug action.

A great deal of attention and research efforts are being concentrated on the synthesis of diverse biodegradable polymers and on the investigations of their viability as drug carriers in the design of these new types of therapeutics [6]. Among the numerous macromolecular systems studied for drug delivery purposes, the polymers with phosphorus ester (C-O-P-O-C) repeating units in the backbone occupy a particularly important place, because they can degrade into biocompatible and non-toxic components under physiological conditions. These polymers possess reactive functional groups in their backbone, which allows for conjugation of bioactive molecules to the chains and gives much opportunities for the preparation of new drug delivery systems with improved therapeutic indexes. On the basis of poly(oxyethylene H-phosphonate)s we synthesized poly(oxyethylene aminophosphonete)s – alternating copolymers built only of aminophosphonate units with potential biological activity and non-toxic poly(ethylene glycol) links.

The immobilization of aminophosphonates to biodegradable polymer carriers like poly(oxyethylene H-phosphonate)s appears a promising approach in the design of new polymer drug carriers, as well of new polymers with own activity.

Chemistry



Scheme 1. Synthesis of poly(oxyethylene aminophosphonate)s 5-8.

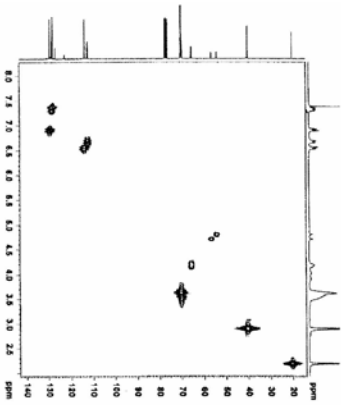
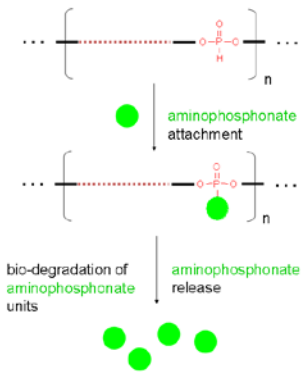


Figure 1. CH COSY diagram of poly(oxyethylene aminophosphonate) 5 in $CDCl_3$

Possible Application



Pharmacology

The compounds were tested for cytotoxicity in a panel of human tumor cell lines, representative for some clinically important types of neoplastic diseases, namely HL-60 (acute promyelocyte leukemia), its multi-drug resistant sub-line HL-60/DOX (characterized by overexpression of MRP-1 efflux pump), LAMA-84 and K-562 (chronic myeloid leukemias). The cells were exposed to serial dilutions of the tested compounds for 72 h and thereafter their viability was assessed using the MTT-dye reduction assay. The clinically used antineoplastic drug cisplatin was used as reference cytotoxic agent.

Table 1. Cytotoxic effects of the poly(oxyethylene aminophosphonate)s 5-8 vs. the clinically applied antineoplastic drug cisplatin, as assessed by the MTT-dye reduction assay after 72 h continuous exposure.

Compounds	IC_{50} (μmol/L)			
	HL-60	HL-60/Dox	LAMA-84	K-562
5	105. 9	> 400. 0	> 400. 0	> 400. 0
6	19. 2	27. 2	17. 2	14. 9
7	19. 9	20. 4	14. 0	15. 2
8	14. 2	14. 4	12. 3	13. 7
Cisplatin	7. 8	14. 5	18. 2	25. 7

Conclusion

Novel poly(oxyethylene aminophosphonate)s 5-8 were synthesized via addition of poly(oxyethylene H-phosphonate)s 1 and 2 to the Schiff bases N-(4-dimethylaminobenzylidene)-p-toluidine 3 and N-furfurylidene-p-toluidine 4.

The polymers 5-8 obtained on the basis of biodegradable polymer carriers 1 and 2 consist only of aminophosphonate (active substance) and non-toxic poly(ethylene glycol) units.

The polymers 5-8 have coordination centres in their repeating units and can be used as new biodegradable polymer carriers for physical immobilization of bioactive substances.

Compounds 6-8 caused prominent cytotoxic effects with low micromolar IC_{50} values.

The N-furfurylidene-p-toluidine-Schiff base with longer (14 units) PEO moiety abundant in 8 were identified as sturtucral prerequisites affording superior activity, while the analogues bearing N-(4-dimethylaminobenzylidene)-p-toluidine was generally less active than 8.

In spite of the Schiff base fragment however, in all sub series of compounds the reduction of the length of the PEO miety from 13 to 4 units was consistent with significant reducitpon in relative potency and in case of 5 with dramatic loss of activity.

The established cytotoxicity of compounds 6-8, similar or comparable to that of the reference drug cisplatin findings give us reason to consider the presented compounds as a novel class of aminophosphonate-based cytotoxic agents.

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БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ
ИНСТИТУТ ПО ПОЛИМЕРИ

Double Networks of Poly(2-Acrylamido-2-Methyl-1-Propanesulfonic Acid)-Polyacrylamide as Templates for Calcium Phosphates Crystallization

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INTRODUCTION

Double networks (DN) are a specific type of interpenetrating polymer networks which hydrogels have very good mechanical performance [1]. Recently, we have observed a nano-domain phase-separated morphology of DN made by polyacrylamide and polysulfobetaine [2]. This specific structure along with the chemical bonding between two components [3] was proposed as the reason for the unusual mechanical properties of DNs films and hydrogels.

AIM

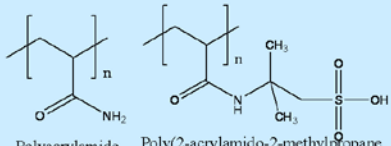
In the present study we aim to explore the specific DN structure in order to induce controlled crystallization of calcium phosphates. To this purpose we have synthesized and characterized poly(2-acrylamido-2-methyl-1-propanesulfonic acid) (PAMPS) - polyacrylamide (PAAm) DNs with different molar ratios between the two components and performed in situ calcium phosphates crystallization.

EXPERIMENTAL PART

Synthesis of DN

1M AMPS, 4 mol. % MBAA, 0.1 mol. % $K_2S_2O_8$
60°C, 6h
Swelling in 1M, 2M, 3M AAm, 0.1 mol. % MBAA, 0.1 mol. % $K_2S_2O_8$
60°C, 6h
DN

Synthesis: The first step is preparing of PAMPS network by using as cross-linking agent N,N'-methylenbisacrylamide (MBAA) and $K_2S_2O_8$ (potassium persulfate) as an initiator. Polymerization took place at 60°C for 6h. The second step is swelling of the PAMPS network into the precursor solution for the second network of PAAm for 24 h. After swelling the obtained hydrogel was heated for 6h at 60°C. DN obtained in this way was washed in distillate water for 1 week to remove the residual chemicals.



Polyacrylamide (PAAm) — Poly(2-acrylamido-2-methylpropane sulfonic acid (PAMPS)

DN CHARACTERIZATION

Microhardness of dry DNs

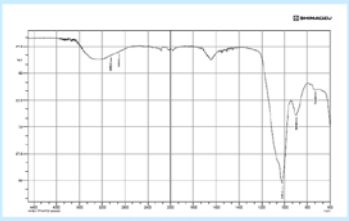
Sample	MH [MPa]
PAMPS	112,2 ± 1,3
PAMPS/1M PAAm (1:10)	256 ± 37
PAMPS/2M PAAm (1:10)	301 ± 40
PAMPS/3M PAAm (1:10)	347 ± 25
PAAm	315 ± 4

The microhardness of the DNs increases as the PAAm content increases. This is most probably due to the increased network density, proved by the decreasing of the swelling ratio.

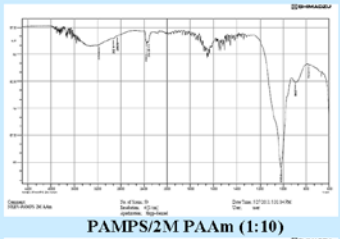
The elastic modulus of the DN`s hydrogels increases as the PAAm content increases. This coincides with the trend observed for the microhardness of dry samples.

CALCIUM PHOSPHATES CHARACTERIZATION

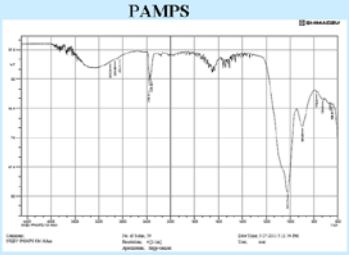
IR Spectroscopy of calcium phosphates crystallized on:



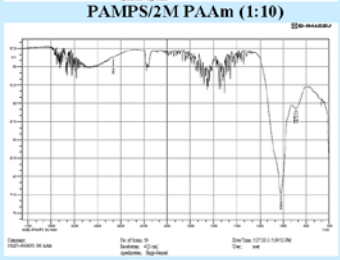
PAMPS



PAMPS/2M PAAm (1:10)



PAMPS/1M PAAm (1:10)



PAMPS/3M PAAm (1:10)

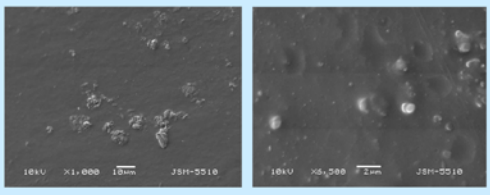
The increase in PAMPS content results into increasing of the formed hydroxyapatite (HA). On the surface of the neat PAMPS, HA occurs which upon "dissolution" of PAMPS with PAAm transforms to amorphous calcium phosphate (ACP). Thus, on the surface of the PAMPS/3M PAAm (1:10) only ACP is formed. The transformation of HA to ACP with increasing the PAAm content is confirmed by the appearance of a shoulder in the bands characteristic for IR spectra of HA (band in the interval 900 - 1200 cm^{-1}). Similar conclusion could be drawn for the DN samples with less excess of PAAm (1:4), IR spectra not shown here.

