

Пета постерна сесия

„Младите учени в света на полимерите“

организирана в рамките на
проект POLINNOVA “Укрепване на научноизследователския капацитет и
иновационен потенциал на ИП към БАН” по 7РП

и

проект „Изграждане на научния потенциал за устойчиво кариерно развитие на
младите учени, докторанти и постдокторанти в приоритетни области на
полимерната наука“

по схема за предоставяне на безвъзмездна финансова помощ: Подкрепа за
развитието на докторанти, постдокторанти, специализанти и млади учени, ЕСФ,
МОН, ОП “Развитие на човешките ресурси” 2007-2013



5 юни 2014 г.
Институт по полимери, БАН
гр. София

ПЕТА ПОСТЕРНА СЕСИЯ
„МЛАДИТЕ УЧЕНИ В СВЕТА НА ПОЛИМЕРИТЕ“

организирана от Институт по полимери – БАН

в рамките на

проект POLINNOVA *“Укрепване на научноизследователския капацитет и иновационен потенциал на ИП към БАН” по 7РП*

и

проект *„Изграждане на научния потенциал за устойчиво кариерно развитие на младите учени, докторанти и постдокторанти в приоритетни области на полимерната наука“*

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5 юни 2014 г.

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Електроовлакнени матове от поли(L-млечна-съ-D,L-млечна киселина) с включен куркумин: получаване и свойства

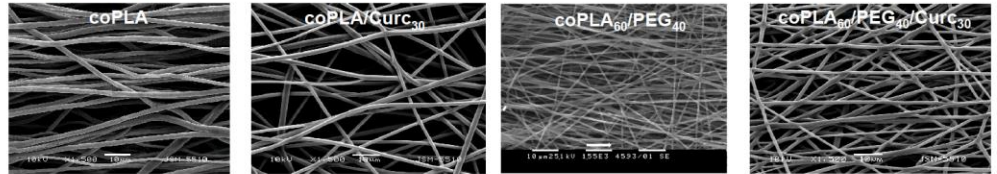


Гюлджан Якуб, Антония Тончева, Невена Манолова, Илия Рашков,
Лаборатория Биологично активни полимери, Институт по полимери – БАН

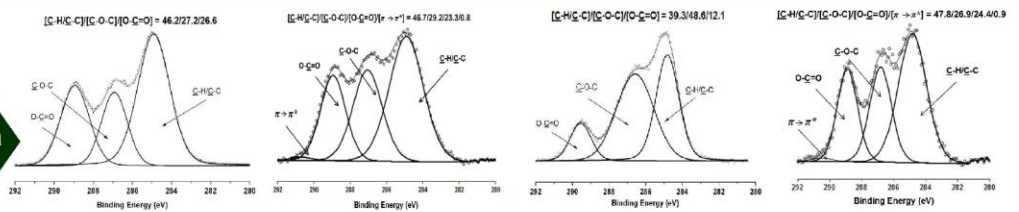
ЦЕЛ

Получаване и охарактеризиране на влакнести материали от поли(L-млечна-съ-D,L-млечна киселина) (coPLA) и полиетиленгликолу (PEG), съдържащи различни количества куркумин (Curc). Изследване на влиянието на състава на полимерната матрица върху някои свойства на влакната.

СЕМ микрографии на получените матове

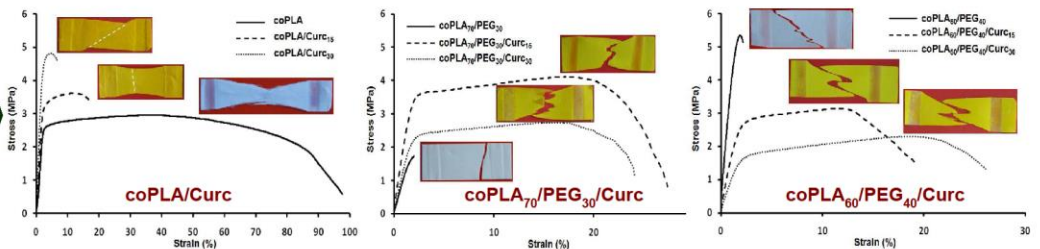


Рентгенова фотоелектронна спектроскопия

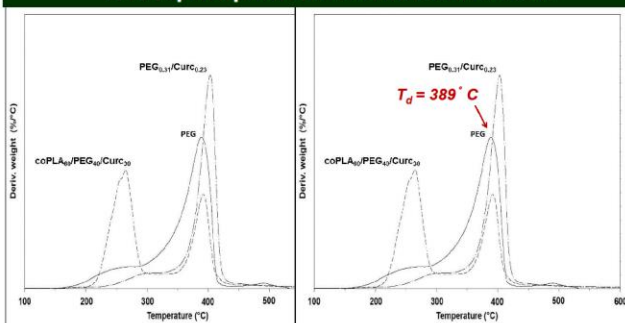


Повърхността на влакната е обогатена на въглеродни атоми, участващи в етерна връзка

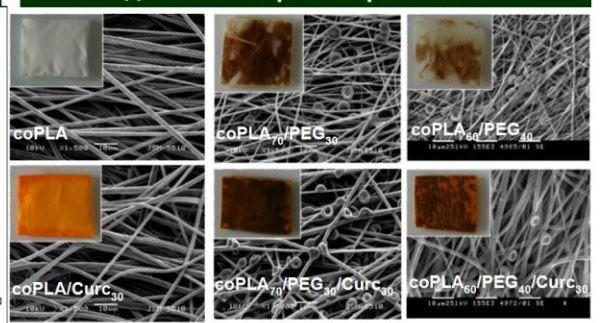
Физико-механични изпитания на влакнестите материали



TGA термограми на влакна и на смеси



Адхезия на червени кръвни клетки



Антиоксидантна активност на матовете

Антиоксидантната активност на матовете, съдържащи куркумин, е оценена спектрофотометрично при отчитане на абсорбцията (при 513 nm), характерна за радикала 2,2-дифенил-1-пикрилхидразил (DPPH•). След 30 мин. контакт на разтвора на DPPH• с матовете от coPLA/Curc₃₀, coPLA₇₀/PEG₃₀/Curc₃₀ и coPLA₆₀/PEG₄₀/Curc₃₀, абсорбцията на DPPH• се понижава с 71-72%, което показва, че Curc проявява антиоксидантната си активност.

ИЗВОДИ: Куркуминът повишава термичната стабилност на PEG. Повърхността на матовете от coPLA, coPLA/Curc и coPLA/PEG/Curc е обогатена на C-H/C-C връзки, което обяснява и хидрофобните им отнасяния. Пълно хидрофилизиране на матовете с включен куркумин се постига при добавяне на по-голямо количество PEG. Включването на PEG във влакната води до получаване влакнести материали с по-добри механични показатели. При контакт на матовете coPLA/Curc₃₀ с пълна кръв не се наблюдава адхезия на червени кръвни клетки. Адхезията на еритроцитите върху влакната, съдържащи PEG се дължи на взаимодействието му с тях.

Благодарности

Г.Я. благодари на договор "Полинова" за финансовата помощ и на д-р Добри Данчев (Военномедицинска академия) за възможността за провеждане на тестовите с кръв.



Polyphosphoesters Bearing Aminophosphonate Units: Synthesis and Biological Activity

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The synthesis of poly(oxyethylene aminophosphonate)s and poly[oxyethylene(aminophosphonate-co-H-phosphonate)s] through an addition of poly(oxyethylene H-phosphonate)s to Schiff bases: N,N-dimethyl-N'-furfurylidene-1,3-diaminopropane (**3**), N-furfurylidene-p-toluidine (**4**), N-(4-dimethylaminobenzylidene)-p-toluidine (**5**) and 9-anthrydine-p-toluidine (**6**), respectively, is reported.

Chemistry

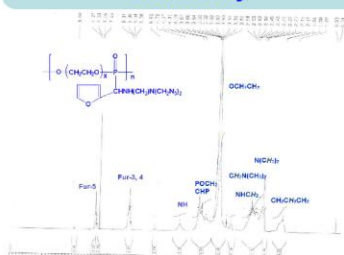


Figure 1. ¹H NMR spectrum of poly(aminophosphonate) obtained from **3**: x=4, n=18.

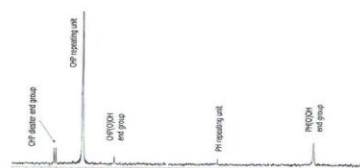


Figure 3. ³¹P{¹H} NMR spectrum of polyphosphoesters bearing aminophosphonate units (90%).

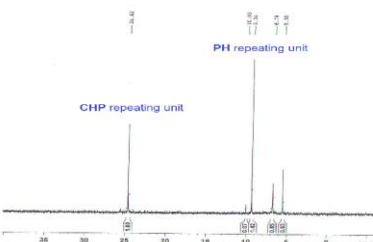
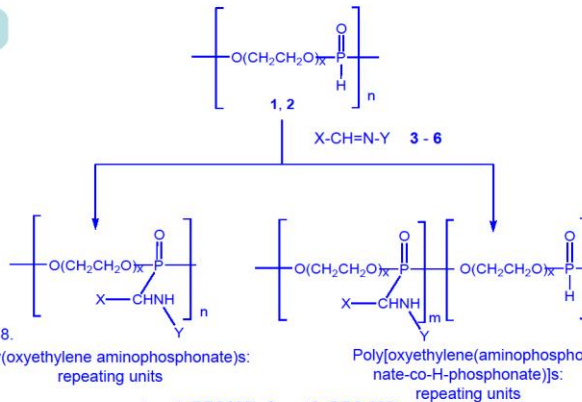


Figure 4. ³¹P{¹H} NMR spectrum of polyphosphoesters bearing aminophosphonate (43%) and H-phosphonate units.

Biological Activity

Table 1. Cytotoxic effects of the aminophosphonates the clinically applied antineoplastic drug cisplatin, as assessed by the MTT-dye reduction assay after 72 h continuous exposure.

Polymers	x	IC ₅₀ (μmol/L)			
		HL-60 ^a	HL-60/Dox ^{a,c}	LAMA-84 ^a	K-562 ^b
	4	105.9	> 400.0	> 400.0	> 400.0
	13	19.2	27.2	17.2	14.9
	4	19.9	20.4	14.0	15.2
	13	14.2	14.4	12.3	13.7
	4	157.5	159.1	88.8	62.3
	13	66.2	16.2	41.9	18.3
Cisplatin		7.8	14.5	18.2	25.7



1: x=4 (PEG200); 2: x=13 (PEG 600)

3: X = , Y = -(CH₂)₃N(CH₃)₂

4: X = , Y =

5: X = , Y =

6: X = , Y =

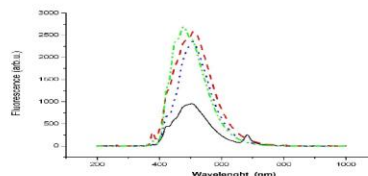


Figure 5. Fluorescence spectra of polymers and copolymers bearing anthracene derived aminophosphonate units in DMSO (λ_{EX}=375 nm).

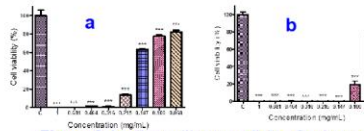


Figure 6. In vitro antitumor activity of polymer **6** (a) and **7** (b) against 647-V cell.

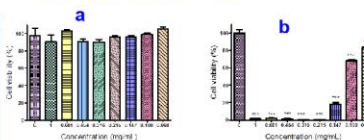


Figure 7. Cytotoxicity of **6** (a) and **7** (b) on BALB/c 3T3 cell line.

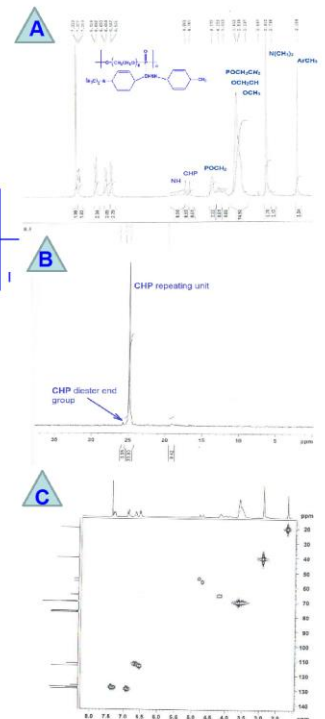


Figure 2. ¹H (A), ³¹P{¹H} (B) and HSQC (C) NMR spectra of poly(aminophosphonate) obtained from **5**: x=4, n=18

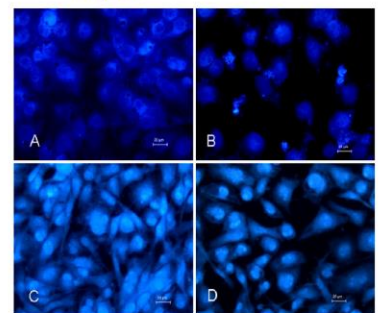


Figure 8. Fluorescence microscopy of subcellular distribution of copolymer **6** in Balb/c 3T3 (clone 31) cells (A), HepG2 cells (B), HBL-100 cells (C) and MDA-MB-231 cells (D) after 24 h treatment (A and C) and 72 h treatment (B and D).

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PULP POST BLEACHING WITH XYLANASE AND PEROXIDE COMPOUNDS

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The main object of bleaching is to remove the incrusting substances and thus obtain a pure white product, therefore, the manufacturing requires a further delignification and bleaching of the fibres. Residual lignin is a major contributing factor in colour. The bleaching process must be carried out as gently as possible, so that the carbohydrate is not attacked. The target brightness cannot be achieved in only one bleaching step without sacrificing pulp strength. Therefore pulp is bleached in several steps, and the pulp is washed between them. The resulting pulp after ECF and TCF bleaching not always has sufficient brightness, which decreases during storage. That requires the application of post bleaching stage for improve the pulp brightness.

The purpose of this work is an investigation into hydrogen peroxide, peracetic acid, tetra acetyl ethylene diamine (TAED) and xylanase treatment as a final stage in pulp bleaching.

Pulp post bleaching optimal conditions

The hardwood kraft pulp has been bleached in the Svilcoell EAD in Bulgaria by the O D₀ Eop D₁ sequence.

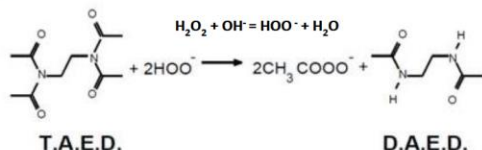
Xylanase (X): T 60° C; pH 8 – 9; charge 0.05 - 0.20%; pulp consistency 10%; 90 min.

Hydrogen peroxide (P): T 80° C; pH 10.8 - 11.2; charge 0.05 - 0.20%; pulp consistency 10%; 90 min.

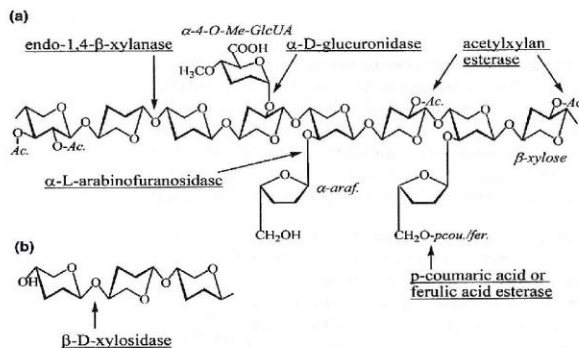
Peracetic acid (Paa): T 70° C; pH initial 5.1 - 11.2; pH final 4.0 - 9.7; charge 0.05 - 0.20%; pulp consistency 10%; 90 min.