DNs hydrogels properties

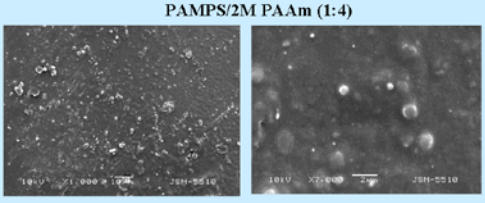
Sample	Swelling ratio	Elastic Modulus [MPa]	
		Ball 1 (small)	Ball 2 (medium)
PAMPS/1M PAAm (1:10)	**23 ± 1.9**	1.8	4
PAMPS/2M PAAm (1:10)	**20 ± 2.7**	1.9	5
PAMPS/3M PAAm (1:10)	**9 ± 1.6**	5.6	17
PAMPS/2M PAAm (1:4)	**71 ± 1.7**	1.7	4.5
PAMPS/3M PAAm (1:4)	**80**	2.8	5
PAAm	**34 ± 1.3**	0.63	1.6
PAMPS	**104**		-

SEM pictures show a phase-separated structure with PAAm domains (white) dispersed into PAMPS. The higher the PAAm content, the number of PAAm domains is higher and their size is smaller. Besides these domains are better dispersed.

Scanning Electron Microscopy



PAMPS/2M PAAm (1:4)



PAMPS/3M PAAm (1:4)

CONCLUSIONS

In this study, PAMPS-PAAm DNs were used as templates for calcium phosphates crystallization. DNs were characterized in terms of their mechanical properties in dry (microhardness) as well in swollen state (elastic modulus). The morphology, revealed by SEM, shows phase separation with small inclusions of PAAm into PAMPS matrix, the number of these domains increasing with increasing PAAm content, while at the same time their size decreased. The crystallization of calcium phosphates took place on the surface of the DNs, the formation of HA was dependent on the DN composition. The increasing of PAMPS content resulted into ACP → HA transition.

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БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ
ИНСТИТУТ ПО ПОЛИМЕРИ

2.06.2011
ИП - БАН

ТРЕТА ПОСТЕРНА СЕСИЯ "МЛАДИТЕ УЧЕНИ В СВЕТА НА ПОЛИМЕРИТЕ", организирана в рамките на Модул 2: Нови материали за медицината и фармацията на проект UNION (ДИДВП 02/2-2009)

EFFECT OF GAMMA-IRRADIATION ON PBI-BASED MEMBRANES

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Institute of Polymers – Bulgarian Academy of Sciences
* - Technical University of Sofia

Materials and Methods

Materials studied: three types of PBI-based membranes (dry films):

- Non-modified PBI-membrane (PBI-0);
- Modified PBI-membrane with 10 % hydroxyalkyl groups (PBI-10);
- Modified PBI-membrane with 40 % hydroxyalkyl groups (PBI-40)

Methods applied: gamma-irradiation in air, at dose rate 5.5 kGy/h; doses – 264 and 450 kGy.

Objectives:

cross-linking of the membranes at appropriate irradiation conditions.

Results and Discussion

Solubility test: solubility of the membranes in dimethylacetamide (DMAA) – starting membrane is soluble; cross-linked membrane is insoluble.

Non-irradiated samples dissolve completely in DMAA at room temperature (T_{room}) as follows:

- PBI-0 dissolves completely at T_{room} by intensive shaking for 10 min;
- Modified membranes (PBI-10 and PBI-40) dissolve completely at T_{room} without shaking for 3 days.

The solubility of the irradiated samples (Table 1 & Table 2) considerably differs from the solubility of the non-irradiated samples; only PBI-10, irradiated at 264 kGy, dissolves almost completely for 3 days at T_{room}. The rest of the samples irradiated exhibit different solubility behavior:

- PBI-0, irradiated at 264 kGy:
  - partially dissolves for 6 days;
  - gel fraction - about 1 wt.%;
- PBI-0, irradiated at 450 kGy:
  - the membrane starts to split into two thin sheets after 2 hours in the solvent;
  - after one month the membrane is still not fully dissolved.
- PBI-40, irradiated at 264 kGy: after one month in the solvent the membrane has rendered several clearly visible flocks;
- PBI-40, irradiated at 450 kGy: after two days in the solvent the membrane disintegrates to fine flocks, which are still visible after one month.
- PBI-10, irradiated at 450 kGy: after two days in the solvent the membrane splits into two thin sheets, which are still visible after one month.

Scheme 1. Modification with glycidol

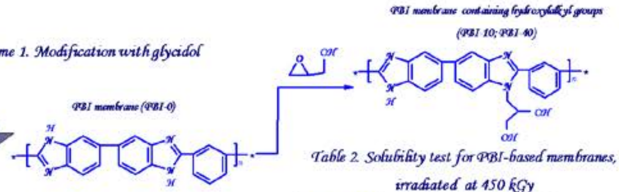

Table 1. Solubility test for PBI-based membranes, irradiated at 264 kGy

Treatment in solvent, [hours/days]	PBI-0	PBI-10 (fully soluble)	PBI-40
18/0.75			
33/1.4			
44/1.8			
57/2.4			
139/5.8			
314/13			
504/21			
788/33			

Table 2. Solubility test for PBI-based membranes, irradiated at 450 kGy

Treatment in solvent, [hours/days]	PBI-0	PBI-10	PBI-40
0/0			
2/0	Splitting		
6/0			
48/2			
51/2		Splitting	
144/6			
336/14			
504/21			
720/30			

Conclusions

The treatment of PBI-based membranes (PBI-0, PBI-10 and PBI-40) with gamma-rays results in considerable changes in their solubility properties which strongly suggests partial cross-linking.

- PBI-0, irradiated at 264 kGy: only about 1 wt. % insoluble fraction.
- PBI-40, irradiated at 264 kGy: after irradiation the membrane is partially soluble.
- PBI-based membranes (PBI-0, PBI-10 and PBI-40), irradiated at 450 kGy: all samples exhibit considerable insoluble fractions after treatment in the solvent for more than one month.

Only PBI-10, treated at dose 264 kGy, does not change after gamma-irradiation; the membrane is fully soluble in DMAA.

Future work

- Irradiating samples at higher doses (up to 1000 kGy) and studying the changes induced in the membranes.
- Studying the mechanical properties (elastic module, tensile strength, elongation at break, microhardness) of the membranes treated.

Acknowledgement: Part of this study has been performed in the frame of the project PEMHYDROGEN funded by the National Science Fund of Bulgaria (Grant 02/68, 2009).

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БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ
ИНСТИТУТ ПО ПОЛИМЕРИ

UNIVERSITY OF OXFORD

Effect of the chain architecture upon spontaneous multilayer formation at the air/water interface in polyamine/SDS mixtures

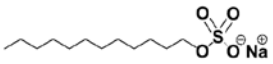
S. Halacheva, J. Penfold and R. K. Thomas

I. Introduction

Recent neutron reflectivity (NR) and surface tension (ST) studies[1,2] from mixtures of sodium dodecyl sulfate (SDS) and commercially available, high molecular weight, linear and branched polyamines (LPEI and bPEI, respectively) have revealed strong correlations between the multilayer (ML) formation at the air/water interface and a range of experimental parameters, including SDS concentration, solution pH, polymer architecture and polymer molecular weight (MW). It was demonstrated[3] that small oligoamines are also able to induce the formation of multilayer structures at the air/water interface under similar conditions to the PEI/SDS systems. In order to control the extent of the polymer/surfactant interaction and to tune the adsorption behaviour, a detailed understanding of the physicochemical properties of the ML structures and the conditions necessary for their formation is essential.

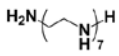
II. The System

Surfactant

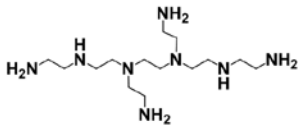


Sodium Dodecyl Sulfate (SDS)

Polyamines



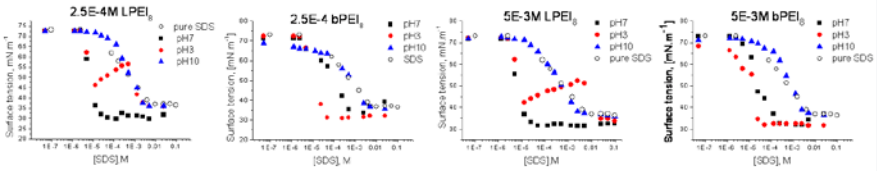
Linear Octamine ($LPEI_8$)



Branched Octamine ($bPEI_8$)

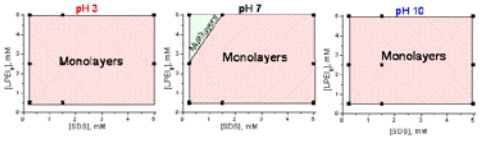
III. Surface Tension

For the $bPEI_8$, ST data are broadly similar to those reported for commercially available pentamine/SDS and hexamine/SDS mixtures.[3]
The ST data at pH 3 for $LPEI_8$ was described in terms of competition between bulk and interface polymer/SDS complexation.

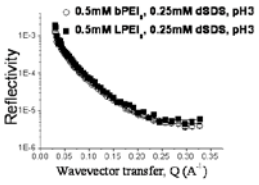


IV. Neutron Reflectivity

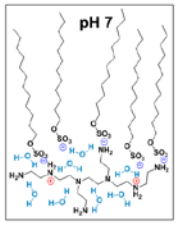
Evolution of the surface structure for $LPEI_8$/SDS/nrw mixtures



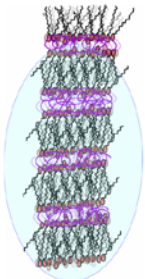
Monolayer characterisation



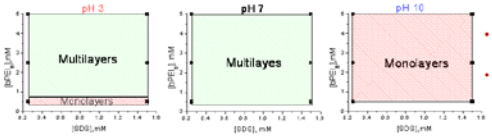
Monolayer structure of $bPEI_8$/SDS at the air-water interface



Multilayer structure

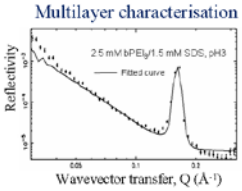


Evolution of the surface structure for $bPEI_8$/SDS/nrw mixtures



- **Monolayer thickness: 18-22 Å**
- **Area per molecule, (A): 32-64 Å²**
- **$A^{pH3} < A^{pH7} < A^{pH10}$**
- **Multilayers are most favoured at pH 7 and when the architecture is branched rather than linear**

Multilayer characterisation



- **Number of layers: ~ 40**
- **Bilayer thickness: ~ 39 Å**
- **Thicker initial monolayer for $bPEI_8$**

V. Conclusions

- Significant enhancement of the SDS adsorbed at the interface was observed, down to very low SDS concentrations, with both $LPEI_8$ and $bPEI_8$
- The optimal conditions for multilayer formation in the $bPEI_8$/SDS and $LPEI_8$/SDS systems have been established
- $bPEI_8$ formed multilayer structures at high solution pH values, where the [amine]:[SDS] ratio was greater than one
- Multilayer formation is both more extensive for the branched polyamines and occurs over a much wider pH and concentration range

VI. References and Acknowledgements

[1] Penfold, J.; Sivia, D. S.; Tucker, I.; Thomas, R. K. *Langmuir* **2004**, *20*, 2265.
[2] Penfold, J.; Tucker, I.; Thomas, R. K.; Zhang, J. *Langmuir* **2005**, *21*, 10061.
[3] Penfold, J.; Thomas, R. K.; Zhang, X. L.; Taylor, D. J. F. *Langmuir* **2009**, *25*, 3980.

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A Comparison Study on Microwave-Assisted and Conventional Cationic Ring-Opening Polymerization of 2-Ethyl-2-Oxazoline by Using Allyl Bromide as a New Functional Initiator

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ABSTRACT

This work describes the synthesis of poly(2-ethyl-2-oxazoline)s end-capped by an α-allyl and a ω-hydroxy group and further polymer chain functionalization/extension trough subsequent thiol-ene click reactions.
For the first time, highly reactive allyl bromide was applied as a functional initiator of the cationic ring-opening polymerization (CROP) of 2-ethyl-2-oxazoline. The polymerization kinetic in thermal and microwave heating conditions were studied by size exclusion chromatography (SEC) and ^{1}H NMR spectroscopy. It has been shown that both thermal and microwave-assisted polymerization produced poly(2-ethyl-2-oxazoline)s of pre-determined molecular weight and low polydispersity, typically below 1.11. In microwave conditions, however, the polymerization was completed within 45 min compared to the conventional thermal polymerization which took more than 7 hrs. Polymer homogeneity and end-group functionality of the obtained poly(2-ethyl-2-oxazoline)s has been evaluated by MALDI TOF mas spectrometry.
To demonstrate the usability of the terminal allyl group, chain extension of the functionalized poly(2-ethyl-2-oxazoline)s with α-methoxy-ω-mercapto-poly(ethylene oxide) (MPEO-SH) as well as end-group transformation with thioglycolic acid has been carried out under photochemical irradiation. The obtained results confirmed a high conversion of the free-radical thiol-ene reactions.

RESULTS and DISCUTION

Synthesis of α-allyl-ω-hydroxy poly(2-ethyl-2-oxazoline) by CROP

Conventional CROP of 2-ethyl-2-oxazoline in acetonitrile

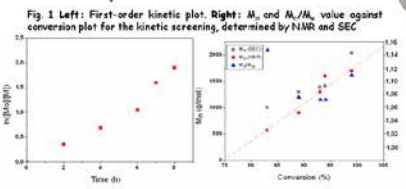


Fig. 1 Left: First-order kinetic plot. Right: M_n and M_w/M_n value against conversion plot for the kinetic screening, determined by NMR and SEC

Table 1. Kinetic date for CROP of 2-ethyl-2-oxazoline with different ratios of the reagents

Code	Time (h)	T (°C)	M_n (NMR)	M_n (SEC)	M_w/M_n (SEC)
PEtOx 1	2	70	570	990	1.15
PEtOx 2	4	70	900	1280	1.09
PEtOx 3	6	70	1300	1370	1.07
PEtOx 4	7	70	1600	1400	1.07
PEtOx 5	8	70	1700	1600	1.11

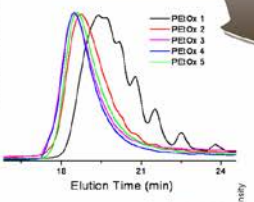


Fig. 2 SEC curves of PEtOxs (Table 1)

CROP of 2-ethyl-2-oxazoline under microwave irradiation in acetonitrile

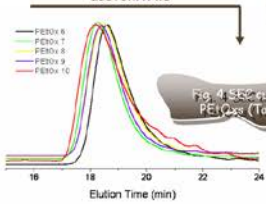
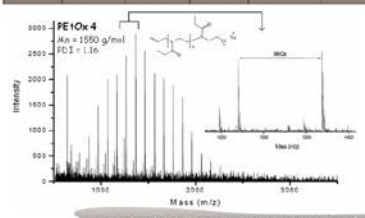


Fig. 4 SEC curves of PEtOxs (Table 2)



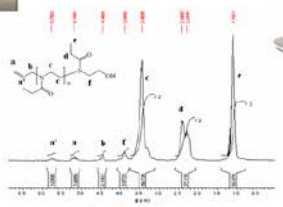
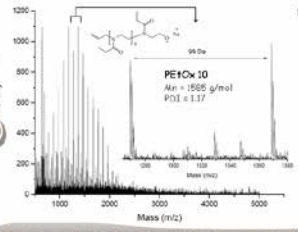


Fig. 3 MALDI-TOF-MS and ^{1}H NMR spectra of poly(2-ethyl-2-oxazoline) (PEtOx 4 in Table 1)



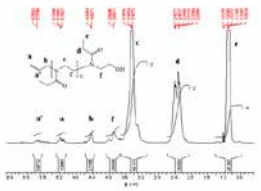
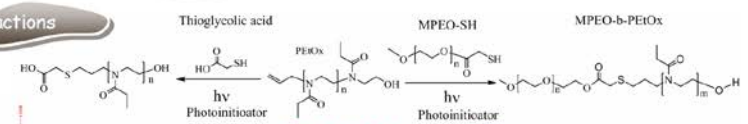


Fig. 5 MALDI-TOF-MS and ^{1}H NMR spectra of poly(2-ethyl-2-oxazoline) (PEtOx 10, in Table 2)

Table 2. CROP of 2-ethyl-2-oxazoline under microwave irradiation at different reaction conditions

Code	Convertion (%)	Time (min)	T (°C)	M_n (NMR)	M_n (SEC)	M_w/M_n (SEC)
PEtOx 6	88	50	58	1130	1200	1.08
PEtOx 7	93	90	70	1400	1500	1.06
PEtOx 8	94	60	90	1600	1400	1.06
PEtOx 9	95	75	70	2200	1400	1.08
PEtOx 10	96.5	45	95	2150	1470	1.08

Thiol-ene click reactions



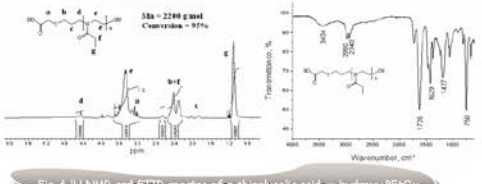


Fig. 6 ^{1}H NMR and FTIR spectra of α-thioglycolic acid-ω-hydroxy PEtOx

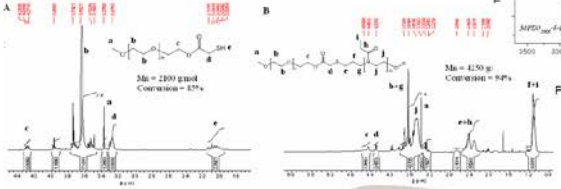


Fig. 8 ^{1}H NMR spectra of (A) MPEO-SH and (B) MPEO-b-PEtOx

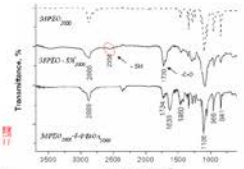


Fig. 7 FTIR spectra of MPEO, MPEO-SH and MPEO-b-PEtOx

CONCLUSIONS

In this study, the successful application of highly reactive allyl bromide as an initiator of the CROP of 2-ethyl-2-oxazoline is described. In order to prove the high activity of this new initiator, we utilized both the convenient CROP (studying the kinetic of this reaction) and the microwave assisted one. The obtained results clearly showed, that the homopolymerization of 2-ethyl-2-oxazoline initiated by allyl bromide is feasible via both pathway. The end products were assessed by ^{1}H NMR spectroscopy, SEC and MALDI-TOF analysis. The obtained α-allyl-ω-hydroxy poly(2-ethyl-2-oxazoline)s exhibited well-defined composition, structure and macromolecular characteristics. Furthermore, we demonstrated the usability of the allyl-head group in the macromolecule of poly(2-ethyl-2-oxazoline)s upon reaction with different mercapto-compounds such as MPEO-SH and thioglycolic acid by using photochemical irradiation. High conversions of these free-radical thiol-ene reactions have been confirmed.

The financial support by the National Science Fund (Grant # DCVP 02/2/2009) is gratefully acknowledged.

Synthesis of poly(vinyl alcohol) graft copolymers containing quaternized ammonium monomer units: Atom Transfer Radical Polymerization versus Ceric Ion Mediated Polymerization

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Introduction

The increasing interest in polyelectrolytes (PEL) is motivated by their versatile applications in industrial processes and daily life. They are abundantly provided by nature but the advances in polymer chemistry gave rise to a variety of man-made PEL. Among the synthetic PEL the cationic polymeric quaternary ammonium compounds have historically been the most extensively studied and used.