Tetra acetyl ethylene diamine (TAED): T 60° C pH initial 7 - 8, charge Paa 0.2%, 60 min.

Dry ageing was carried at 0 % relative humidity in a dedicated forced air circulation oven with excess oxygen at 105 ° C for 4 h according to UM 200, tappi.



Reaction mechanism of H₂O₂ and TAED



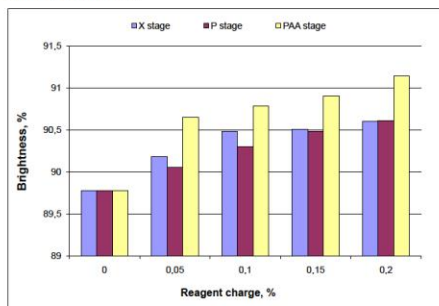
(a) Structure of xylan and the sites of its attack by xylanolytic enzymes. The backbone of the substrate is composed of 1,4- b-linked xylose residues. Ac., Acetyl group; a-araf., a-arabinofuranose; a-4-O-Me-GlcUA, a-4-O methylglucuronic acid; pcou., p-coumaric acid; fer., ferulic acid. (b) Hydrolysis of xyloligosaccharide by beta-xylosidase.

Pulp post bleaching with xylanase and peroxide compounds

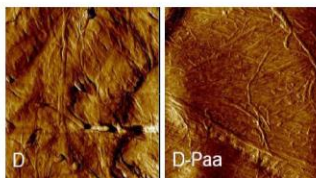
The comparison of the results of pulp post bleaching with xylanase, peracetic acid and hydrogen peroxide shows that the greatest effect on pulp brightness is achieved by the peracetic acid treatment.

The application of Paa not only cleans the fibre surface, but also eliminates microbes and reduces the chemicals consumption in papermaking.

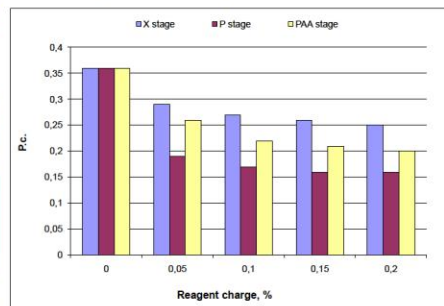
The peroxide treatment leads to lowest P.c. number, but the selectivity of the pulp bleaching with this reagent is lowest, too.



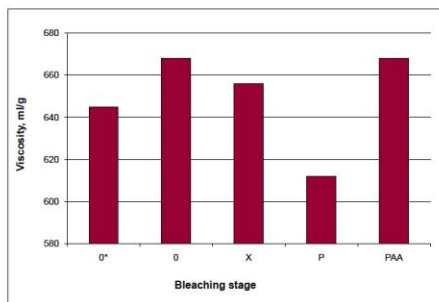
Effect of the reagent type and charge on the pulp brightness.



Surface images taken with Atomic Force Microscope (microscope with high resolution, wide - 2µm x 2µm)



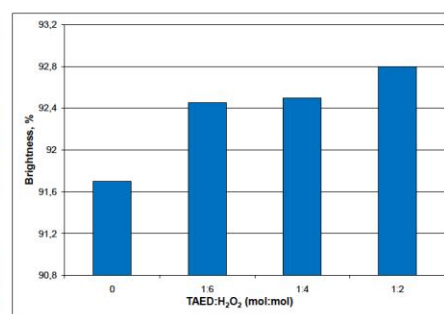
Effect of the post bleaching on the pulp P.c. number.



Effect of the post bleaching on the pulp viscosity (0* - initial pulp, 0 - 90 min. treatment without reagents, optimal conditions and reagents charge 0.20%).

The peroxide proves to be relatively most non-selective, an indicator of which is the established decrease of pulp viscosity. The peracetic acid and xylanase practically do not affect the cellulose under the applied conditions of the last bleaching stage.

The application of pulp post bleaching does not require additional capital investment, and the effect achieved justifies the expense for bleaching reagents.



Effect of TAED:H₂O₂ ratio on the pulp brightness



Synthesis of Poly(alkylene Amidophosphate)s via Staudinger Reaction

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 1113 Sofia, Bulgaria



Introduction

Biopolymers (Nucleic Acids, Proteins, Carbohydrates, Lipids) are organic biodegradable polymers, produced by living organisms. Since they make up much of human bodies and the majority of the biosphere, it is safe to say that *Life depends on polymers*.

Well-defined Poly[alkylene trimethylsilylphosphite(III)]s were prepared for the first time via silylation of Poly(oxyethylene H-phosphonate)s with N,O-bis(trimethylsilyl)acetamide or trimethylsilyl chloride. They were applied as a precursor in a chemoselective STAUDINGER-POLYPHOSPHITES REACTION for the synthesis of **Polyphosphoramides**.

Purpose

For a better understanding of the vital role biopolymers play in nature, polymers with structures and functions complementary to those in nature (**GLYCOPOLYMERS**) are synthesized.

GLYCOPOLYMERS (synthetic sugar-containing polymers) possess a wide range of biological recognition properties and can mimic the multivalent effect seen in nature. Inspired by the most important biopolymers, this study aims to develop a new method for the preparation of **Multivalent Carbohydrate-Polyphosphoramidate-Conjugates** (Pic. 1)

Specific Objectives:

- Use a biocompatible, highly reactive, water soluble precursor;
- Synthesis of a novel polymers with a well-defined structure and phosphate ester backbone;
- Functionalization of the novel polymers with different carbohydrate ligands;
- Achieving a non-expensive and simple method
- Mild conditions of the reaction.

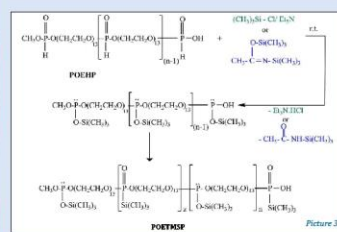
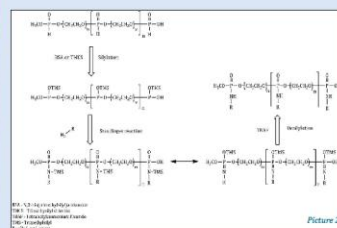
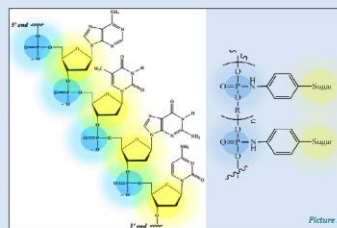
HOW? (Pic. 2)

Methods

MOST KNOWN SYNTHETIC PROTOCOLS	STAUDINGER REACTION between azides and trivalent phosphorus species
<ul style="list-style-type: none"> acid lability of the P(RO)-NH bond harsh reaction conditions involve protection of nucleophilic side chains and their removal 	<ul style="list-style-type: none"> convenient synthetic route under acid-free conditions mild reaction conditions does not require the protection of nucleophilic side chains

- The polymeric H-phosphonates were synthesized via a polytransesterification reaction of dimethyl H-phosphonate and poly(ethylene glycol) (PEG 600).
- The structures of the compounds were studied by MS and NMR (¹H, ¹³C and ³¹P) spectroscopy.

Tools



Picture 1: DNA structure vs. Sugar-Polyphosphoramidate-Conjugates.

Picture 2: Staudinger-Polyphosphite reaction protocol.

Picture 3: Silylation of POEHP with TMCS or BSA.

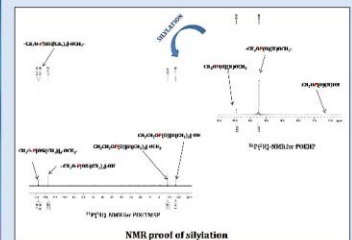
Results

- Silylation with **TMCS** or **BSA** (Pic. 3)

Degree of conversion of POEHP into POETMSP with **TMCS** after 0.5h (molar ratio POEHP:TMCS=1:4) – 100 %

Degree of conversion of POEHP into POETMSP with **BSA**, %:

Time, h	Molar ratio POEHP:BSA		
	1:1	1:2	1:4
1	70.22	NA	100
2.5	88.28	100	NA
4	11.92	10.04	15.92
24	24.02	NA	NA

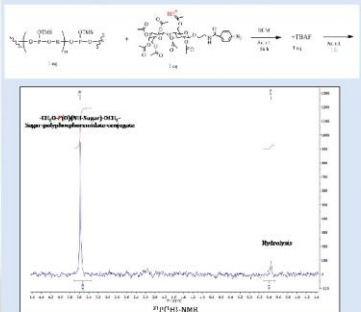


- Staudinger reaction with Aryl and Alkyl Azides:

Alkyl azide	Aryl azide	Conversion (According to ³¹ P{H} NMR)	+TRAF	
Benzyl azide	Phenyl azide	Full 5.28 ppm	5.37 ppm (90%)	
Dodecyl azide	4-nitrophenyl azide	Full 1.47 ppm	5.39 ppm (98%)	
3-phenyl propyl azide	Phenyl azide	Full 5.02 ppm	3.39 ppm (-84%)	
The results were un satisfactory (lower yields, a lot of byproducts!)		p-Azidobenzoic acid	Full 4.41 ppm	2.70 ppm (-65%)

SS: 1:1 POEHP:Phosphite-Azide; TMCS; Ac. Et. 1h
 Trifluoromethane; 1:1 PEG-TMCS; Ac. Et. 1h

- Staudinger reaction with Sugar Azides:



Acknowledgement

Financial support of this work was provided by the NSF of Bulgaria (National Center for Advanced Materials (UNION) Module 2 "New Materials for Medicine and Pharmacy" Grant: DCVP 02-2/2009), the Ministry of Education and Science (BG051PO001/3.3-06 Operational Program "Human Resources Development") and by the Bulgarian Academy of Sciences. Thanks also due to POLINNOVA GA No 316086 and Leibniz-Institut für Molekulare Pharmakologie im Forschungsverbund Berlin e.V. (FMP, AG Hackenberger).

The fifth poster session "Young scientists in the world of polymers", IP-BAS, 5 June 2014, Sofia, Bulgaria

ANTIBACTERIAL ACTIVITY OF WELL-DEFINED CATIONIC COPOLYMERS OBTAINED VIA AQUEOUS ATRP OF 2-(ACRYLOLOXY)ETHYL TRIMETHYLAMMONIUM CHLORIDE

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INTRODUCTION

Water-soluble polycations have been investigated for various technical and biomedical applications. Among different classes of polycations, the quaternary ammonium compounds are the most effective germicides and hence find wide application in the field of biomaterials and smart surfaces. For biomedical applications such polymers have been used as micro- and nanosized drug carrier systems and are known to show excellent antimicrobial properties.¹

A series of well-defined linear copolymer were obtained. The chemical structure and copolymer composition were analyzed through ¹H-NMR, FTIR and size exclusion chromatography (SEC).

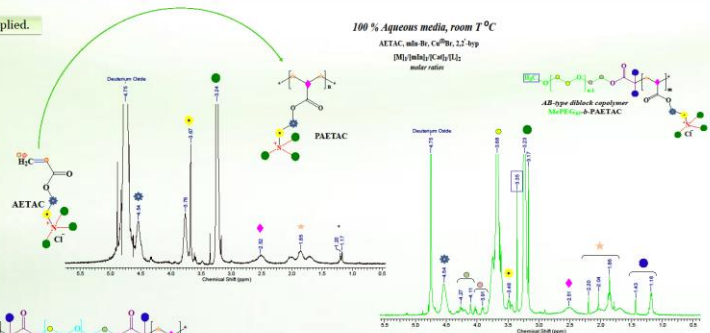
Polymer synthesis and characterization

In this work, the synthesis of cationic polyelectrolytes of various copolymer compositions by means of atom transfer radical polymerization (ATRP) was studied. The ATRP polymerization in aqueous media of [2-(acryloyloxy)ethyl trimethylammonium chloride, AETAC] was applied and investigated.

As initiators, mono- and difunctional poly(ethylene glycol)s were applied.

AETAC based copolymers obtained via aqueous ATRP	Type and macromolecular architecture of the copolymer	Reaction time [r. h]	Average M _n (PDI)	Average M _w (PDI)	Dispersity ^a [g/mol]
PAETAC	homopolymer	24	3 100	2 400	1.86
MePEG ₄₅ -b-PAETAC	diblock copolymer	24	4 000	1 100	1.23
PAETAC-b-PEG ₄₅ -b-PAETAC	triblock copolymer	24	4 500	1 400	4.84

^aQuaternary PAETAC and its block copolymers were characterized by aqueous SEC



DLS/Zetasizer measurements

Solution properties and aggregation in aqueous media were followed by DLS and ζ-potential measurements as a function of pH and temperature.

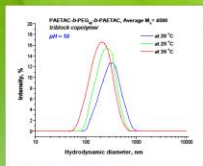


Figure 3. Aggregation behavior of the obtained PAETAC-b-PEG-b-PAETAC block copolymer at pH 10

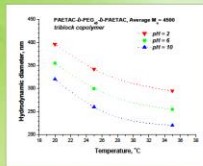


Figure 2. Aggregation behavior of the obtained PAETAC-b-PEG-b-PAETAC block copolymer as a function of the T°C

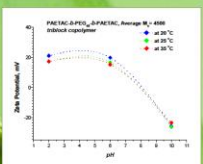


Figure 4. Zeta-potential alteration of the obtained PAETAC-b-PEG-b-PAETAC block copolymer as a function of the T°C and pH

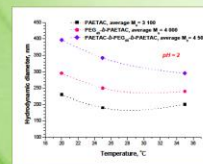


Figure 5. Aggregation behavior of the obtained copolymers as a function of the T°C at pH 2

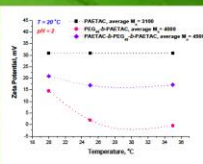
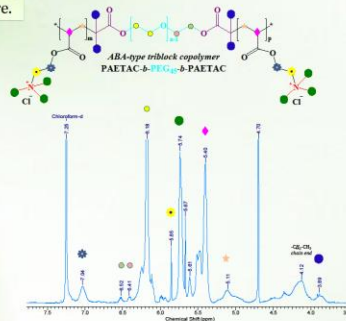


Figure 6. Zeta-potential alteration of the obtained copolymers as a function of the T°C at pH 2



Antibacterial activity investigations

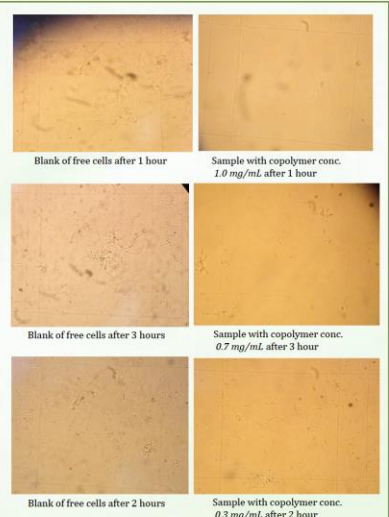


Figure 8. Antibacterial activity of the obtained PAETAC-b-PEG-b-PAETAC block copolymer

The antibacterial activity of the PAETAC block copolymers was determined against the Gram-positive bacteria *Arthrobacter oxydans* 1388 through a viable cell counting method.

The amount of the microbial cells in a 1 cm³ of the test suspension was calculated through the following equation:

$$M = \frac{\alpha \cdot 10^5}{(h \cdot S) \cdot D}$$

M – number of cells in a 1 cm³ suspension;
 α – average number of cells in the network;
 h – counting camera depth, mm, 0.1 mm;
 S – the square area of the network in mm² (small square = 1/400 mm²);
 D – conversion factor of mm³ in 1 cm³;
 D – dilution of the test suspension.

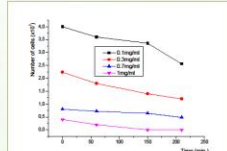


Figure 9. Antibacterial activity of PAETAC-b-PEG-b-PAETAC against *Arthrobacter Oxydans* Strain 1388

In vitro bacterial activity study demonstrated a significantly reduced number of *Arthrobacter Oxydans* Strain 1388. This indicating that the obtained copolymers possessed a good antibacterial activity. As a prove of that is the low proliferation observed. The minimal inhibition concentration of the obtained triblock copolymer PAETAC-b-PEG-b-PAETAC was estimated to be up to 0.7 mg/mL.

CONCLUSIONS

The systematic investigations on the solution properties of the synthesized copolymers and their aggregation in aqueous media as well as the investigated antibacterial activity of the new developed polycations renders their potential application in the biomedical fields such as smart drug delivery carriers, scaffolds for tissue engineering, sensors, etc.

FUTURE WORK

This investigation will be continued in order to establish the minimal inhibition concentration against Gram-negative *Pseudomonas* species bacteria.

References

1. N.K. Goel, Ravijoshi, YK.Bhardwaj, L.Varshney; Role of radiolytically generated species in polymerization of [2-(acryloyloxy)ethyl]trimethylammonium chloride (AETC) in aqueous medium: Steady state and pulse radiolysis study, *Radiation Physics and Chemistry*, **92** (2013) 66–70

Acknowledgments

The presentation of the results at the fifth poster session "Young scientists in the world of polymers", IP-BAS, 5 June 2014, Sofia, Bulgaria is funded by the EU project "Building of scientific potential for sustainable career development of young researchers, PhD-students and post-docs in the field of polymer science" granted by the Operational Program "Human resources development" 2007-2013, ESF (Contract BG051P0001-3.3.06 – 0017)



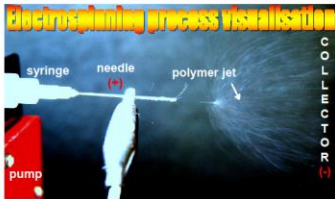
Electrospun drug containing poly(lactic acid) (PLA) fibrous materials for biomedical application



Antoniya Toncheva, Dilyana Paneva, Nevena Manolova, Iliya Rashkov
 Laboratory of Bioactive Polymers, Institute of Polymers, Bulgarian Academy of Sciences

Production of novel microfibrillar materials from poly(L-lactic acid) (PLLA) and poly(L-lactic-co-D,L-lactic acid) (PDLLA) containing ionogenic bioactive substances by electrospinning. Improvement of the electrospinning setup for individual fiber self-organization into bundles. Demonstration of some potential applications of the novel fibrous materials.

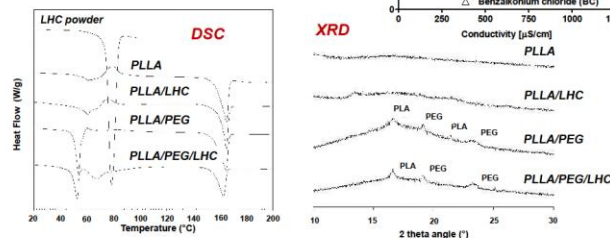
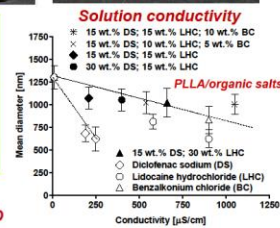
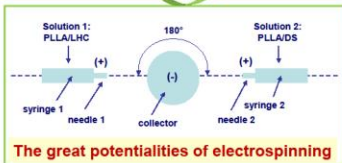
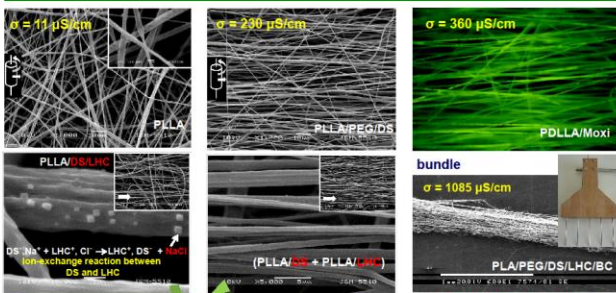
Electrospinning



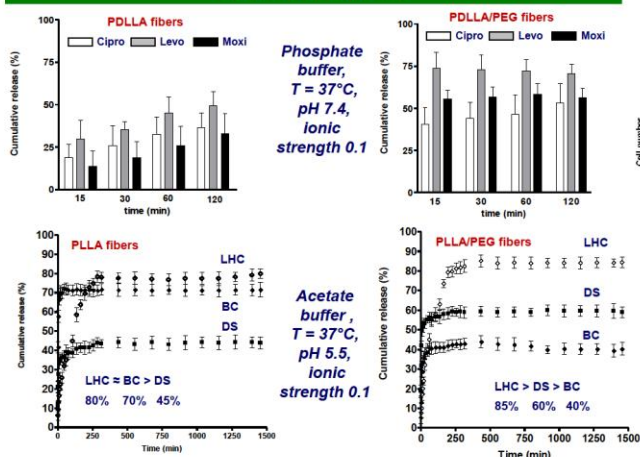
Electrospinning: a fascinating method for the preparation of micro- and nanofibrous materials

Micro- and nanofibers: high specific surface area and highly porous structure, easy to manipulate, diverse morphology

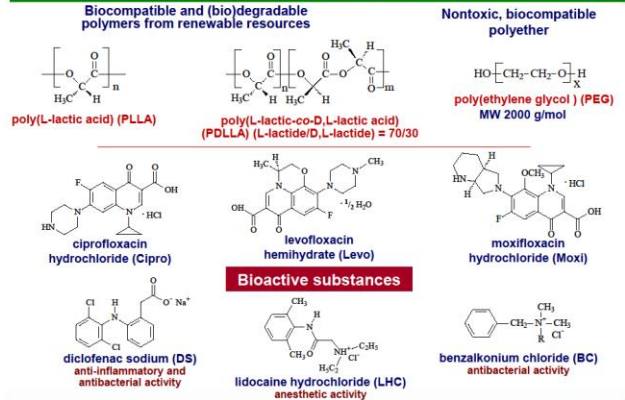
SEM, fluorescence microscopy, solution conductivity, DSC and XRD



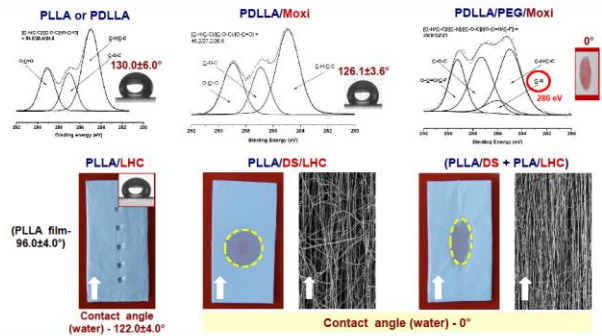
Drug release profile



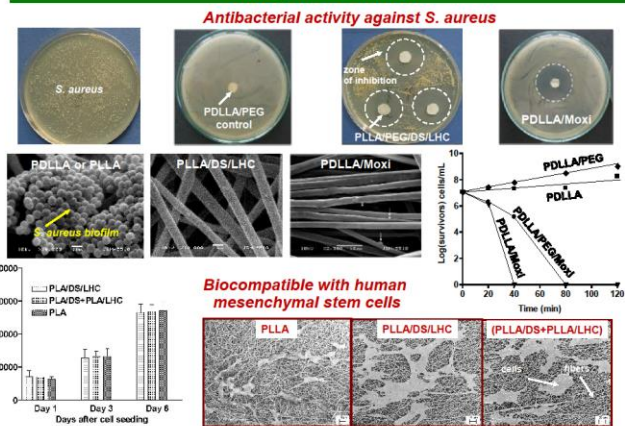
Polymers and bioactive substances



XPS and contact angle



Biological behavior



Conclusion

- The present contribution is the first report on the preparation of materials based on PDLLA or PDLLA/PEG - containing highly efficient fluoroquinolone antibiotics Cipro, Levo or Moxi, by electrospinning;
- Micro- and nanofibrous electrospun membranes from PLLA and PLLA/PEG containing drugs (DS, LHC, BC) with anti-inflammatory, anesthetic and antibacterial properties have been developed;
- It was found that the polymer matrix composition (PLLA, PLLA/PEG, PDLLA or PDLLA/PEG) and the nature of the biologically active substances influence the drug's release profile;
- Tuning of the solution conductivity is used as an original approach to induce micro- and nanofibers self-organization into bundles, in a way that the selected drugs increase the solution conductivity by themselves;
- Microbiological studies have demonstrated that the PLLA and PDLLA membranes, containing antibiotics - Cipro, Levo, or Moxi, DS or BC exhibit antibacterial activity against *S. aureus*. The drug-loaded PLLA, PLLA/DS/LHC and (PLLA/DS+PLLA/LHC) mats are compatible with human mesenchymal stem cells.

References: Toncheva A., Spasova M., Paneva D., Manolova N., Rashkov I., Poly(lactide) (PLA)-based electrospun fibrous materials containing ionic drugs as wound dressing materials: A review, *Int. J. Polym. Mater. Polym. Biomater.*, 2014 63: 657-671

Some of the results were presented at the European Polymer Congress EPF 2013, June 16-21, 2013, Italy

Contact: rashkov@polymer.bas.bg



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An environmentally friendly extraction technique: Application to amides

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Abstract

1

In the 21st century, one of the missions of green chemical engineering is to promote innovative technologies that reduce or eliminate the use of organic solvents. Supercritical fluid extraction (SCFE) is a typical example of a sustainable technology which applies cheap, non-flammable, non-explosive, non-toxic and easily accessible solvents as carbon dioxide and can thus have wide applications in chemical and biochemical engineering, food and pharmaceutical industries. To model, design and optimize a SCFE process knowledge of the solubility of substances in supercritical CO₂ (SC CO₂) is essential.

Introduction

2

Primary amides can act as model systems for the study of complex biochemical systems as peptides and proteins in solutions. The particular importance of those components is that they have an amide bond, similar to the essential bond between amino acids in proteins and are used as a starting material in the synthesis of many other organic compounds. Propionamide is a key intermediate in the synthesis of hydroxamic acid and of different drugs with a strong hypnotic effect.

This study is devoted to the experimental measurement of the solubility of butanamide in SC CO₂. All experiments were carried out at the Chemical Engineering and Biotechnology Research Center, Lisboa, Portugal. To correlate the solubility of butanamide we applied the Soave-Redlich-Kwong cubic equation of state (SRK EoS) with the two-binary interaction-parameter-per-pair version of the van der Waals one fluid mixing rule. Furthermore, those of the properties of butanamide, which are not available but are required for the modeling, were estimated and reported.

To the best of our knowledge, the solubility of butanamide in SC CO₂ hasn't been investigated previously and no such data is available in the open literature.

Materials and Methods

3

The supercritical fluid extraction experiments were performed in a flow apparatus. This equipment allows carrying out studies at a temperature up to 120°C and a pressure up to 60 MPa. The equipment and the scheme of the experiments are shown on Figure 1 and Figure 2, respectively.



Figure 1 – The equipment

Figure 2- Scheme of the supercritical fluid extraction apparatus. G, CO₂; C, compressor; E, extractor; S, separator; BP, back-pressure regulator; MMV, micrometer valve; MV, flow meter; Tot, totalizer; TI, temperature indicator; PT, pressure indicator.

The liquid CO₂ flowing from the cylinder was compressed to the desired pressure into the extraction vessel, which is heated. Then CO₂ was passed through a bed consisting of a sequence of glass spheres, propylene wool, and the sample. The total volume of CO₂ was determined with a mass flow meter GFM and a totalizer. The CO₂ (99.995 % purity) was supplied by Air Liquide (Portugal). The extracts were collected in a system of glass U tubes, at atmospheric pressure and a temperature controlled with an ice bath.

The solubility of butanamide in supercritical CO₂ was measured at T= (308, 313 and 323) K and at pressures range (9 to 40) MPa.

Results and Conclusions

4

The solubilities of butanamide in SC CO₂, measured at the three temperatures of interest to the experiment, are shown on Figure 3. With the increase of pressure at constant temperature, the solid solubility increases due to an increase of the fluid density. The solubility isotherms exhibit a crossover pressure at around 12.0 MPa.

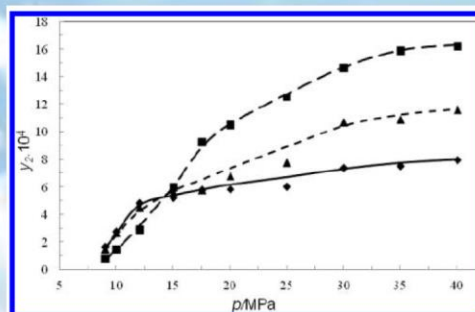


Figure 3 - Solubility of butanamide in SC-CO₂. Symbols represent experimental solubility; Lines represent the solubility, correlated by the SRK EoS. •, measured, and —, correlated solubility at T = 308.2 K; ▲, measured, and —, correlated solubility at T = 313.2 K; ■, measured, and —, correlated solubility at T = 323.2 K.

Figure 3 also shows the correlation of butanamide solubility by the SRK cubic EoS. The agreement between the experimentally measured and correlated solubility of butanamide at the three temperatures of interest to the experiment is very good.

Funding

5

The authors acknowledge with gratitude the financial support from the Bulgarian Science Fund, Ministry of Education and Science. (CONTRACT GRANT No: ДФНИ Б01/23).

Using different nanostructure ferrite-type catalysts for obtaining substituted polyphenylacetylenes by coupling reactions

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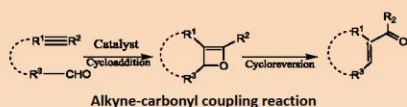
²Institute of Catalysis, Bulgarian Academy of Sciences, "Acad. G. Bonchev" St., bl.11

During the last decade a new synthetic route for the preparation of oligomeric products, bases on carbonyl-olefin exchange reaction and reductive coupling of conjugated dicarbonyl compounds, has been developed. The products thus obtained are well soluble, stable in air and still possess the physical properties of conjugated polymers. This approach provides the possibility for synthesizing polyphenylacetylenes with different end-groups [1].

AIM

The goal of our investigations is to study a nanosized ferrite-type materials with different chemical composition and stoichiometry $M_xFe_{3-x}O_4$ ($M=Zn, Mg; x=0.5; 1$) as catalysts for the coupling reactions between alkynes and aldehydes. To determine suitable preparation conditions for synthesis of substituted polyphenylacetylenes .