We have already develop a convenient method to synthesize novel synthetic PEL, namely graft copolymers of poly(vinyl alcohol) (PVA) containing permanently charged quaternary ammonium groups in the side chains. PVA has been chosen for its hydrophilicity and excellent film-forming and mechanical properties. Moreover, PVA can be used for a variety of biomedical applications such as implants and devices, coatings, pharmaceutical products, etc. It is the only polyvinyl type synthetic polymer confirmed to be biodegradable and its water solubility imply the advantages of easier degradation and elimination. Series of poly(vinyl alcohol) copolymers with grafted poly[2-(methacryloyloxy)ethyl]-trimethylammonium chloride side chains have been obtained by applying the Ceric Ion Mediated Polymerization (CIMP) method. The advantages of this grafting reaction are mild reaction conditions and ecologically preferable aqueous reaction media.

The development of controlled polymerization techniques during the last decades has made it possible to obtain various well defined polymer structures, such as block, multiblock, graft, etc. Atom Transfer Radical Polymerization (ATRP) can be conducted in a range of solvents, such as toluene, ethyl acetate, acetone, methanol, water and supercritical carbon dioxide. Aqueous ATRP has received significant attention, due to increased environmental concern and also the perspectives for diverse biomedical applications of the hydrophilic polymers obtained.

Objectives

The aim of this work is to explore the aqueous Atom Transfer Radical Polymerization technique for controlled grafting of the charged cationic monomer [2-(methacryloyloxy)ethyl]-trimethylammonium chloride on poly(vinyl alcohol) and to compare the copolyelectrolytes thus obtained with those synthesized through Ceric Ion Mediated Polymerization

Results and discussions

General scheme of grafting charged monomer [2-(methacryloyloxy)ethyl] trimethylammonium chloride (Q6) onto PVA by ATRP

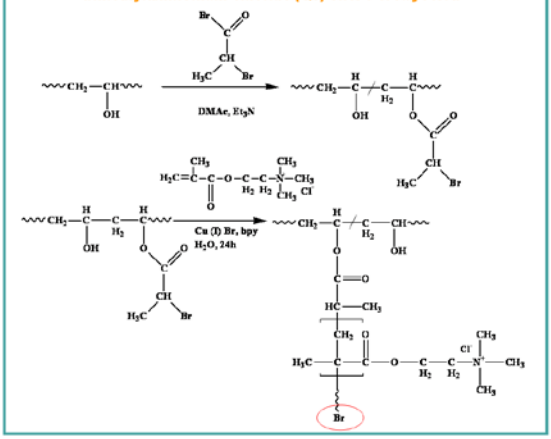
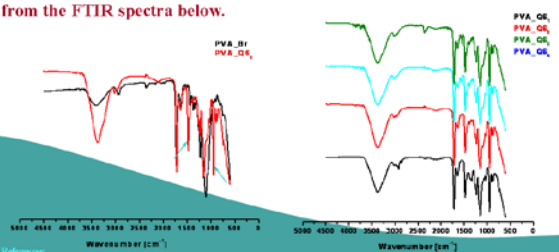


Table 1

Code	Concentration of PVA macroinitiator, [wt %]	Concentration of Q6, [wt %]	Reagents' molar ratio in the reaction mixture, PVA : Q6 : Cu(I)Br : bpy	*Copolymer composition, Q6/PVA
PVA_Q6_2	12	75	30 : 1 : 1 : 2.5	5
PVA_Q6_3	6	75	30 : 0.5 : 2 : 5	7
PVA_Q6_4	6	75	30 : 0.5 : 1 : 2.5	4

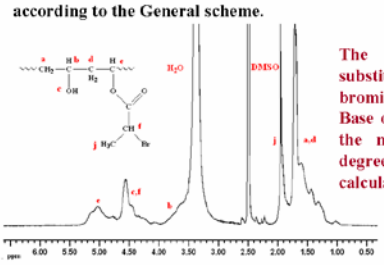
$PVA\_Q6_{2\,3\,4}$ stay for the grafted charged monomer Q6 onto PVA by ATRP
** expressed as average number of grafted Q6 monomer molecules per one PVA unit, as calculated from the ^{1}H NMR spectra*

The successful grafting of Q6 on PVA macroinitiator has been confirmed by FTIR. The structure of copolyelectrolytes obtained via aqueous ATRP was compared with those prepared through CIMP. Good agreement with chemical structure of the newly developed copolyelectrolytes is visible from the FTIR spectra below.



Synthesis of PVA macroinitiator

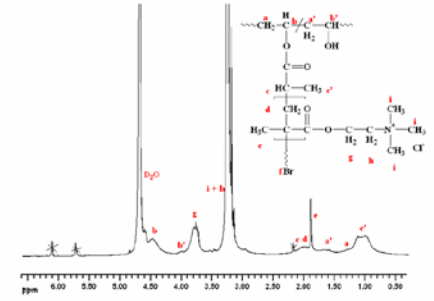
The first step of synthesis of copolyelectrolyte by ATRP was to obtained the macroinitiator [1] by reacting PVA with 2-bromopropionyl bromide according to the General scheme.



The extend of OH-groups substitution with 2-bromopropionyl bromide was estimated by ^{1}H NMR. Base on the integrated spectrum of the macroinitiator (PVA_Br) the degree of modification was calculated to 20 mol %.

ATRP grafting of Q6 onto PVA

In the second stage, Q6 was grafted onto PVA_Br by using Cu(I)Br as catalyst and 2,2′-bipyridine (bpy) as ligand in aqueous media. Series of grafted polyelectrolytes of different composition have been synthesized by varying the reagents' ratio [Table 1].



The copolymers composition has been obtained from the integrated proton NMR spectra.

Conclusions

Novel copolyelectrolytes have been synthesized by grafting the charged cationic monomer [2-(methacryloyloxy)ethyl]-trimethylammonium chloride onto PVA through Atom Transfer Radical Polymerization. Compared to the similar copolymers previously prepared by using Ceric Ion Mediated Polymerization, these newly obtained copolyelectrolyte structures contain uniform size Q6 grafts which are expected to change the solution properties. Moreover, the utilized ATRP method provides possibility for further grafts' chain extension and/or end groups fictionalization with respect to potential biomedical applications.

References:
1. Julien Bernard, Arnaud Favier, Thomas P.Davis, Christopher Barner-Kowollik, Martina H. Stenzel, Synthesis of poly(vinyl alcohol) combs via MADIX/RAFT polymerization, Polymer 47 (2006) 1073–1080

Acknowledgments:
This investigation has been carried out with the financial support of the National Science Fund, project UNION (Contract DCVP 02/2/2009).

БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ

ИНСТИТУТ ПО ПОЛИМЕРИ

Electrochemical synthesis of polyaniline in the presence of poly(2-acrylamido-2-methyl-1-propanesulfonic acid). Electrogravimetric study.

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[2]Physikalische Chemie und Elektrochemie, Technische Universitaet Dresden, 01062 Dresden, Germany

Open questions ?

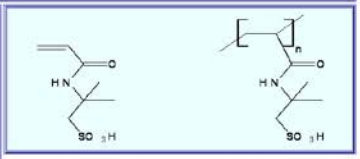
- What is the effect of PAMPSA on the polymerization of aniline in acidic solutions in terms of electromicrogravimetry?
- What is the nature of the ion transport during oxidation and reduction of PANI/PAMPSA layers in neutral media?
- What is the effect of pH on the electroactivity of PANI/PAMPSA composites?

Experimental Studies

ELECTROLYTES

- 0.055 M aniline/0.4 M $HClO_4$ (or 0.4 M H_2SO_4)/ 0.7 mM PAMPSA
- 0.1 M Na or Cs PBS (pH 6.7)
- 0.1 M NaPBS (pH 8, 9 and 10.7)
- 0.1M TrisCl or TrisClO_4 (pH 7)
- 0.4 M HCl, 0.4 M $HClO_4$

- Chronoamperometric and microgravimetric measurements during the potentiostatic synthesis of PANI layers
- Voltammetric and microgravimetric measurements of PANI layers
  - in buffer solutions with different pH containing one and the same type of ions
  - in buffer solutions with constant pH and various types of ions (differing markedly in their molar mass)
- Observation of the surface morphology of PANI layers by SEM

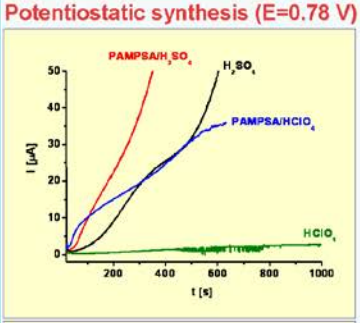


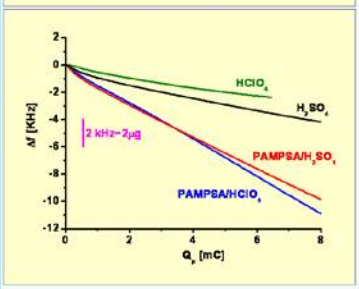
2-acrylamido-2-methyl-1-propanesulfonic acid (AMPSA)

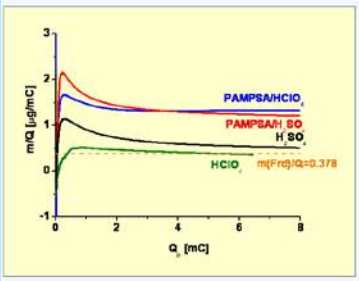
poly(2-acrylamido-2-methyl-1-propanesulfonic acid) (PAMPSA)

Synthesis

Potentiostatic synthesis (E=0.78 V)