EXPERIMENT



Experimental conditions

Monomer	Comonomer	Catalyst	T, °C	Time, h	Product
1-phenylacetylene 0.007mmol	Isobutyraldehyde 0.005mmol	$Zn_{0.5}Fe_{2.5}O_4$ 0.0001mmol	80	4	polyphenylacetylenes with a carbonyl end group (PPA-1)
1-phenyl-1-propyne 0.007mmol	Isobutyraldehyde 0.005mmol	$Zn_{0.5}Fe_{2.5}O_4$ 0.0001mmol	80	4	polyphenylacetylenes with an olefin end group (PPA-2)
1-phenylacetylene 0.07 mmol	Isobutyraldehyde 0.011 mmol	$Mg_{0.5}Fe_{2.5}O_4$ 0.010 μmol	80	4	polyphenylacetylenes with a carbonyl end group (PPA-3)
1-phenylacetylene 0.07 mmol	Isobutyraldehyde 0.011 mmol	$MgFe_2O_4$ 0.010 μmol	120	4	polyphenylacetylenes with an olefin end group (PPA-4)
1-phenyl-1-propyne 0.07 mmol	Isobutyraldehyde 0.011 mmol	$Mg_{0.5}Fe_{2.5}O_4$ 0.010 μmol	120	4	polyphenylacetylenes with an olefin end group (PPA-5)

As solvent was used 1,2- Dichloroethane.
The crude mixture was purified by column chromatography with a mixture hexane: ethyl acetate = 1:10.
The products were isolated as a yellow and dark viscous liquids [2].
The electroconductivity of samples PPA-3 and PPA-4 was measured by the four-probe in plane method at RT (Tesla multimeter: BM518). The products were prepared as a thin film and 1×10^{-3} cm thickness [2].

Preparation of zinc and magnesium ferrite-type catalysts

The magnesium ferrite-type catalysts $Mg_{0.5}Fe_{2.5}O_4$ with spinel ferrite and different quantity of intermediate phase - $\beta\text{-FeOOH}$; iron-magnesium hydroxalcalite ($(Mg,Fe)O(OH)$) and $Zn_{0.5}Fe_{2.5}O_4$ containing except ferrite phase and additional akaganelite (iron oxide hydroxide) were prepared by chemical co-precipitation procedure. The prepared initial 0.03 M aqueous solutions of $FeCl_3 \cdot 4H_2O$, $FeCl_2 \cdot 6H_2O$ and $MgCl_2 \cdot 6H_2O$ or $ZnCl_2$ were mixed in a ratio of 1:4:1. As precipitant was dropped 0.3 M NaOH at continuous stirring until pH of the mixture became 12.5 (for magnesium contained ferrites) or 13 (for zinc contained ferrites). After co-precipitation procedure the mixture was stirred for one hour. The prepared brown precipitates were centrifuged and washed with distilled water up to neutral reaction (pH=7). The products were dried at 35 °C. The phase composition and structure of prepared magnesium and zinc ferrite powders were investigated by X-ray diffraction, Moessbauer and FTIR spectroscopy and reported in our previous study [3,4].

Conclusions

- An effective synthesis of substituted polyphenylacetylenes with carbonyl or olefin end groups has been prepared for the first time in intramolecular coupling reactions catalyzed by nanodimensional zinc and magnesium contained ferrites.
- The obtained results indicate that isomerization of the cis- and trans- units. The FT-IR spectroscopy shows that vibration bands around 1700 cm^{-1} corresponding to the stretching vibrations of the carbonyl groups. As well as the absorption peaks around 1600 cm^{-1} are attributed to the presence of conjugated backbones.
- The obtained products PPA-1 and PPA-4 showed the best electroconductivity - $0.9 \times 10^{-3} - 1.2 \times 10^{-3}\text{ S/cm}$.
- The structures of PPA may find applications in various areas, including use as light emitting diodes or sensing devices.

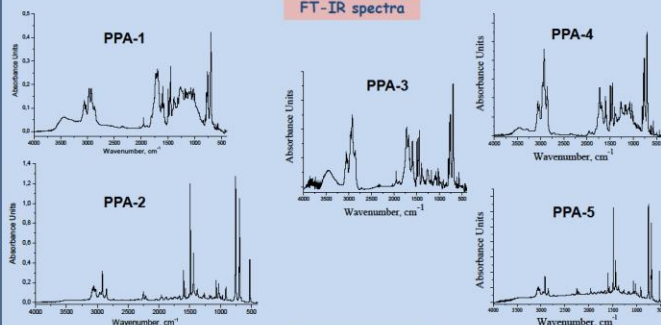
RESULTS



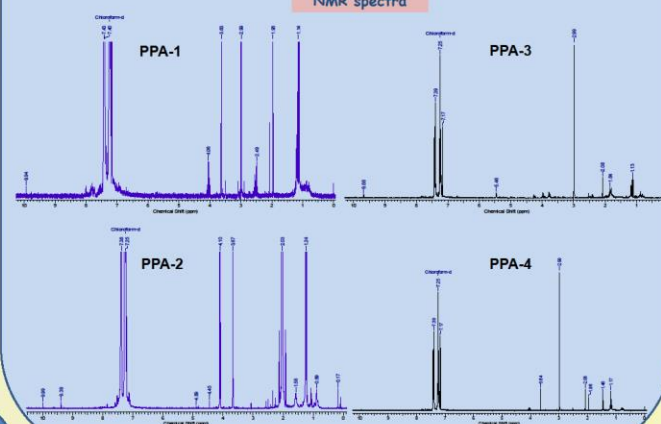
Samples prepared using zinc contained ferrite catalysts

Samples prepared using magnesium contained ferrite catalysts

FT-IR spectra



NMR spectra



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PREPARATION AND CHARACTERIZATION OF CURCUMIN LOADED PCL-PDEMA MICELLES

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1. Aim of the study

Polymeric micelles are alternative drug delivery systems due to the high capacity to incorporate hydrophobic drug molecules in the inner micelle core. Curcumin is a highly hydrophobic molecule possessing antioxidant, anti-inflammatory, anticancer effects etc. However, the low water solubility and instability at various conditions (e.g. pH, light exposure) influenced its oral absorption.

The present study aims to overcome these problems by encapsulation of curcumin in newly developed polymeric micelles based on the copolymer of poly(*ε*-caprolactone) and poly(dimethylamino)ethyl methacrylate. The efficient curcumin loading was considered taking in account the hydrophobicity of polycaprolactone core. On the other hand, the positive charge of PDEMA micellar corona could influence the interaction between the micelles and cell membranes.

2. Results and Discussion

Preparation of PDEMA-PCL-PDEMA micelles by dialysis method

The copolymer PDEMA₂₀PCL₂₀PDEMA₂₀ with M_w of 11000 g/mol was synthesized in the Laboratory of Structure and Properties of the Polymers (Institute of Polymers, Bulgarian Academy of Science).

The PDEMA-PCL-PDEMA micelles were prepared by dialysis method as presented in Fig. 1.

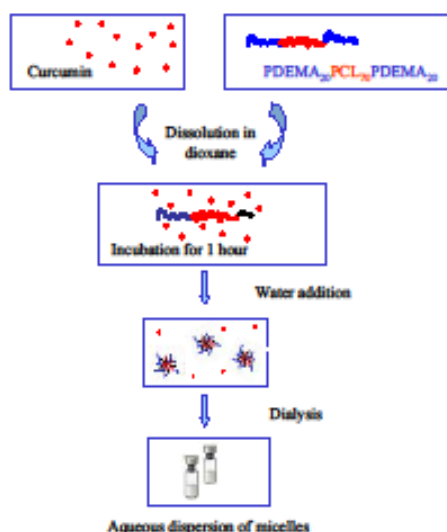


Fig. 1. Preparation of PDEMA-PCL-PDEMA micelles by dialysis method.

Physico-chemical characteristics of the micelles

The main physico-chemical characteristics of the micelles like size, polydispersity and zeta-potential were determined by photon correlation spectroscopy and electrophoretic laser doppler anemometry using a Zetasizer analyzer (Malvern Instruments, UK). As shown, the average diameter of the micelles was approximately 134 nm (Fig. 2). The zeta-potential was +65.5 mV which was expected regarding the micellar corona based on PDEMA chains.

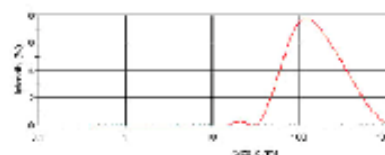


Fig. 2. Size distribution of polymeric micelles.

The amount of curcumin incorporated into the micelles was determined by spectrophotometry at a wavelength of 480 nm. The curcumin loading was calculated as a difference between its initial concentration and the concentration found in the aqueous fractions collected after the dialysis procedure. According to the applied procedure, the curcumin loading was highly efficient (higher than 60 %) (Fig. 3).

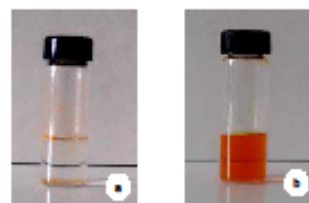


Fig. 3. Photographic images of free curcumin (a) and curcumin loaded into micelles (b).

The cellular uptake was investigated by incubation of free curcumin and curcumin loaded in micelles in chronic myeloid leukemia derived K-562 cells (Fig 4 and 5).

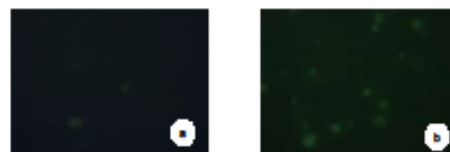


Fig. 4. Cellular uptake after 1 h incubation of free curcumin (a) and micellar curcumin (b) in K-562 cell line (concentration 2.5 μM).

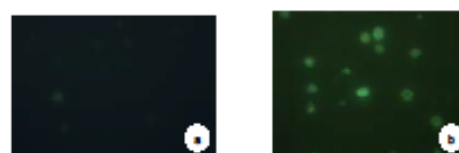


Fig. 5. Cellular uptake after 1 h incubation of free curcumin (a) and micellar curcumin (b) in K-562 cell line (concentration 5 μM).

3. Conclusion

The triblock poly(dimethylamino)ethyl methacrylate – poly(*ε*-caprolactone) – poly(dimethylamino)ethyl methacrylate micelles could be appropriate vehicles for curcumin because of the small size and improved cell internalization.

Acknowledgements

The financial support of the National Science Fund of Bulgaria (001-25/2012) is gratefully acknowledged.



ПОЛУЧАВАНЕ НА НЕТЪКАН ТЕКСТИЛ ОТ ПОЛИ(L-ЛАКТИД) И ЦИНКОВ ОКСИД ЧРЕЗ ЕЛЕКТРООВЛАКНЯВАНЕ ИЛИ ЕЛЕКТРООВЛАКНЯВАНЕ/ЕЛЕКТРОРАЗПРЪСКВАНЕ



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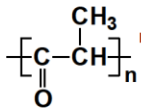
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ЦЕЛ

Получени са нови хибридни влакнести материали PLA/наноразмерен цинков оксид тип "in" или тип "on", посредством прилагането на електроовлакняване или електроовлакняване/електроразпръскване. Показана е фотокаталитичната и антибактериалната им активност.

Поли(L-лактид) (PLA)

Биосъвместим, (био)разградим полимер



Получава се от възобновяеми източници

Няма собствена химична и биологична активност



МАТЕРИАЛИ

- ZnO – необработен
- ZnO(Si) – силинизиран
- ZnO(amino) – аминофункционализиран
- ZnO(ester) – естернофункционализиран

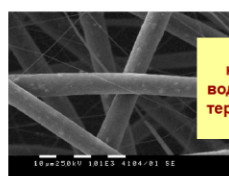
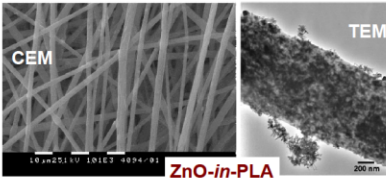


Цинков оксид (наноразмерен)

Притежава фотокаталитично и антибактериално действие, не е токсичен за хората и околната среда, подходящ е за биомедицински приложения, за пречистване на отпадни и питейни води.

ЕЛЕКТРООВЛАКНЯВАНЕ

Цинковият оксид е включен в **обема** и на **повърхността** на влакната



ZnO(Si)-in-PLA

Включването на наноразмерен ZnO води до понижаване на термичната стабилност на матове от PLA

ТИП IN



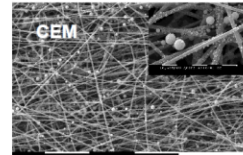
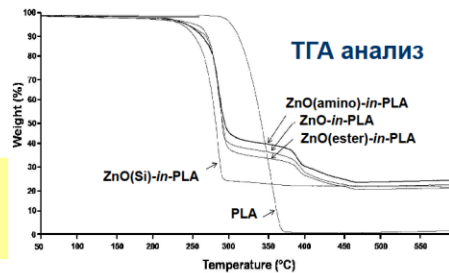
ТИП ON



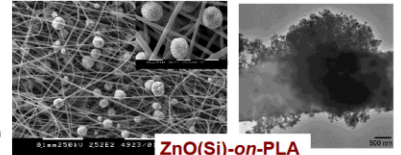
ЕЛЕКТРООВЛАКНЯВАНЕ/ЕЛЕКТРОРАЗПРЪСКВАНЕ

Цинковият оксид е включен на **повърхността** на влакната

ОХАРАКТЕРИЗИРАНЕ

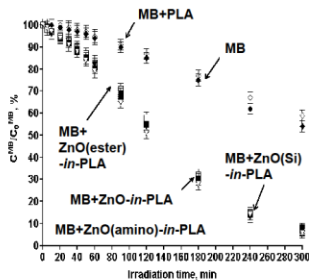


ZnO-on-PLA

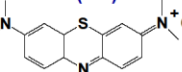


ZnO(Si)-on-PLA

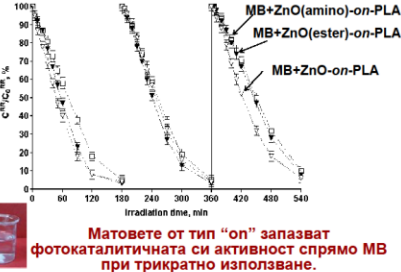
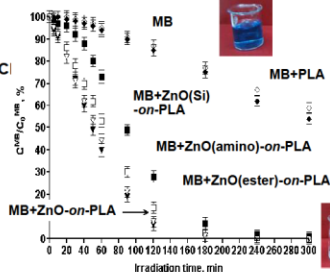
ФОТОКАТАЛИТИЧНА И АНТИБАКТЕРИАЛНА АКТИВНОСТ



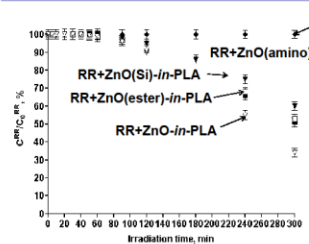
Метиленово синьо (MB)



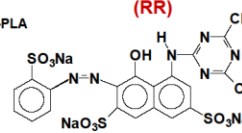
Матове тип "in" разграждат почти напълно багрилото MB за 5 часа.



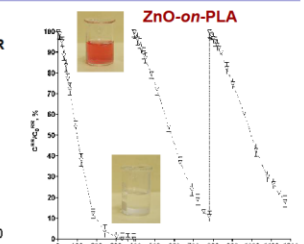
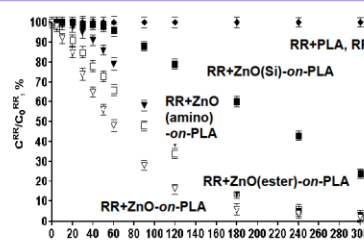
Матове от тип "on" запазват фотокаталитичната си активност спрямо MB при трикратно използване.



Реактивно червено (RR)



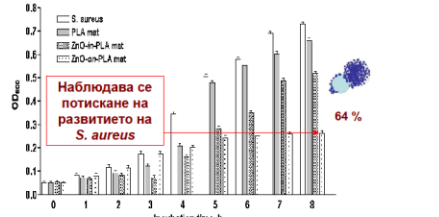
Остатъкът неразградено багрило RR е по-голям в сравнение с този на MB



ЗАКЛЮЧЕНИЕ

Установено е, че прилагането на техниката електроовлакняване/електроразпръскване (матове тип "on") е по-ефективна за получаване на хибридни материали по отношение на фотокаталитична (спрямо MB и RR) и на антибактериална активност на матове от PLA/наноразмерен цинков оксид. Новите хибридни материали тип "on" могат да бъдат използвани както за биомедицински цели (като антибактериални подложки), така и за хетерогенно фотокаталитично разграждане на органични замърсители на околната среда.

Изследванията са осъществени с финансовата подкрепа на Фонд Научни изследвания (договор ДЦВП 02/2/2009). Д.В. благодарни на ОПРЧР (договор ВГ051Р0001-3.3.06-006) на Европейския социален фонд и на проект ПОЛИНОВА за средствата за различаване на постера. Авторите благодарят на доц. д-р А. Куюмджиева за проведените микробиологични тестове. За контакти: rashkov@polymer.bas.bg



Наблюдава се потискане на развитието на S. aureus 64%



Polymer electrolyte membrane (PEM) used in H₂S/O₂ fuel cell

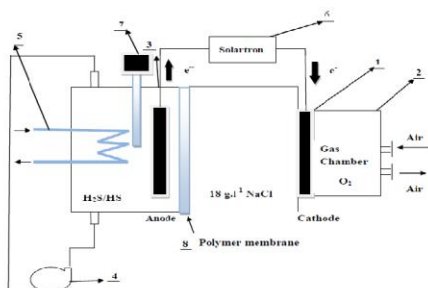
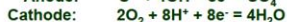
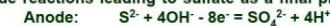
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The electrochemical process for conversion of H₂S in a fuel cell using a polymer membrane for producing in electricity and products like poly-sulfides and sulfates is very desirable. This work is focused to the study of electrocatalysts for H₂S oxidation at low concentrations for use in a newly developed H₂S/O₂ fuel cell, the final aim being energy production from the hydrogen sulfide in Black Sea waters.

The electrode reactions leading to sulfate as a final product are as follows:



Scheme 1. H₂S/O₂ PEM fuel cell: 1 – Gas Diffusion Electrode (GDE); 2 – gas chamber; 3 – working electrode (anode); 4 – peristaltic pump; 5 – water heater; 6 – Solartron; 7 – H₂ Reference electrode; 8 – Polymer Membrane (Nafion).

Four different catalysts have been studied: 1. (Degusa Carbon + 20 % CoPc(cobalt phthalocyanine) + 35 % teflonized Vulcan XC-72 (DGCPV); 2. (DG + 20% CoPc) + 35 % teflonized Acetylene Black (DCPAB); 3. La_{1.3}Sr_{0.7}NiO₄ + 35 % teflonized Vulcan XC-72 (LSNV) 4. Bulk Graphite.

All electrodes studied are immersed type and have geometrical area of 10 cm². The electrodes are prepared from a mixture of the catalysts and teflonized carbon black (35% Teflon) as a binder. Two types of carbon black have also been used – Vulcan XC-72 and acetylene blacks. The mixture is pressed onto both sides of a stainless steel current collector at 300°C and pressure of 300 atm.

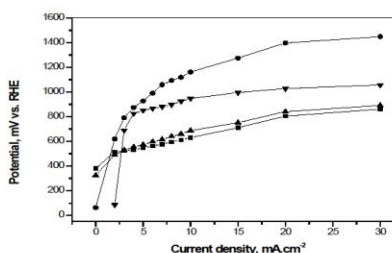


Figure 1. Working electrode potential vs. current density for the oxidation of H₂S with different catalysts: ● – Graphite, ▼ – DCPAB, ▼ – DGCPV, ■ – LSNV; electrolyte - 1g.l⁻¹ sulfide ions + 18 g.l⁻¹ NaCl.

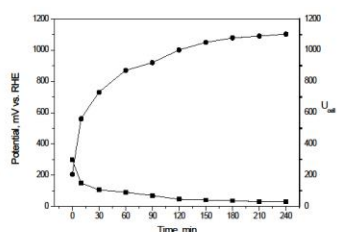


Figure 2. Fuel cell mode test (working electrode potential variation with time at constant current density, $i = 10 \text{ mA.cm}^{-2}$). Working electrode - DGCPV. Electrolyte – 186 mg.l⁻¹ sulfide ions; + 18 g.l⁻¹ NaCl.

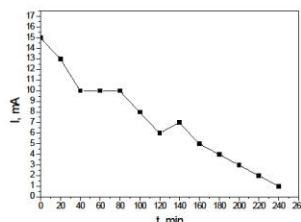


Figure 3. Fuel cell mode test (short circuited current variation with time) at $T=60^\circ\text{C}$. Working electrode - LSNV. Counter electrode - air GDE; Reference electrode - “Gaskatel”; electrolyte - 200mg.l⁻¹sulfide ions; supporting electrolyte 18 g.l⁻¹ NaCl.

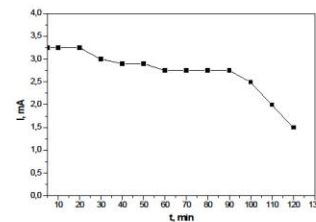


Figure 4. Fuel cell mode test (short circuited current variation with time). Working electrode - 2 grams perovskite (La_{1.3}Ni_{0.7}SrO₄) and 12 % PTFE powder. Counter electrode - air GDE; Reference electrode - “Gaskatel”; electrolyte - 182 mg.l⁻¹sulfide ions; supporting electrolyte 18 g.l⁻¹ NaCl; $T = 25^\circ\text{C}$.

Table 1. Experimental data for the time variation of sulfide and sulfite concentrations in the fuel cell mode under galvanostatic conditions: $i = 10 \text{ mA.cm}^{-2}$.

Time, hour	Potential, mV	Concentration of sulfide, mg.l ⁻¹	Concentration of sulfite, mg.l ⁻¹
0	204	186	243
2	1001	69,7	354
4	1103	10	470

Acknowledgements: This work was supported by the project HYSULFCEL (bs-era.net) of the 7 FP of the European Union, contract DNS7RP 01/32 of the Ministry of Education and Science of Republic of Bulgaria.

The authors wish to thank POLINNOVA Project funded under the FP7 Grant Agreement No 316086 and European Social Fund, Structural Funds, Operational Programme “Human Resources Development” Grant No. BG051PO001-3.3.06-0017, 2007-2013 for the opportunity to attend the V poster session “Young scientists in the world of polymers.”

Conclusions: Several catalysts have been tested for the anodic oxidation of sulfide to sulfite and sulfate. The electrodes prepared with CoPc and perovskite (La_{1.3}Ni_{0.7}SrO₄) have been optimized and showed very good electrochemical characteristics. The adequacy of a new developed sulfide driven fuel cell has been tested and proved using optimized electrodes and conditions. H₂S/O₂ PEM fuel cell at room temperature and low HS⁻ concentrations has reached reasonable current densities due to sulfide to sulfite and sulfate oxidation without electrode poisoning.

Изследване на микрофбрилизирани структури на вторични ПП/ПЕТ смеси



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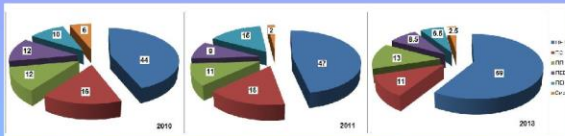
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** Лаборатория по структура и свойства на полимерите, Факултет по химия и фармация, Софийски университет

ВЪВЕДЕНИЕ

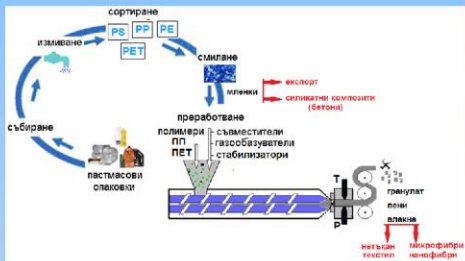
През последните десетилетия потреблението на пластмаси в индустрията, обществения живот и бита многократно нараства поради техните уникални свойства, адаптивност и сравнително леснодостъпни и производителни методи за преработването им в изделия. При широкото им използване е невъзможно да се избегне натрупването на огромни количества отпадъци от тях, които създават сериозни екологични и икономически проблеми, когато техният полезен живот завърши. Механичното рециклиране е приемлив подход за намаляване на отделияните в околната среда пластмасови отпадъци и същевременно осигуряване на суровини за полимерната индустрия.

Състояние на проблема в България



Фигура 1. Разпределение на използваните полимери за опаковки по видове в проценти, съгласно доброволно проведен статистически експеримент.

Резултат - нараства частта на ПЕТ в опаковки в бита, което налага необходимост от разработване на стратегия за неговото повторно използване.



Фигура 2. Технологична схема за получаване на смеси и изделия от вторични пластмаси

ЦЕЛ

Целта на настоящата работа е получаване на рециклирани ПП/ПЕТ смеси и изследване на техните реологични и термични свойства, както и морфологията на получените микрофбрилизирани структури.

ЕКСПЕРИМЕНТАЛНА ЧАСТ

МАТЕРИАЛИ

- Изотактен ПП "Булен" 6631 (MFR = 2.3 g/10 min)
- ПЕТ-мленки от бутилки за мин. вода и газирани напитки

Получаване на смеси - двущнеков екструдер Brabender DSE 17/35D

Състав: 95ПП/5ПЕТ; 87.5ПП/12.5ПЕТ; 75ПП/25ПЕТ и 50ПП/50ПЕТ

Технологичен режим :

Температура на стопилката по зони - от T1(200°C) до T5(260°C)

Скорост на екструзия Ue=30 гр/м

Получаване на микрофбрили



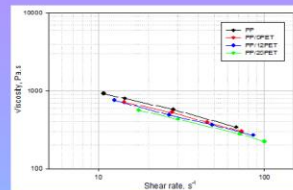
Фигура 3. Технологична схема и параметри за получаване микрофбрили

МЕТОДИ

- Реология (Криви на течене; Адаптиран апарат за индекс на стопилка)
- Диференциална сканираща калориметрия (TA Instruments Q200 Calorimeter) ;
- Сканираща електронна микроскопия (JEOL 5510 microscope);

РЕЗУЛТАТИ

Реология

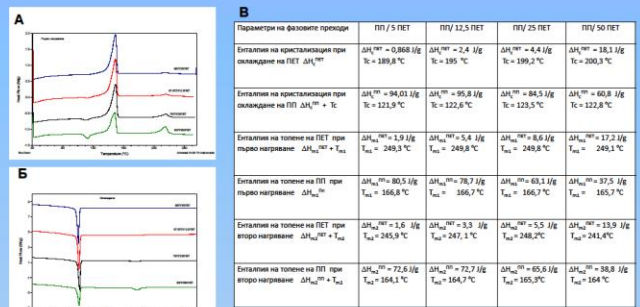


Фигура 4. Криви на течене на ПП/ПЕТ смеси, определени при Tm= 250



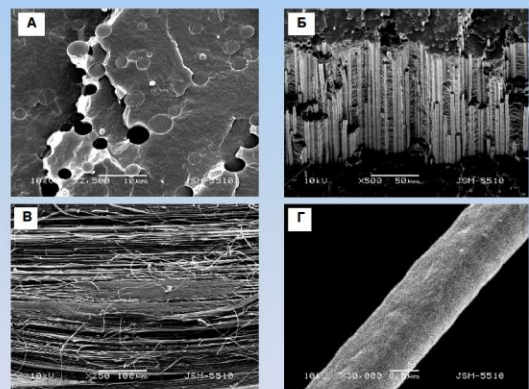
Фигура 5. Адаптиран апарат за определяне на индекс на стопилка

Диференциална сканираща калориметрия



Фигура 6. А.) DSC криви на топене на вторични ПП/ПЕТ смеси; Б.) DSC криви на кристализация на вторични ПП/ПЕТ смеси; В.) Параметри на фазовите преходи

Сканираща електронна микроскопия



Фигура 7. Морфология на микрофбрилизирани 75ПП/25ПЕТ смеси: А.) Напрежен срез на екструдирани смеси; Б.) Надлъжен срез на екструдирани смеси; В) Изтеглени фибрили; Г) Единична фибрила на ПЕТ

ЗАКЛЮЧЕНИЯ

- Проведен е доброволен статистически експеримент, въз основа на който е представена стратегия за повторното използване на ПЕТ.
- Получени са смеси на основата на вторичен ПЕТ и ПП и са определени кривите на течене и параметрите на фазовите преходи.
- Получени са микрофбрилизирани структури на 75ПП/25ПЕТ смеси и е изследвана тяхната фазова морфология.
- SEM показва че, след екструдиране ПП ламелите са разположени напречно на ПЕТ фибрилите, като размерът на ПЕТ фибрилите е между 5÷7 μm, а след изтегляне размерът им достига до 1 μm.

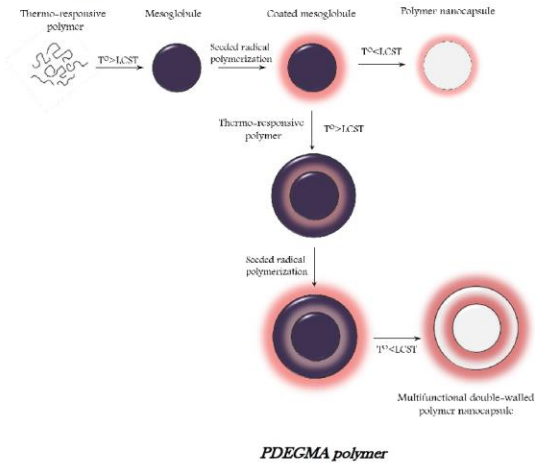
Multifunctional double-walled polymeric nanocapsules obtained by template-assisted technique

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Introduction

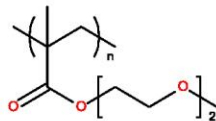
In our previous work¹ we have shown the preparation of polymeric nanocapsules by a simple method, which comprises (i) formation of thermoresponsive polymeric core-templates, (ii) construction of polymeric shell on the surface of the obtained core-template and (iii) removal of the core-template by lowering the temperature below the LCST of the thermosensitive polymer.

In this contribution we demonstrate the ability to obtain multi-functional **double-walled capsules** prepared in a similar manner by repeating steps i - iii.

Due to their multicompartiment architecture the resulting multi-functional double-walled capsules resemble cell structure and can be used as artificial cells in medicine and pharmacy as bioreactors or as drug delivery vehicles.

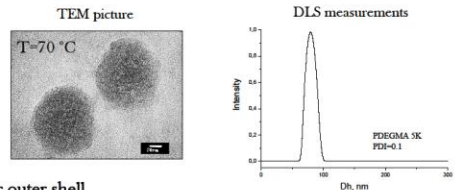
Obtaining of thermoresponsive polymeric core-templates

It is well known that in aqueous solution and at temperatures above their lower critical solution temperature (LCST), conditions can be found at which thermoresponsive polymers form well-defined and narrowly distributed colloidal particles called *mesoglobules*. In this work poly(methoxydiethyleneglycol methacrylate) (PDEGMA) was used to obtain small in size and narrowly distributed thermoresponsive core-templates.