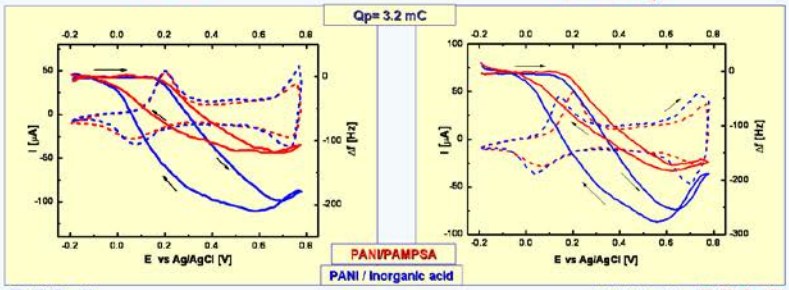




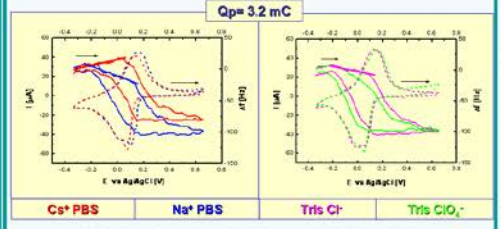
RESULTS

Characterization

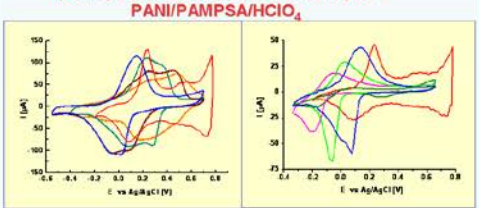
In acidic solutions



In neutral solutions

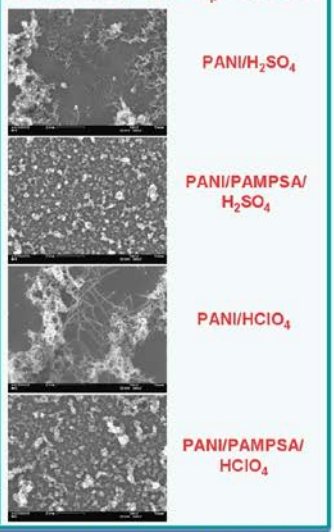


pH dependence of the electroactivity of PANI/PAMPSA/$HClO_4$



0.4 M HCl, pH 4, pH 5, pH 6, pH 7, pH 8, pH 9, pH 10.7

SEM micrographs Q_p= 12.8 mC



CONCLUSIONS

- The microgravimetric frequency shift during aniline polymerization in PAMPSA-containing electrolytes is much higher in comparison to the corresponding shift, measured in polymerization solutions containing inorganic acids alone. This effect indicates the incorporation of PAMPSA in the PANI layers in the course of polymerization.
- The voltammetric and microgravimetric measurements of thin PANI/PAMPSA layers in acidic media show that PAMPSA anions are probably partially involved as charge compensating species during the PANI redox transition.
- The microgravimetric studies of PANI/PAMPSA layers in neutral media show that the frequency shift, measured in the course of redox transition, does not depend on the molar mass of cations or anions available in the buffer solutions. This indicates that the charge compensating species are most probably protons, available in the PANI/PAMPSA composite layers.
- PANI/PAMPSA composite layers preserve their electroactivity in buffers with pH as high as 9. With increasing pH from 7 to pH 10.7 the redox activity gradually decreases due to deprotonation of the PANI/PAMPSA complex.

ACKNOWLEDGEMENTS

Financial support of the Alexander von Humboldt foundation (grants for V.L. and V.T.) and project VUH 307/207 of the Bulgarian Ministry of Education and Science is gratefully acknowledged.

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БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ
ИНСТИТУТ ПО ПОЛИМЕРИ

Електроовлакнени мембрани с антибактериални свойства от поли(L-лактид), съдържащи лекарствени вещества

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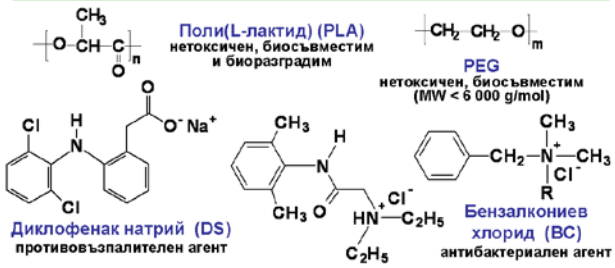
Цел: Получаване и охарактеризиране на микро- и нановлакнести мембрани от поли(L-лактид) (PLA) или PLA/полиетиленгликол (PEG), съдържащи диклофенак натрий (DS), лидокаин хидрохлорид (LHC), бензалкониев хлорид (BC) или техни комбинации, проследяване на профила на освобождаване на лекарствените вещества *in vitro* и микробиологични тестове.

Електроовлакняване

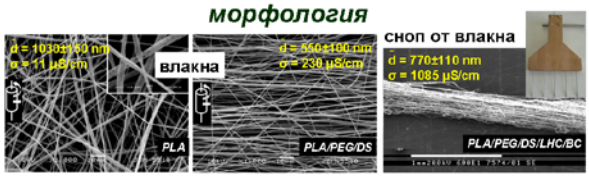
многоиглен електрод

Материали: полимери и органични соли

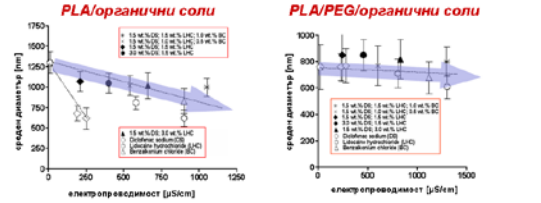


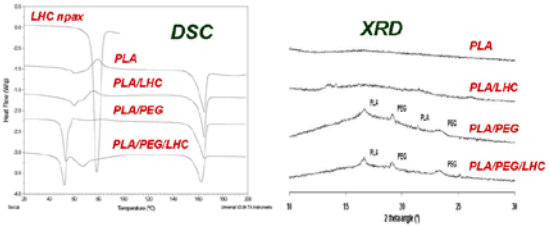
Охарактеризиране

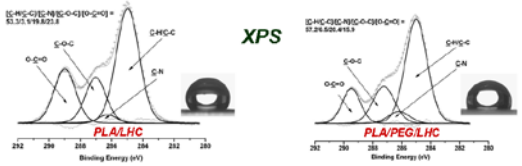
морфология



електропроводимост на разтворите

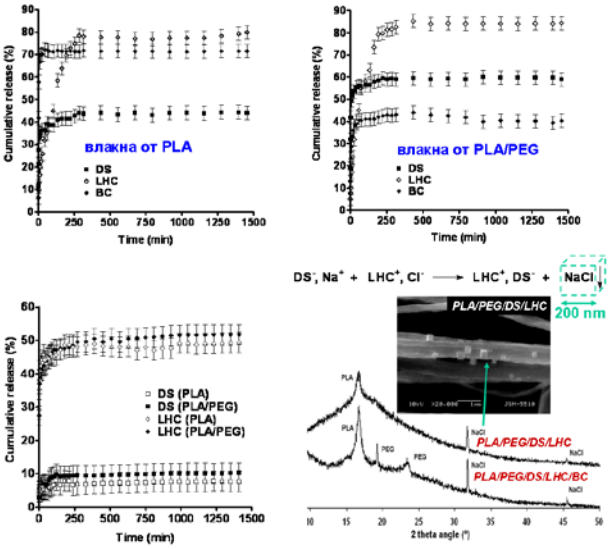




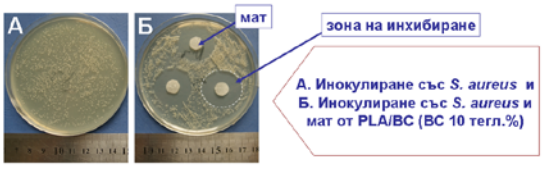


Профил на освобождаване и антибактериална активност

профил на освобождаване (pH 5.5, I = 0.1)



антибактериална активност



Заключение

Получени са микро- и нановлакнести мембрани от PLA и PLA/PEG, съдържащи лекарствени вещества (DS, LHC, BC) или техни комбинации. Самоорганизиране на влакната, съдържащи лекарствените вещества, в снопове беше постигнато при използване на многоиглен електрод. DSC и XRD анализите показаха, че в мембраните лекарствата се намират в аморфно състояние. В случая на PLA/DS, PLA/PEG/DS, PLA/BC, PLA/PEG/BC се наблюдава бърз етап на освобождаване на DS и на BC. Из PLA/LHC и PLA/PEG/LHC LHC се освобождава по-бавно вероятно поради хидрофобния характер на тези мембрани. Профилът на освобождаване на DS и на LHC от PLA/DS/LHC и от PLA/PEG/DS/LHC е различен от този от мембрани PLA или PLA/PEG, съдържащи само DS или LHC, вероятно поради йонно взаимодействие между двете соли. Мембраните, съдържащи DS, BC или техни комбинации проявяват антибактериална активност спрямо *S. aureus*.