Molecular weight characteristics and cloud point value of PDEGMA polymers		
Mn g/mol	Mw/Mn	LCST °C
6400	1.5	29

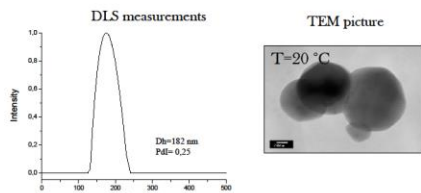
PDEGMA mesoglobules



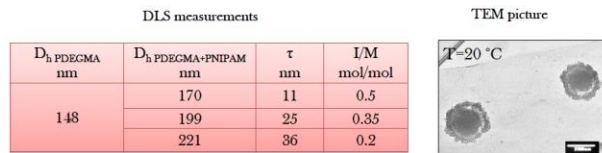
Construction of the first polymeric outer shell

PDEGMA mesoglobules were coated with a surface-cross-linked shell formed by seeded radical polymerization of N-isopropylacrylamide and 2-hydroxyethylmethacrylate. N,N-methylenebis(acrylamide) was used as a cross-linker. By varying the monomer to initiator ratio the shell thickness, τ , was controlled. The received core-shell particles displayed different morphology depending of the polymer used for construction of outer shell. Particles composed of cross-linked PNIPAM were of raspberry-like and uneven shell in contrast to those obtained of cross-linked PHEMA which were smooth, uniform in thickness and homogeneous.

✓ PHEMA shell



✓ PNIPAM shell



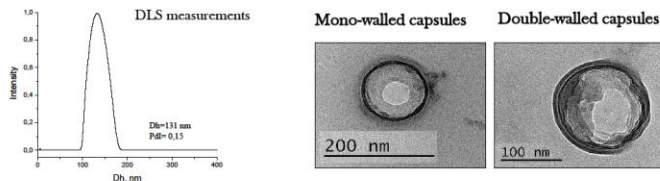
Construction of the second polymeric outer shell

An appropriate amount of PDEGMA was added to the core-shell particles obtained in the first step. The increase in temperature above the LCST resulted in formation of a PDEGMA layer on the surface of the core-shell particles. The second polymeric shell (membrane) was formed by seeded radical polymerization of HEMA in the presence of N,N-methylenebis(acrylamide) as a cross-linker.

	First core	First shell	Second core	Second shell	Double-walled capsules	
T °C	70	70	20	70	20	
D_h , nm	59	69	215	108	120	250
PDI	0,07	0,05	0,51	0,18	0,09	0,48
						0,31

Capsule preparation

Polymeric mono- or double-walled nanocapsules were prepared by dissolving and removing of PDEGMA core-template from the coated with PNIPAM or PHEMA particles. After construction of the outer shell(s), the polymer dispersions were dialysed against water for 7 days at temperature of 10 °C.



Conclusions

- For the first time polymers of the family of polymethacrylates with pendant oligo(ethylene glycol) chains, which have been reported to exhibit LCST properties, were employed as templates for preparation of polymeric nanocapsules.
- PDEGMA core-templates and shells based on PNIPAM as well as PHEMA were combined to produce the intermediate core-shell structures.
- Obtaining of a PDEGMA layer and construction of the second PHEMA shell were also performed for the first time.
- Following extensive dialysis against water at temperatures below the LCST of PDEGMA, the core-templates were removed and unique mono- and double-walled nanocapsules were obtained.

Acknowledgement

The authors would like to express gratitude to the EC project POLINNOVA and by Operational Program "Human resources development" - BG03/PO001-3.3.06/001/ under project "Building of scientific potential for sustainable career development of young researchers, PhD-students and post-docs in the field of polymer science".



References:

1. E. Haladjova, S. Rangelov, Ch. Tsvetanov, P. Simon, *Polymer* 55 (2014) 1621-1627.

САМОАСОЦИРАНЕ ВЪВ ВОДЕН РАЗТВОР НА ТРИБЛОКОВИ АМФИФИЛНИ СЪПОЛИМЕРИ ПОЛИГЛИЦИДОЛ-ПОЛИ(АЛИЛ ГЛИЦИДИЛОВ ЕТЕР)-ПОЛИГЛИЦИДОЛ (PG-PAGE-PG)

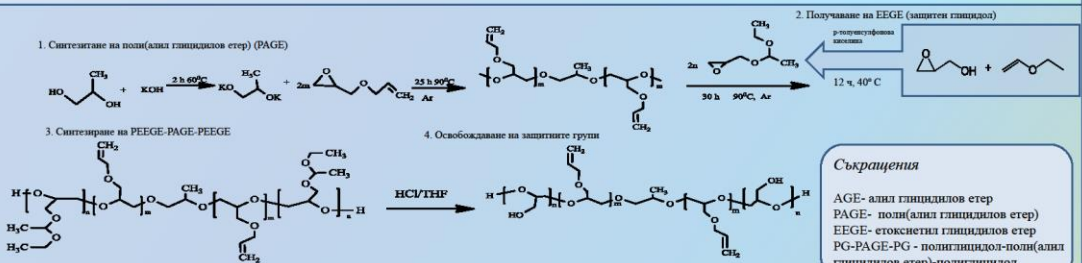


Бояна Стоянова, Христо Новиков, Станислав Рангелов, Христо Цветанов
Институт по полимери, Българска академия на науките
E-mail: bstoyanova@polymer.bas.bg

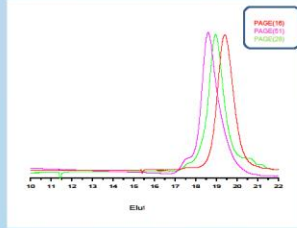
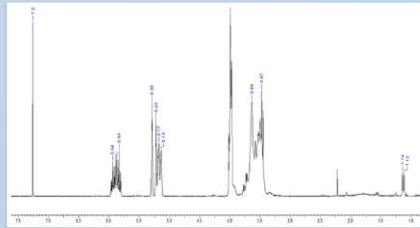


Синтезът на амфибилни триблокови съполимери полиглицидол-поли(алил глицидилов етер)-полиглицидол (PG-PAGE-PG) се извършва в три стъпки: (I) анионна полимеризация с отваряне на пръстен на алил глицидилов етер (AGE), последвана от (II) анионна полимеризация на етоксетил глицидилов етер (EEGE, защитен глицидол) и (III) освобождаване на защитните етоксетилни групи. Съполимерите се различават по молекулярна маса и по съотношение между съставните блокове. Първоначално бяха синтезирани серия от три PAGE комополимера с молни маси от 2000, 4000 и 6000 Da, които бяха използвани като макроинициатори за полимеризация на EEGE. Полимеризациите на AGE и EEGE бяха извършени в маса по контролиран начин. След освобождаване на защитните групи бяха получени 3 серии от линейни PG-PAGE-PG съполимери с фиксирана молна маса на средния блок PAGE и нарастващо съдържание на PG от 35 до 60 mol% във всяка серия. Блоковите съполимери са охарактеризирани чрез ¹H NMR спектроскопия и GPC.

Получаване на триблокови съполимери PG-PAGE-PG

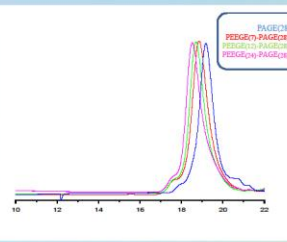
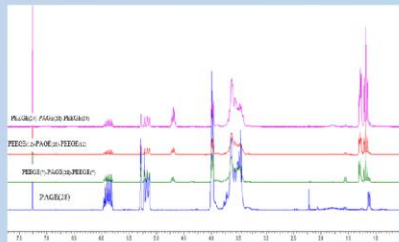


Охарактеризиране на поли(алил глицидилов етер) (PAGE)

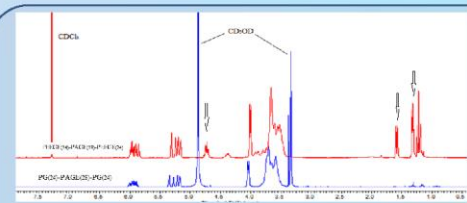


НАИМЕНОВАНИЕ	M _n (NMR)	M _n (GPC)	PDI
PAGE ₍₁₆₎	1800	1900	1.12
PAGE ₍₅₁₎	5800	6000	1.13
PAGE ₍₂₈₎	3200	3400	1.1

Охарактеризиране на съполимерите



НАИМЕНОВАНИЕ	M _n (NMR)	M _n (GPC)	PDI
PEEGE ₍₃₎ -PAGE ₍₁₆₎ -PEEGE ₍₃₎	2700	2800	1.12
PEEGE ₍₇₎ -PAGE ₍₁₆₎ -PEEGE ₍₇₎	4200	4500	1.13
PEEGE ₍₁₃₎ -PAGE ₍₁₆₎ -PEEGE ₍₁₃₎	5700	5800	1.15
PEEGE ₍₁₃₎ -PAGE ₍₅₁₎ -PEEGE ₍₁₃₎	9800	10000	1.14
PEEGE ₍₂₃₎ -PAGE ₍₅₁₎ -PEEGE ₍₂₃₎	12600	13000	1.15
PEEGE ₍₂₈₎ -PAGE ₍₅₁₎ -PEEGE ₍₂₈₎	14100	14100	1.17
PEEGE ₍₃₃₎ -PAGE ₍₅₁₎ -PEEGE ₍₃₃₎	15500	15600	1.15
PEEGE ₍₇₎ -PAGE ₍₂₈₎ -PEEGE ₍₇₎	5300	5400	1.11
PEEGE ₍₁₃₎ -PAGE ₍₂₈₎ -PEEGE ₍₁₃₎	6900	7000	1.12
PEEGE ₍₂₄₎ -PAGE ₍₂₈₎ -PEEGE ₍₂₄₎	10200	10500	1.15



Освобождаване на защитните етоксетилни групи

За успешно освобождаване на защитните етоксетилни групи се съди по изчезването на сигналите на 4.6-4.7 ppm за метиловия протон и сигналите на 1.1-1.2 ppm и 1.3 ppm за метиловите протони на ацеталните групи.

Самоасоциране във воден разтвор

ДРС данни PG-PAGE-PG

наименование	концентрация (ng/ml)	диаметър, D _z (nm)
PG ₍₇₎ -PAGE ₍₂₈₎ -PG ₍₇₎	1	530
	0.1	307
	0.05	170
PG ₍₁₇₎ -PAGE ₍₂₈₎ -PG ₍₁₇₎	1	257
	0.1	124
	0.05	-
PG ₍₂₄₎ -PAGE ₍₂₈₎ -PG ₍₂₄₎	5	190
	2.5	98
	1	-

Благодарности:

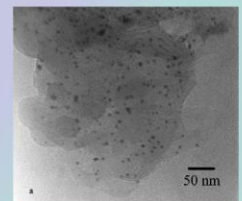
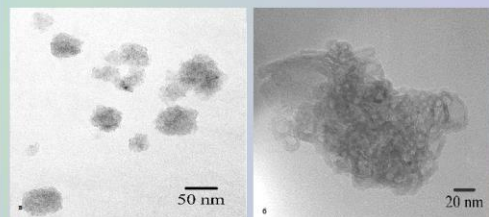
ОП РЧР- BG051P0001-33 06-0017. Изграждане на научния потенциал за устойчиво качествено развитие на младите учени, докторанти и постдокторанти в приоритетни области на полимерната наука и "POLINNOVA"



Изводи:

- ✓ Чрез анионна полимеризация с отваряне на пръстен са синтезирани три серии PEEGE-PAGE-PEEGE съполимери с различна дължина на съставните блокове.
- ✓ Полимеризациите на AGE и EEGE бяха извършени по контролиран начин в маса.
- ✓ След освобождаване на защитните етоксетилни групи бяха получени амфибилни триблокови съполимери PG-PAGE-PG със съдържание на PG 35, 45 и 60 мол. %
- ✓ При самоасоциране на съполимерите във водни разтвори се наблюдава образуване на частици с размери между 98 и 530 nm в зависимост от концентрацията и съотношението между блоковете.

Чрез динамично разсейване на светлина е изследвана способността на съполимерите да самоасоцират във воден разтвор като образуват частици с различни размери и морфологии в зависимост от състава, молната маса, концентрацията и съотношението между съставните блокове. Самоасоциралите структури са визуализирани чрез TEM.



TEM снимки на PG₍₇₎-PAGE₍₂₈₎-PG₍₇₎ (а), PG₍₁₇₎-PAGE₍₂₈₎-PG₍₁₇₎ (б), PG₍₇₎-PAGE₍₂₈₎-PG₍₇₎ (в), във воден разтвор

"CLICKABLE" POLYMERS FOR POTENTIAL BIOMEDICAL APPLICATIONS

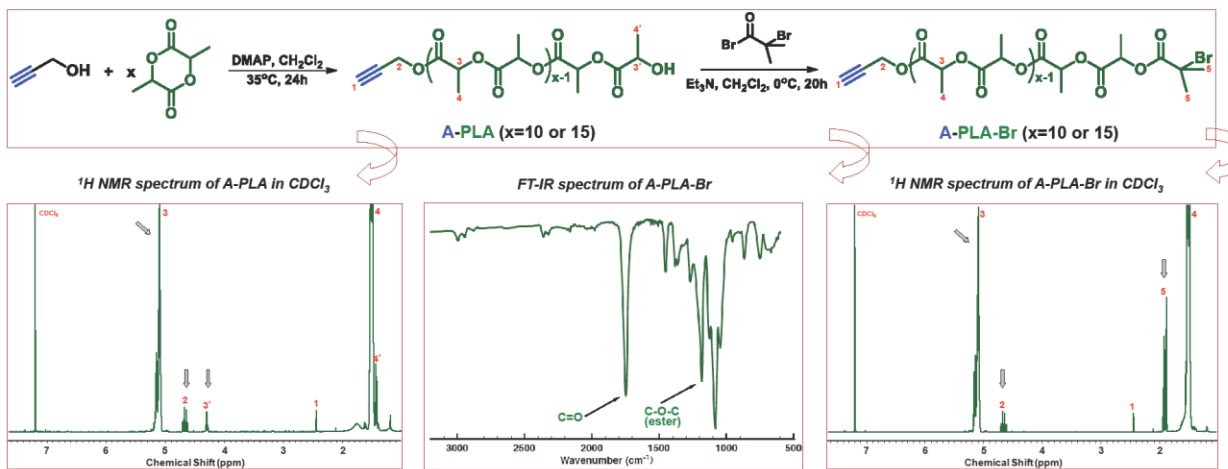
Dimitrina Babikova, Ivaylo Dimitrov

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

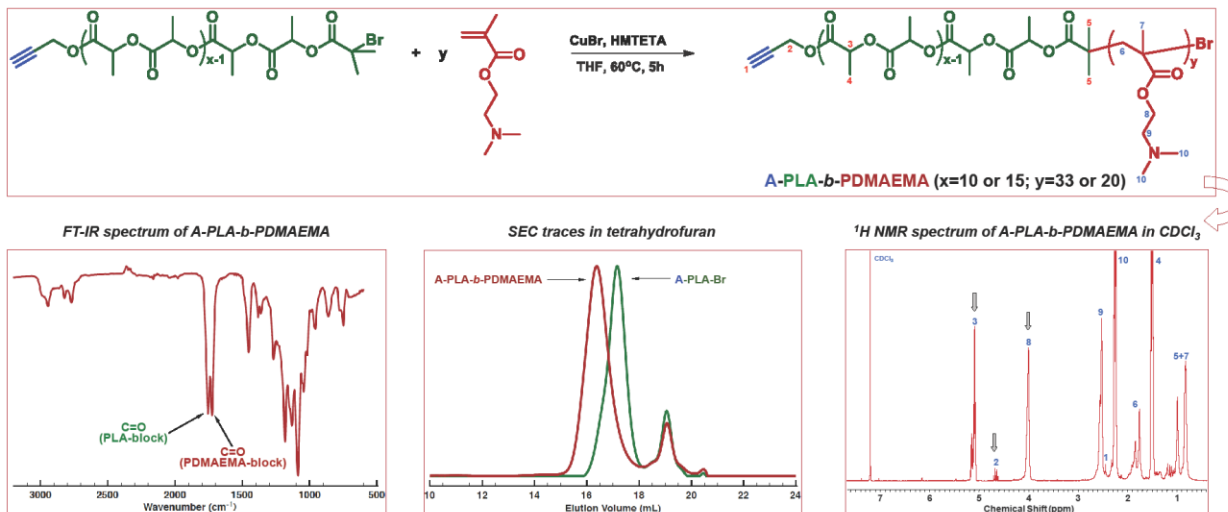
POLYMER NANOCARRIERS ARE GOOD CANDIDATES FOR DRUG DELIVERY AT CELLULAR AND SUB-CELLULAR LEVEL. MODERN NANOMEDICINE REQUIRES A DESIGN OF MULTIFUNCTIONAL DRUG CARRIERS THAT ARE ABLE TO OVERCOME VARIOUS CELLULAR BARRIERS. CONTROLLED POLYMERIZATION METHODS COMBINED WITH HIGHLY EFFICIENT MODIFICATION TECHNIQUES SUCH AS "CLICK" CHEMISTRY APPROACH, OFFER THE POSSIBILITY FOR THE DEVELOPMENT OF MULTIFUNCTIONAL NANOPARTICLES WITH UNIQUE PROPERTIES AND FUNCTIONS FOR BIOMEDICAL APPLICATIONS.