Авторите благодарят за финансовата помощ на Национален Фонд Научни Изследвания (ДО 02-237/08)

За контакти: rashkov@polymer.bas.bg

БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ
ИНСТИТУТ ПО ПОЛИМЕРИ

ПОЛУЧАВАНЕ НА ЕЛЕКТРОПРОВОДЯЩИ НАНОКОМПОЗИТИ ЧРЕЗ ОТЛАГАНЕ НА МОДИФИЦИРАНИ ВЪГЛЕРОДНИ НАНОТРЪБИ ВЪРХУ МАКРОПОРЕСТИ КРИОГЕЛОВЕ

Георги Георгиев, Петър Петров и Христо Б. Цветанов

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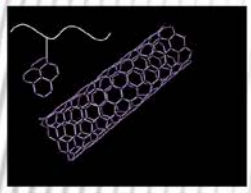
Въведение

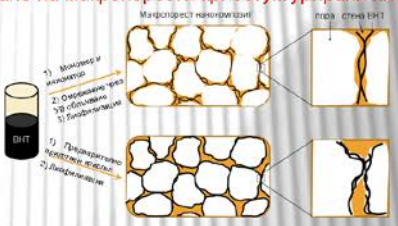
Въглеродните нанотръби (ВНТ) имат уникален набор от свойства които ги правят атрактивни за приложение в електронните устройства, дисплеи, резервоари за водород, полимерни композитни материали и т.н. Немодифицираните въглеродни нанотръби, под действието на ван дер Ваалсови сили, лесно образуват големи агломерати, което възпрепятства получаването на стабилни дисперсии и хомогенни стопилки и съществено затруднява работата с тях. Модифицирането на въглеродните нанотръби с полимери предоставя възможност за решаване на гореспоменатия проблем.

Стратегия

1. Модифициране чрез присаждане пирен съдържащ съполимер

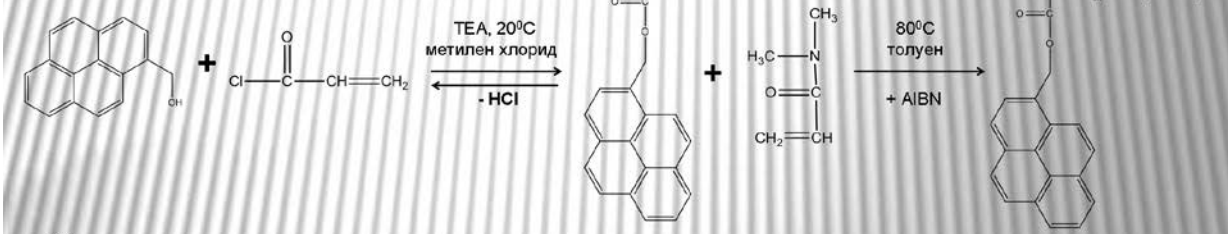


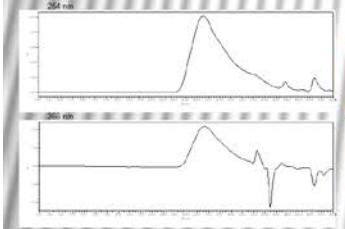
2. Получаване на макропорести криоструктурирани хибридни материали



Резултати

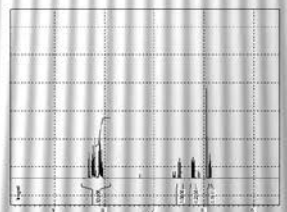
1.Синтез на пиренсъдържащ водоразтворим полимер



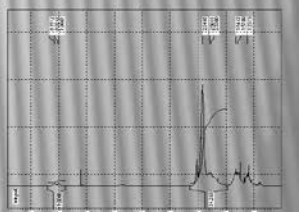


Съдържание на РуМА [мол.%]	Съдържание на ДМААм [мол.%]
2	98
6	94
10	90

Двете хроматограми, снети при дължина на вълната съответстваща на поглъщането от карбонилната група (горе) и тази съответстваща на поглъщането от пиреновата група(долу) са идентични. Следователно можем да заключим че съмономера е включен в полимерната верига



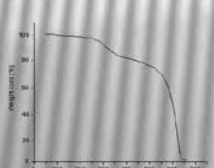
Протонен ЯМР спектър на получения мономер съдържащ пиренова група



Протонен ЯМР спектър на получения полимер съдържащ пиренова група

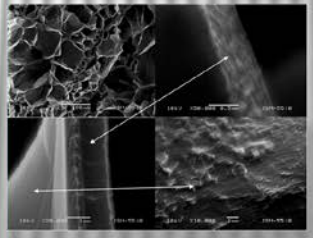
2. Получаване на стабилни водни дисперсии на ВНТ

Снимка на водни дисперсии на: вляво – немодифицирани ; вдясно – модифицирани с пиренсъдържащ полимер



ТГА крива показваща топлоустойчивостта на получения полимер спрямо въглеродните нанотръби

3. Получаване на супер-макропорести нанокомпозити



СЕМ снимка на макропорести криогелове: вляво – криогел без тръби; вдясно горе – с вградени в стените нанотръби; вдясно долу – отложени по стените нанотръби

Снимка на :
a – предварително приготвен аерогел и стъбилна водна дисперсия от модифицираните нанотръби;
b – полученият след потапяне в дисперсията с тръби хибриден материал;
c – филм от пресования хибриден материал

Material	CNTs type	CNTs [wt%]	Density (g cm^{-3})	Conductivity (S m^{-1})
HEC-spw	SWNTs	0.14	0.007	5.9×10^{-2}
HEC/PAAm-hydro	SWNTs	0.12	0.013	3.4×10^{-2}
HEC/PAAm-film	SWNTs	0.12	0.8	2.4×10^{-2}
PNIPAAm-cryo	SWNTs	0.15	0.021	4.9×10^{-2}
PNIPAAm-cryo	SWNTs	0.15	0.021	1.1×10^{-2}

Acknowledgement: This research work was supported by Bulgarian Ministry of Education and Science, Structural Funds and Educational Programs Directorate, Project "Support for the development and realization of PhD-students, post-docs and young researchers in the field of polymer chemistry, physics and engineering", **Grant 51, financed by the Operational Program "Human resources development" at the scheme BG051PO001/07/3.3-02; Projects Funded by the National Science Fund**
Center of Excellence: NATIONAL CENTER FOR ADVANCED UNION Module 2: New materials in medicine and pharmacy, ДЦВП-02/2 and Project "Ideas" ДО 02 247/18.02.08

БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ
ИНСТИТУТ ПО ПОЛИМЕРИ

ДИЗАЙН НА ПРИСПОСОБЛЕНИЯ КЪМ АПАРАТУРА ЗА ЕЛЕКТРООВЛАКНЯВАНЕ ЗА ПОЛУЧАВАНЕ НА КОАКСИАЛНИ СНОПОВЕ

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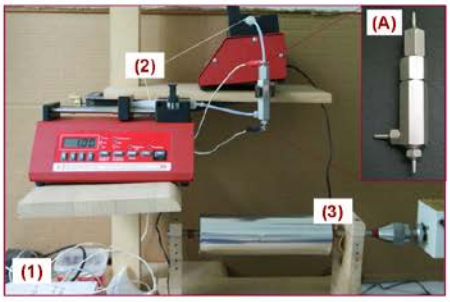
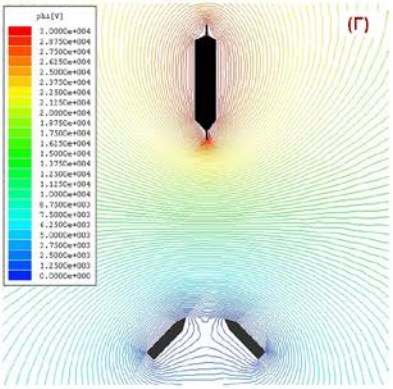
Лаборатория Биологично активни полимери, Институт по полимери – БАН

Електроовлакняването е върхова технология за получаване на непрекъснати полимерни микро- и нановлакна с дължина, достигаща до няколко метра. Класическата лабораторна апаратура включва три основни елемента: източник на високо напрежение (1), спринцовка с капиляра за подаване на предилния разтвор (2) и колектор (3), върху който се отлагат получените влакна. **Целта на изследването** е да се конструират приспособления към апаратурата за електроовлакняване за получаване на снопове от коаксиални влакна.

Дизайн на приспособления към апаратура за електроовлакняване

Беше конструирано и пуснато в действие специално приспособление "игла в игла" (А) за получаване на коаксиални влакна и два прототипа на вертикален въртящ се колектор тип "диск" с шипове (Б) и иглен (В). За да се изясни влиянието на дизайна на конструираните колектори върху траекторията на предилната струя беше използвана програмата *Ansoft Maxwell SV 2D* за теоретично симулиране на електричното поле (Г).

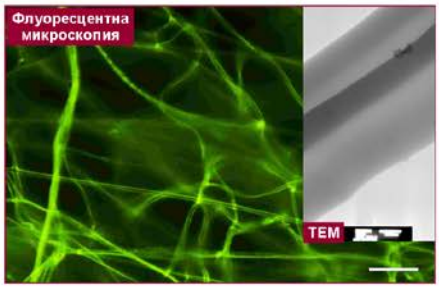


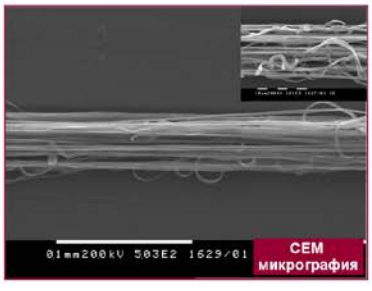


Симулациите показаха, че добавянето на шипове води до контролирано намаляване на амплитудата на камшикообразното движение на полимерната струя, осигурява стабилизирано изтегляне на струята и насочено отлагане на сноповете от влакна върху въртящия се дисков колектор.

Получаване на коаксиални снопове

Коаксиални снопове бяха получени чрез електроовлакняване при използване на приспособлението "игла в игла". За получаване на сърцевина беше използван разтвор на ПВА/Fe_3O_4 (ферофлуид), получен по зол-гел метода, а на обвивка - разтвор на поликапролактон. Условия за електроовлакняване: 35 kV, 15 cm, 1 ml/h (ядро) и 3 ml/h (обвивка).





За да покажем, че влакната са коаксиални, към разтвора на обвивката беше добавен флуоресцеин. От анализите с флуоресцентна микроскопия се вижда, че влакната са коаксиални с ясно изразена сърцевина и флуоресцираща обвивка. Сърцевината и обвивката бяха наблюдавани и с ТЕМ. Направените СЕМ анализи показват организирането на влакната в снопове, тяхната морфология и ориентация.

Благодарности

Изследванията са осъществени с финансовата подкрепа на Фонд Научни изследвания при МОМН (Договор ДО 02-237/2008).

Изводи

Намерени са подходящи условия за получаване на коаксиални снопове с включен Fe_3O_4 чрез електроовлакняване.

БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ
ИНСТИТУТ ПО ПОЛИМЕРИ

НОВИ АНТИБАКТЕРИАЛНИ ВЛАКНЕСТИ МАТЕРИАЛИ, ПОЛУЧЕНИ ЧРЕЗ МОДИФИЦИРАНЕ НА МАТОВЕ ОТ СЪПОЛИМЕРИ НА СТИРЕН И МАЛЕИНОВ АНХИДРИД С КВАТЕРНИЗИРАНИ ПРОИЗВОДНИ НА ХИТОЗАНА

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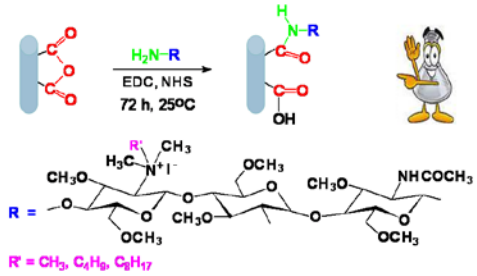
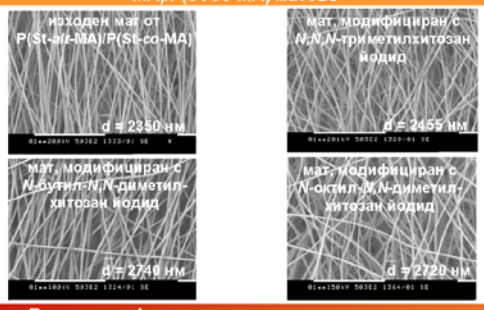
Микро- и нановлакнестите материали в последните години са обект на голям интерес, който е предизвикан от богатите възможности за тяхното практическо приложение, особено в биомедицинската област. Все повече нараства интересът към полимерите от възобновяеми източници. Такъв полимер е хитозанът - полизахарид, който притежава комплекс от ценни химически, биологични и физикохимични свойства. Ограничената му разтворимост във водна среда в някои случаи представлява ограничение за неговите приложения. Това е причина да се изследват все повече неговите водоразтворими производни, например кватернизирани N-алкилхитозани. Тяхната биоразградимост и силно антимикробно действие ги правят особено привлекателни за редица биомедицински приложения. Един от методите от особена важност при получаването на микро- и нановлакнести полимерни материали е електроовлакняването. Получаването на микро- или нановлакнести материали, които съчетават функционални синтетични полимери с кватернизирани производни на хитозана може да направи възможно получаването на материали със зададени свойства, отнасяния и функционалност, които могат да намерят приложение в редица области, като материали с антибактериална активност и с антиадхезивни свойства спрямо патогенни микроорганизми.

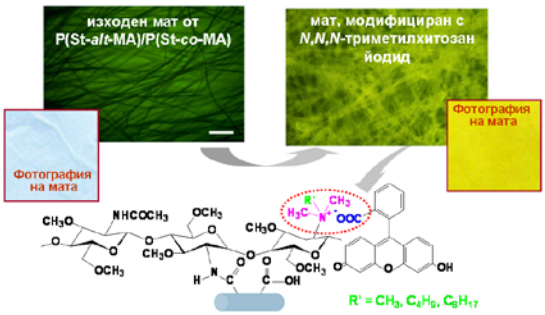
Модификация на микровлакнести P(St-*alt*-MA)/P(St-*co*-MA) матове с кватернизирани производни на хитозана (QCh)



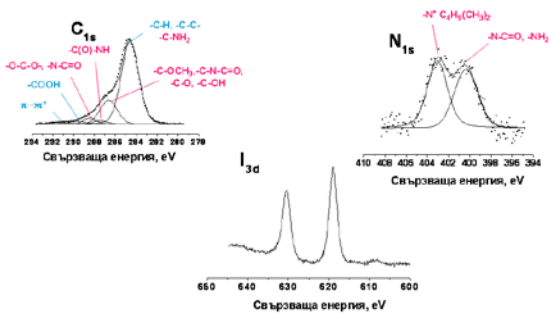
СЕМ микрографии на изходните и модифицираните P(St-*alt*-MA)/P(St-*co*-MA) матове



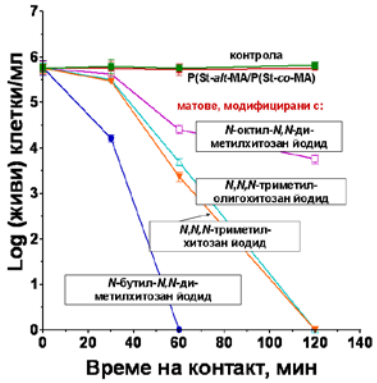
Флуоресцентна микроскопия на изходните и модифицираните матове



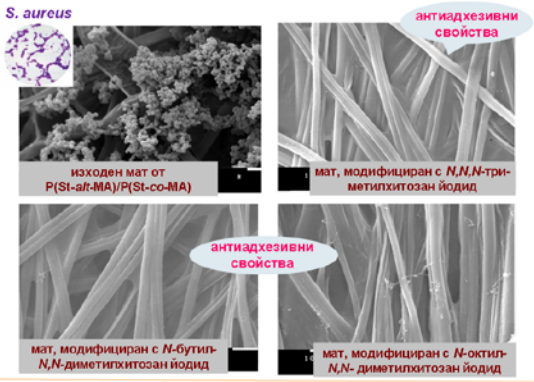
Рентгенова фотоелектронна спектроскопия на модифицираните матове



Оценяване на антибактериалната активност на модифицираните матове спрямо *E. coli*



Изследване на адхезията на *S. aureus* върху модифицираните матове



Изследванията са разработени с финансовата подкрепа на Фонд Научни изследвания (Договор ДО-02-164/2008) към МОМН

За контакти: rashkov@polymer.bas.bg; manolova@polymer.bas.bg; mil_ign@yahoo.com; janina_petkova@abv.bg

ИЗВОДИ: За първи път при меки условия и едноетапно са получени насочено модифицирани с QCh микровлакнести матове от съполимери на стирен и малеинов анхидрид. Чрез микробиологични тестове е установено, че за разлика от изходните матове, новите модифицирани матове притежават добра антибактериална активност, както и способност да понижават в значителна степен адхезията на патогенните бактерии *S. aureus*. Тези свойства правят модифицираните матове подходящи за редица приложения в медицинската практика, напр. превръзочни материали, антимикробни филтри, медицински приспособления и устройства.

Българска академия на науките

Институт по полимери

БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ
ИНСТИТУТ ПО ПОЛИМЕРИ

СТАРЕЕНЕ НА МОДИФИЦИРАНИ РЕЦИКЛИРАНИ СМЕСИ ОТ ПОЛИЕТИЛЕН НИСКА ПЛЪТНОСТ И ПОЛИПРОПИЛЕН

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ВЪВЕДЕНИЕ

Поради трудното гравиметрично разделяне на отпадъците от ПЕНП и ПП, ефективен начин за съвместното им оползотворяване и в същото време получаването на нов материал със специфични свойства се явява изготвянето на полимерни смеси. С добавянето на еластомер се подобрява адхезията и съвместимостта между двата термопластични полимери [1-4].

В зависимост от тяхната "предистория" пластмасовите отпадъци могат да се разделят на два типа: технологичен (индустриален скрап) и постконсумативен отпадък.

Процесите на стареене водят до промяна на термичните, морфологичните и механичните характеристики на пластмасите[5,6]. За да се прецени доколко рециклатите са полезни за отделни приложения е нужно да се изследва тяхното поведение при стареене.

ЕКСПЕРИМЕНТАЛНА ЧАСТ

Двойни и тройни смеси са приготвени от два типа полимерни отпадъци: технологични отпадъци (означени с ТХ) и постконсумативни отпадъци (означени с ПК) от ПЕНП и ПП опаковки. Индустриален скрап е предоставен от „Асенова Крепост" АД, Асеновград, а постконсумативен отпадък от "Унитрейд 2002" АД. Тройните смеси са получени като към базова смес ПЕНП:ПП=1:1 е добавен етилен пропилен диен терполимер (ЕПДМ)- Келтан 512 (DSM Elastomer). Концентрацията на еластомер варира от 0 до 15% и модифицираните полимерни смеси са означени съответно 7ТХ, 10ТХ, 15ТХ и 15ПК. Смесването е извършено в двушнеков екструдер Brabender DSE 35/17D при скорост на екструзия - 20 rpm и температура на стопилката в екструдера по зони: I- 175°C; II-190°C III-200 и IV- 210°C.

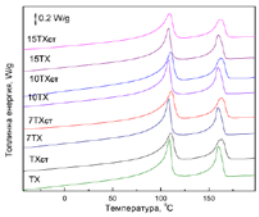
Изкуственото стареене е извършено в камера Q-sun Xenon Test Chamber (Q-panel Lab Products, UK) с времетраене 500ч при следните строго контролирани условия: сух режим-102 мин и режим на впръскване- 18 мин, интензивност (интензитет) на облъчването 0, 51 W/m² при T= 65±3°C с дестилирана вода в съответствие със стандарт EN ISO 2440.

Термичните свойства на полимерните отпадъци са определени с диференциален сканиращ калориметър TA Q100 при скорост на нагряване и охлаждане 10 °C /min.