HEREIN WE PRESENT THE CONTROLLED SYNTHESIS OF ALKYNE-TERMINATED AMPHIPHILIC BLOCK COPOLYMERS COMPRISING POLY(*N,N*-DIMETHYLAMINO-2-ETHYL METHACRYLATE) (PDMAEMA) AND BIODEGRADABLE POLY(*D,L*-LACTIDE) (PLA) SEGMENTS. THE PRESENCE OF "CLICKABLE" TERMINAL GROUP ALLOWS MODULAR ATTACHMENT OF VARIOUS TARGETING AND OTHER FUNCTIONS FOR POTENTIAL BIOMEDICAL APPLICATIONS.

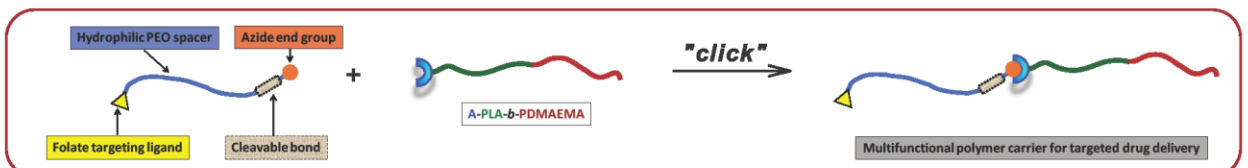
I Controlled synthesis of poly(*D,L*-lactide) ATRP macroinitiator with terminal alkyne group (A-PLA-Br)



II Synthesis of "clickable" amphiphilic block copolymer (A-PLA-*b*-PDMAEMA)



OUTLOOK





Novel Dexamethasone Sodium Phosphate delivery nanosystems based on star-shaped cationic copolymers



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¹Department of Pharmaceutical Technology and Biopharmaceutics, Faculty of Pharmacy, Medical University-Sofia, Dunav Str. 2, 1000 Sofia, ²Institute of Polymers, Bulgarian Academy of Sciences, Acad. G. Bonchev str., Bl.103A, Sofia-1113, Bulgaria

INTRODUCTION

The challenge in the development of drug delivery systems is to achieve targeted delivery of bioactive substances to specific sites of human body, which provides increasing of therapeutic potential and decreasing of undesirable effects. Nowadays more investigations are devoted to the use of nanoparticles (NPs) in order to achieve targeted drug delivery. Polymeric NPs obtained from natural or synthetic polymers are very interesting as drug delivery systems, owing to their high stability and potential to remodel their surface. They can be altered in such a manner, so that to achieve both controlled release and targeting. This can be accomplished by changing the polymers' characteristics and chemical structure of the surface. Stimuli-responsive nanocarriers offer interesting opportunities for drug delivery, because the delivering system becomes an active participant in the process rather than a passive carrier. The use of stimuli-responsive nanocarriers is very important in cases when the stimuli are unique for certain pathology. Temperature and pH are examples of such stimuli, which can be applied in the design of stimuli-responsive nanocarriers. Dexamethasone sodium phosphate (DSP) is a synthetic glucocorticoid and has anti-inflammatory, anti-allergic and immunosuppressant effects. It belongs to class I/III of BCS. The reported data about encapsulation of DSP in NPs is insufficient. The aim of this investigation is to synthesize novel NPs based on cationic star-shaped polymers and to study their potential as drug delivery systems for DSP.

METHODS AND RESULTS

Synthesis of star-shaped copolymers and DSP-loaded NPs

Star-shaped copolyelectrolytes (CP3) of varied molar mass were synthesized using Ce⁴⁺ initiated redox polymerization of cationic monomer 2-(acryloyloxy)ethyl trimethylammonium chloride in aqueous media at 35 °C. 1,1,1-tris(hydroxymethyl)propane (THMP) was used as a tri-functional initiating moiety. The obtained copolymers were purified by dialysis against water and isolated by freeze-drying. DSP-loaded NPs (CP3-DSP) were prepared by mixing aqueous solutions of the copolymer (0.25 g/l and 0.5 g/l) and DSP (0.665 g/l) at 20 °C at vigorous stirring.

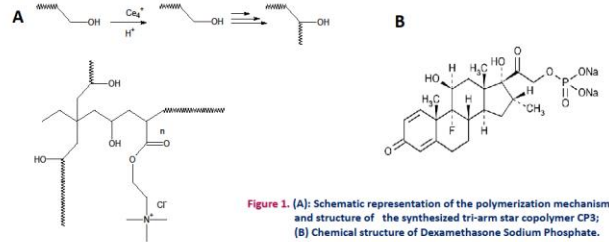


Figure 1. (A): Schematic representation of the polymerization mechanism and structure of the synthesized tri-arm star copolymer CP3; (B) Chemical structure of Dexamethasone Sodium Phosphate.

Characterization of the DSP-loaded NPs

Dynamic light scattering and zeta potential determination

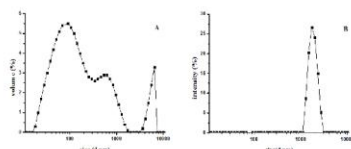


Figure 2. DLS of DSP loaded NPs obtained in: (A) deionized water (B) aqueous media with pH 2

Scanning electron microscopy investigations

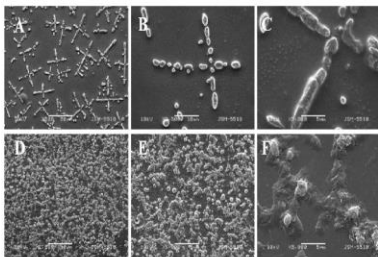


Figure 3. A-D micrographs of CP3 NPs E-H micrographs of CP3-DSP NPs

Transmission electron microscopy investigations

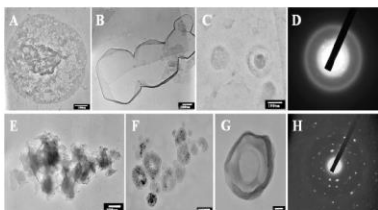


Figure 4. A-D micrographs of CP3 NPs E-H micrographs of CP3-DSP NPs

Nuclear magnetic resonance imaging

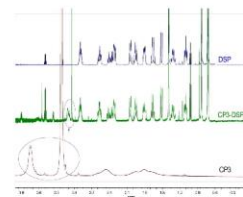


Figure 5. ¹H NMR spectra of DSP, CP3 and CP3-DSP

FTIR-spectroscopy

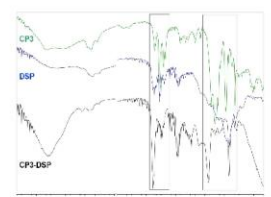


Figure 6. FTIR spectra of CP3, DSP and CP3-DSP

Differential scanning calorimetry

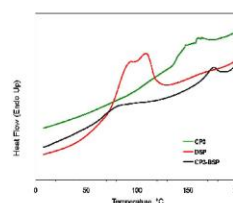


Figure 7. DSC thermograms of CP3, DSP and CP3-DSP

In vitro drug release study

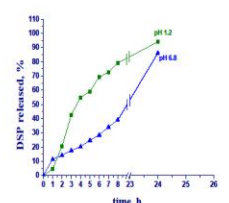


Figure 8. Release kinetics (37 °C; different pH) of DSP from NPs, obtained in deionized water

CONCLUSIONS

The developed pH-responsive NPs based on positively charged three-arm star copolymers showed potential as DSP delivery system and can be further optimized for specific therapeutic purposes.

ACKNOWLEDGMENTS Financial support by National Science Fund of Bulgaria (Project UNION, Grant # DCVP 02/2/2009) is gratefully acknowledged.

Възможности за приложение на хибриден материал на основата на поливинилов алкохол/сребърни наночастици (PVA/AgNps), като консервант при производство на хиперимунен заешки серум за диагностика на *E.coli*

Елена Величкова*¹, Даниела Пенчева¹, Райна Бряскова²

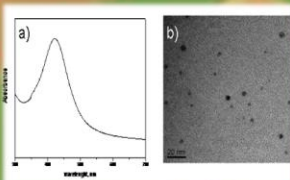
¹ Бул Био – Национален Център Заразни и Паразитни Болести, бул. Я. Сакъзов 26, 1504 София, България; ²Химикотехнологичен и металургичен университет, Катедра "Полимерно инженерство", бул. Климент Охридски 8, 1756 София, България.
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Увод

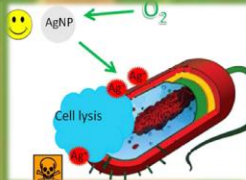
Антимикробните свойства на хибриден материал PVA/AgNps са обект на научен интерес за научния колектив от години [1]. Проучването разкрива много широк спектър от възможности за приложението му. Едно от направленията с практическа насоченост е прилагането му като консервант при производството на диагностични аглутиниращи серуми. Установяване качествата на един консервант при този тип производство изисква дългогодишни изпитвания, свързани с проследяване стабилността на продукта, в който е вложен. В конкретния случай хибридният материал е използван като консервант при получаването на хиперимунен серум *E.coli* O104, през 2011г. [2].

Цел

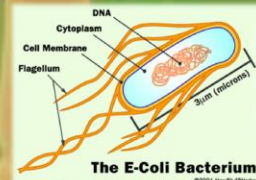
Установяване качествата на хибриден материал PVA/AgNps като консервант чрез проследяване на два критични показателя: стерилност и активност на получен преди 3 години хиперимунен заешки серум *E.coli* O104.



Фигура 1. а) UV-vis спектър и б) TEM на AgNps стабилизирани в PVA (сребърна концентрация - 156.902 mg/L).



Фигура 2. Действие на Ag-наночастици. (www.nanoparticle-blog.com)



Фигура 3. Схема на устройство на *E. coli*. (www.science.howstuffworks.com)



Фигура 4. Щам *E.coli* O 104.

Методи на работа

Метод за получаване на PVA/AgNps

Синтезът на хибриден материал PVA/AgNps (Фигура 1) е подробно описан в [1].

Крайното съдържание на сребро в разтвора на използваната синтезирана проба е определено с ICP-OES като 156.902 mg/L.

Приготвяне на антиген и схема за имунизация

Обработката на антигена и приложената схема на имунизация са представени в [2].

Тест за изпитване стерилност на хиперимунния заешки серум

Тестът за стерилност е проведен чрез накапване на 0.1 ml серум в соево-казеинов бульон и след престой в термостат при 32.5 °C и 22.5°C за 7 дни.

Тест за изпитване на активност на хиперимунния заешки серум

Извършена е титрация в реакция степенна аглутинация с термично обработен за 2 часа на 100°C щам *E.coli* O 104, с цел получаване на термостабилен O-антиген.



Фигура 5. 24-часова култура *E.coli* O 104.

Резултати

Основната цел на извършеното три-годишно проучване е установяване ефективността на синтезирания материал PVA/AgNps като консервант. Периодично, един път годишно след първоначалното определяне стерилността и титъра на изходния серум, той се изпитва отново. При последното изпитване три години след получаване на серума, теста за стерилност отчете липса на микробен растеж в бульона, което потвърждава стерилността на пробата. Изпитването на серума със специфичен антиген в реакция степенна аглутинация с цел проверка стабилността на титъра установи, че до този момент 3 години след получаването му, той все още запазил своя първоначален O-титър, а именно 1600.

Заклучение

Запазената стерилност и O-титър на серум, консервиран преди 3 години с хибриден материал, съдържащ сребърни наночастици – PVA/AgNps дават основание да се приеме, че той е подходящ за приложение като консервант в производството на хиперимунни заешки серуми за *in vitro* диагностика на *E.coli* щамове. Получените от изпитването положителни резултати ни насочват към следващи изпитвания на анти-салмонелни и анти-шигелни серуми, консервирани с PVA/AgNps. Перспективите, които се разкриват са обект на проучване на млад учен с идея за тема на бъдещ дисертационен труд. Разширените изпитвания в тази насока ще позволят използване на хибриден материал като консервант в производството на аглутиниращи диагностични серуми.

[1] Daniela Pencheva, Rayna Bryaskova, Todor Kantardjiev. Polyvinyl alcohol/silver nanoparticles (PVA/AgNps) as a model for testing the biological activity of hybrid materials with included silver nanoparticles. *Materis Science and Engineering: C*, Volume 22, Issue 7, 1 October 2012, Pages 2048–2051

[2] Daniela Pencheva, T. Kantardjiev, R. Bryaskova. Hybrid material based on PVA/AgNps using as an effective preservative for the manufacture of vaccines and pharmaceutical products. *Kragujevac: Proceedings, MICROBIOLOGIA BALKANICA 2011 - 7th BALKAN CONGRESS OF MICROBIOLOGY & 8th CONGRESS OF SERBIAN MICROBIOLOGISTS*, 25-29. oktober 2011, Udruzenje mikrobiologa Srbije, Beograd.

Liposomal formulations for delivery of curcumin-pegylated calix[n]arenes inclusion complexes

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¹ – Medical University of Sofia, Faculty of Pharmacy

² – Bulgarian Academy of Sciences, Institute of Organic Chemistry

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* - dmomekova@yahoo.com

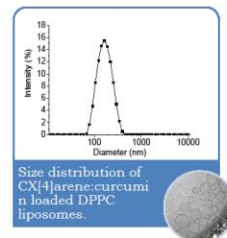
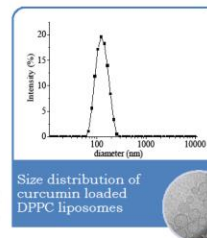
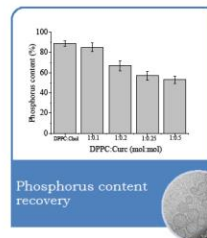
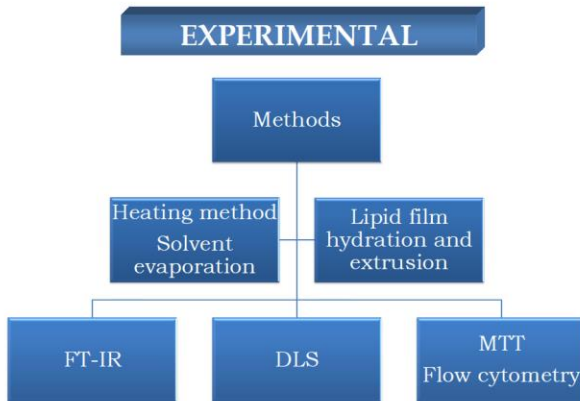


INTRODUCTION

Curcumin, the constituent of *Curcuma longa*, is considered a very promising anticancer agent due to its potent and pleiotropic antineoplastic activity and low nonspecific toxicity to normal cells. However the clinical realization of its potential has been limited due to its poor aqueous solubility and very low systemic bioavailability. A possible approach to overcome these limitations is the design of nanosized vehicles of curcumin.