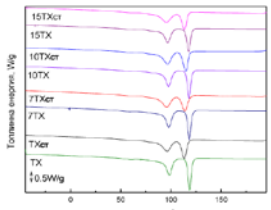
Морфологията на композитите е изучена с апарат JEOL JSM 5510 (Япония)

Якоста на опън е определена на машина "TIRATEST 2300" съгласно EN ISO 527, а якостта на удар е определена с чук на Шарпи "М 1488-4" съгласно БДС EN ISO 179 -1: 2000. Показателите представляват осреднени резултати от изпитването на пет пробни тела.

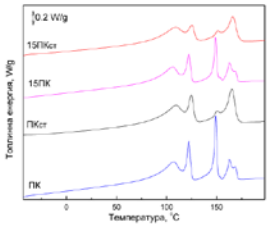
РЕЗУЛТАТИ И ОБСЪЖДАНЕ



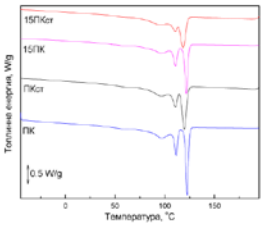
Фигура 1: ДСК термограми от второто топене на технологични смеси с различно съотношение на ЕПДМ преди и след стареене



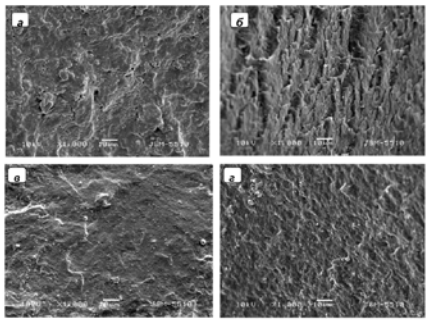
Фигура 2 *ДСК термограми от кристализация на технологични смеси с различно съотношение на ЕПДМ преди и след стареене*



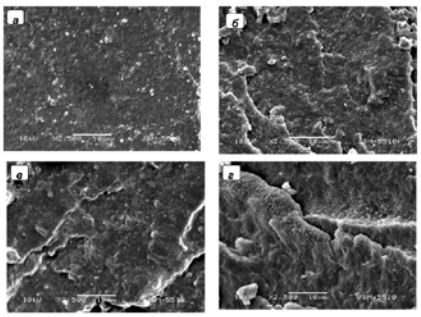
Фигура 3 . ДСК термограми от второто топене на постконсумативна смес със и без ЕПДМ преди и след стареене



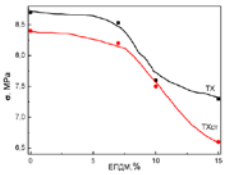
Фигура 4. ДСК термограми от кристализация на постконсумативна смес със и без ЕПДМ преди и след стареене



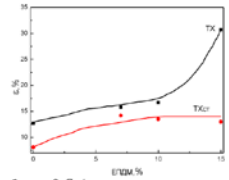
Фигура 5. Морфология на технологични смеси 1)ТХ-преди(в)и след стареене (б); 15ТХ- преди(в)и след стареене(г)



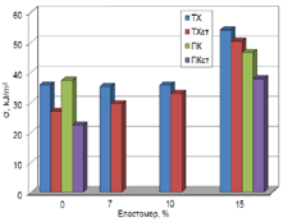
Фигура 6. Морфология на постконсумативни смеси: 1)ПК-преди(а) и след стареене(б); 2) 15ПК- преди(е) и след стареене(г)



Фигура 7: Якост на опън на смеси от технологични отпадъци с различно процентно съдържание на еластомер ЕПДМ преди и след стареене.



Фигура 8. Деформацията на смеси от технологични отпадъци с различно процентно съдържание на еластомер ЕПДМ преди и след стареене.



Фигура 9 : Якост на удар по Шарпи на вторични материали съдържащи различно процентно съотношение на еластомер ЕПДМ преди и след стареене .

ИЗВОДИ

- При съпоставяне на ДСК термограмите от кристализация и второ топене преди и след стареене се вижда че добавката на еластомер не влияе значимо върху процесите на стареене. Пиковете са по- ниски, по- широки и несиметрични на третираните образци в резултат на структурните промени. Имаме изместване на пиковете на топене на полиетилена и полипропилена към по- високите температури.
- ДСК термограмите от второ топене на постконсумативната смес показват значими структурни промени, особено по отношение на полипропилена.
- При изследване на морфологията не се наблюдават ясно отчетливи разлики като наличие на фазово отделяне или микропукнатини.
- Най- драстично се променят свойствата на опън след стареене в сместа от технологичен отпадък съдържаща15 %ЕПДМ.
- При тройните смеси в по-голяма степен се запазва якоста на удар в сравнение с двойните смеси, което е доказателство за противостарителния ефект на ЕПДМ.

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БЛАГОДАРНОСТ

Колективът изказва сърдечна благодарност за финансовата подкрепа на Министерство на Науката и Образованието чрез Договор № BG051PO001/07/3.3-02/51 и Договор ДТК-02/7.

БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ
ИНСТИТУТ ПО ПОЛИМЕРИ

ЖЕЛАТИНОВИ КАПСУЛИ И УТАЯВАНЕ НА КАЛЦИЕВИ ФОСФАТИ В ТЯХНО ПРИСЪСТВИЕ

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ВЪВЕДЕНИЕ

Зъбният емайл е най-твърдата тъкан в човешкия организъм. Неговият основен компонент е хидроксилапатита, ХА ($Ca_{10}(PO_4)_6(OH)_2$). ХА се характеризира чрез своята морфология, размер на кристалитите, чистота, стехиометрия и структура. Най-широко използваният метод за получаване на ХА е чрез утаяване в разтвор. При този метод, обаче, липсва прецизен контрол на стехиометрията, кристалността и морфологията на получения ХА. Методът е модифициран чрез добавянето на повърхностно-активни вещества, микроемулсии и мицели като шаблони.

ЦЕЛ

В настоящото изследване желатинови капсули са получени посредством ултразвуков метод – метод, чиито основни предимства са лесната работа и изключително високата чистота на получените капсули. Капсулите са използвани като среда за утаяване на калциеви фосфати в опит да се имитира естественият процес на получаване на зъбния емайл в среда от нанокапсули (20-40 nm) на естественя белтък амелогенин.

Ход на работа

0.5 тегл. % желатинов разтвор

↓ Ултразвук

Воден разтвор на желатинови капсули

↓

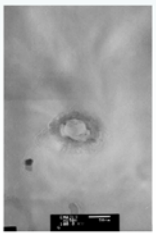
Утаяване на Са фосфат
Ca/P=1.74
(0.37 M $CaCl_2$ + 0.29M K_2HPO_4)
pH=10.5
(с 1M KOH)

↓

Охарактеризиране

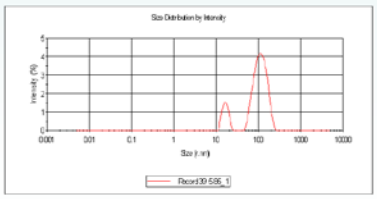
Охарактеризиране на получените желатинови капсули

Трансмисионна електронна микроскопия



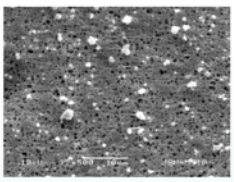
Фиг 1. ТЕМ на желатинови капсули, получени при 90% амплитуда.

Динамично лазерно светоразсейване

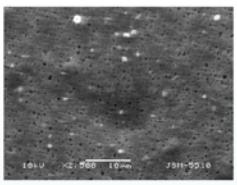


Фиг 2. ДЛС на желатинови капсули, получени при желатинова концентрация 0.5 тегл.% за 3 мин. обработка с ултразвук.

Сканираща електронна микроскопия



Фиг 3. Желатинови капсули, получени при 20% амплитуда.



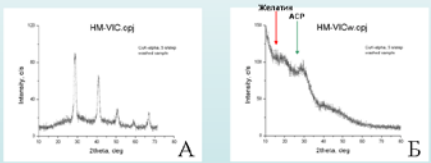
Фиг 4. Желатинови капсули, получени при 90% амплитуда.

Извод

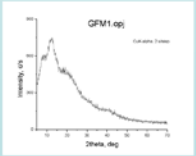
При сонифициране при 20% амплитуда се получават 120 частици за 0.002mm², а при сонифициране при 90% амплитуда- 45 частици за 0.002mm². При 90% амплитуда се получава бимодално разпределени с два средни размера ~18 nm и 180 nm.

Охарактеризиране на калциевите фосфати, получени в присъствие на желатинови капсули

Рентгеноструктурен анализ

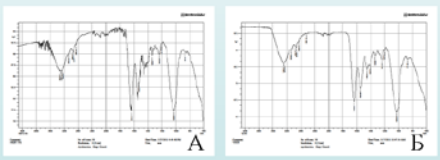


Фиг 5. Дифрактограма на калциеви фосфати: (А) без измиване; (Б) след измиване на KCl.

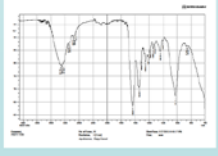


Фиг 7. Дифрактограма на чист желатин

Инфрачервена спектроскопия



Фиг 6. ИЧ спектър на калциеви фосфати: (А) без измиване; (Б) след измиване на KCl



Фиг 8. ИЧ спектър на калциеви фосфати, след 2 дни "зреене".

Заключение

Желатинови капсули, получени чрез ултразвуков метод, са използвани за пръв път като среда за кристализация на калциеви фосфати. При кристализация, проведена при pH=10.5, без "зреене", според данните от ИЧ спектроскопията и рентгенографския анализ, се получава аморфен калциев фосфат (ACP), а след 2 дни "зреене" се наблюдава начало на кристализация. ACP е прекурсор на ХА, който е естествиия градивен елемент на зъбния емайл. Преходът ACP→ХА се осъществява след "зреене" на ACP във водна среда.

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