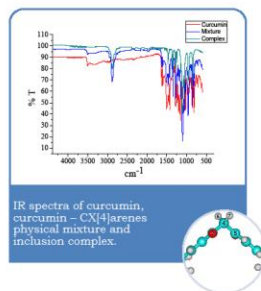
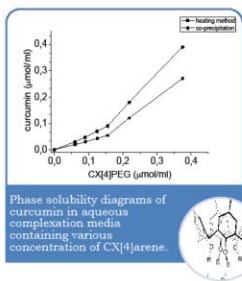
The present work reports the preparation, characterization and in vitro evaluation of antineoplastic activity of novel curcumin-in pegylated calix[4]arenes – in liposomes nanoparticles.

EXPERIMENTAL



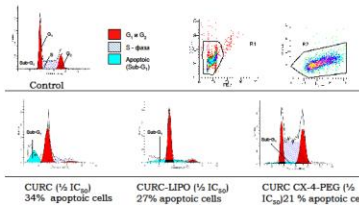
Formulation	Diameter (nm)	IP	ζ-potential (mV)	Entrapment efficacy (%)	Amount of encapsulated curcumin (µg/ml)
DPPC: CHOL	124 ± 4.2	0.096 ± 0.002	-22	-	-
DPPC: CHOL:CURC	145 ± 3.6	0.14 ± 0.04	-26.3	98	240
DPPC: CHOL:CURC: CX[4]arene:curcumin	147 ± 4.2	0.135 ± 0.08	-20,8	82	345

RESULTS



Formulations	IC ₅₀ (µmol/L) (n=8)	
	KG-1*	RPMI-8226*
Curcumin (DMSO solution)	13,45 ± 2,31	2,89 ± 0,77
Liposomal-PEG-CX-4 curcumin	2,19 ± 0,71	0,59 ± 0,21
PEG-CX-4 curcumin complexes	8,70 ± 1,44	2,22 ± 0,79

*acute promyelocyte leukemia; *multiple myeloma; *MI-modulation index = IC₅₀ (free curcumin)/ IC₅₀ (curcumin formulation).



Pro-apoptotic activity of free curcumin, liposomal-PEG-CX-4 (CURC-LIPO)curcumin and PEG-CX-4 curcumin complexes (CURC-CX-4-PEG) after 24 hours treatment.

Parameter	Heating method	Solvent evaporation method
Stability constant (K _s)	325 µM ⁻¹ .ml	1072 µM ⁻¹ .ml
Solubility enhancement factor (β) ¹	40 960 %	59 445 %

CONCLUSION: Thus on the grounds of the excellent in vitro biocompatibility profile and the favorable physicochemical and drug loading characteristics of the tested liposomal nanoparticles, and their ability to retain the intrinsic pharmacological properties of encapsulated drug they could be considered promising drug delivery platforms for lipophilic curcumin.

ACKNOWLEDGEMENTS

Financial support from National Science Fund of Bulgaria, Grant № ДФНИ Б01-25/2012 and ДЦВП 02-2/2009 is gratefully acknowledged.

ПОЛУЧАВАНЕ И ОХАРАКТЕРИЗИРАНЕ НА ЕЛЕКТРООВЛАКНЕНИ НАНОВЛАКНЕСТИ ИМПЛАНТИ ОТ ПОЛИЛАКТИД, ПОКРИТИ С КВАТЕРНИЗИРАН ХИТОЗАН И СЪДЪРЖАЩИ ГОСИПОЛ, С АНТИТУМОРНА АКТИВНОСТ СПРЯМО ТУМОР НА GRAFFI



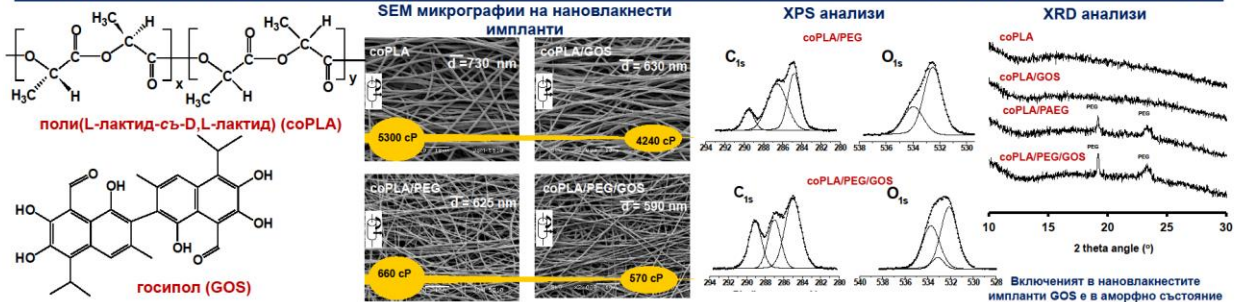
Калин Калинов^a, Милена Игнатова^a, Невена Манолова^a, Ренета Тошкова^b, Марин Александров^b, Илия Рашков^{a*}

^aЛаборатория по Биологично активни полимери, Институт по полимери, БАН, 1113 София, България

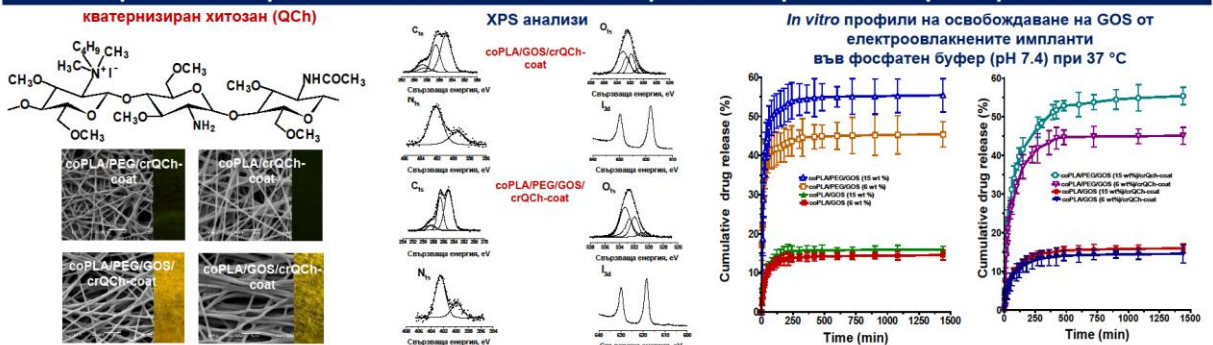
^bИнститут по експериментална морфология, патология и антропология с музей, БАН, 1113 София, България

Използването на електроовлакнени полимерни влакна като носители на антитуморни лекарствени вещества е обещаващ подход с потенциално биомедицинско приложение, особено за локална следоперативна химиотерапия. Тяхната голяма специфична повърхност и възможността за постепенно освобождаване на активното съединение води до намаляване на цитотоксичността и до подобряване на терапевтичния ефект на лекарствените вещества. Природният полизахарид хитозан, както и неговите кватернизирани производни (QCh) притежават висока антитуморна активност, както и много добро антимикробно и антимикотично действие. Съчетаването на биологичната активност на QCh с добрите антитуморни свойства на природното полифенолно съединение госипол е изключително перспективна стратегия за получаването на нановлакнести импланти за локално следоперативно лечение на солидни тумори.

Първи етап: Получаване и охарактеризиране на нановлакнести импланти, съдържащи госипол

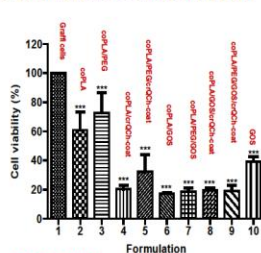


Втори етап: Покриване на имплантите с тънък филм от омрежен кватернизиран хитозан

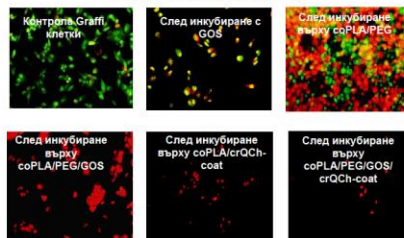


In vitro и in vivo изследване на антитуморната активност на нановлакнестите импланти

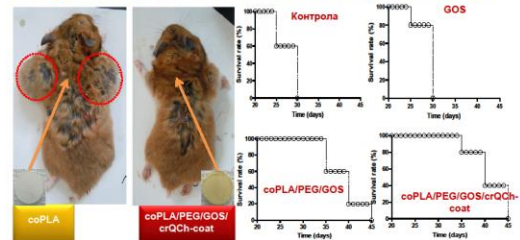
In vitro определяне на антитуморния ефект на нановлакнести матове, съдържащи GOS чрез MTT тест



In vitro флуоресцентни микрографии на Graffi туморни клетки, оцветени с акридиноранж и етидиев бромид, инкубирани за 24 ч. в присъствието на нановлакнести импланти



Фотографии от in vivo експерименти и графики на преживяемост на опитни животни, заразни със солиден миелоиден тумор на Graffi, след екстирпация на тумора и последващо поставяне на имплантите в оперативното поле



ИЗВОДИ:

Установено беше, че *in vitro* профилът на освобождаване на госипола зависи от състава на нановлакнестите импланти. Проведените *in vitro* MTT тестове показват, че нановлакнестите импланти, съдържащи QCh и GOS, проявяват по-висока цитотоксичност спрямо Graffi туморните клетки от тази на GOS. Предиизвикването на апоптоза на Graffi клетките е един от главните механизми на антитуморната активност на нановлакнестите импланти, съдържащи GOS. Локалното поставяне на нановлакнестите импланти от coPLA/PEG, покрити с филм от QCh и съдържащи GOS, в мястото на отстранения тумор води до повишаване на преживяемостта на опитните животни и до намаляване на процента на рецидиви в оперативното поле, както и на метастази в регионалните лимфни възли. Тези свойства правят получените нановлакнести импланти обещаващи като системи за освобождаване на антитуморни лекарствени вещества при локално лечение на солидни тумори.



БЛАГОДАРНОСТИ: Изследванията са разработени с финансовата подкрепа на Фонд Научни изследвания (Договор ДО-02-164/2008). К. К., Н. М. и М. И. изказват благодарност за финансовата подкрепа по Договор Polinnova.

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Получаване на смесени полимерни мицели с потенциално биомедицинско приложение



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²Катедра "Технология на лекарствените средства с Биофармация", Фармацевтичен факултет, Медицински университет-София, ул. "Дунав" 2, 1000 София, България

Въведение:

Амфифилните блокови съполимери са атрактивен клас полимерни материали, поради тяхната способност да се самоорганизират във водна среда, формирайки различни наноразмерни структури. Тези полимерни агрегати и по-специално, сферичните мицели от типа ядро-обвивка имат потенциал за приложение в медицината като системи за доставане на лекарства, туморни маркери и т.н. За синтеза на добре дефинирани блокови съполимери се използват контролираните полимеризационни техники, тъй като чрез тях могат да се получат полимери с желани състав, макромолекулярната структура и функционалност. Всички тези фактори играят важна роля при получаването на полимерните агрегати.

Цел:

Целта на тази работа е да се изследва възможността за получаване на смесени полимерни мицели от АБА - и СДС- тип амфифилни триблокови съполимери. За тази цел бяха избрани два различни триблокови съполимера, поли(етиленов оксид)₂₆-блок-поли(пропиленов оксид)₄₀-блок-поли(етиленов оксид)₂₆ (PEO₂₆-PPO₄₀-PEO₂₆; Pluronic P85) и поли(акрилова киселина)-блок-поли(ε-капролактон)-блок-поли(акрилова киселина) (ПАК-ПКЛ-ПАК). Първо, чрез радикалова полимеризация с пренос на атом (ATRP) бяха синтезирани триблокови съполимери, състоящи се от централен хидрофобен блок от биоразградимия поли(ε-капролактон) и два външни блока, съставени от поли(терт-бутил акрилат) (PtBA). След това, PtBA блоковете бяха хидролизирани до поли(акрилова киселина) с трифлуoroоцетна киселина.

Синтез и характеристики на съполимерите

HO(CH2)6CO
 поли(ε-капролактон)

BrC(CH3)2C(=O)Br
 2-бромоизобутирилбромид

TEA, толуен
20°C, 24ч

BrC(CH3)2C(=O)O(CH2)6COO(CH2)6COO(CH2)6COBr
 Br-ПКЛ-Br макроинициатор

C(CH3)2C(=O)OC(CH3)3
 терт-Бутил акрилат

CuBr/PMDETA
Толуен
50°C, 72ч
ATRP

HO(CH2)6COO(CH2)6COO(CH2)6COO(CH2)6COO(CH2)6COOH
 ПАК-ПКЛ-ПАК

CF₃COOH
CH₂Cl₂
25°C, 48ч

HO(CH2)6COO(CH2)6COO(CH2)6COO(CH2)6COO(CH2)6COOH
 ПАК-ПКЛ-ПАК

¹H ЯМР спектър на PtBA₂₂-ПКЛ₂₆-PtBA₂₂ блок съполимер в CDCl₃

¹H ЯМР спектър на ПАК₂₂-ПКЛ₂₆-ПАК₂₂ блок съполимер в DMSO-d₆

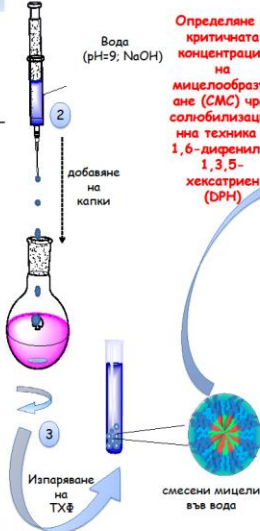
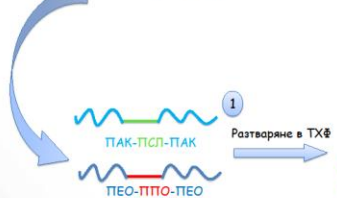
Зададен състав	Получен състав	M _n 1H ЯМР (g/mol)	M _n ГТХ (g/mol)	Mw/Mn
PtBA ₂₅ -ПКЛ ₂₆ -PtBA ₂₅	PtBA ₂₂ -ПКЛ ₂₆ -PtBA ₂₂	8640	10 310	1,17
ПАК ₂₂ -ПКЛ ₂₆ -ПАК ₂₂	ПАК ₂₂ -ПКЛ ₂₆ -ПАК ₂₂	6168	-	-

Получаване на смесени мицели

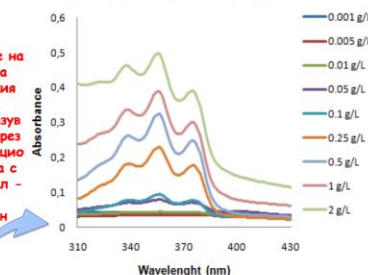
Молекулни характеристики на триблоковите съполимери, използвани в тази работа

Код	Съполимерен състав	Средна мол. маса (g/mol)	M _n ГТХ (g/mol)	Mw/Mn
Pluronic P 85	PEO ₂₆ -PPO ₄₀ -PEO ₂₆	4600*	2600	1,13
KaPCL	ПАК ₂₂ -ПКЛ ₂₆ -ПАК ₂₂	6168	-	-

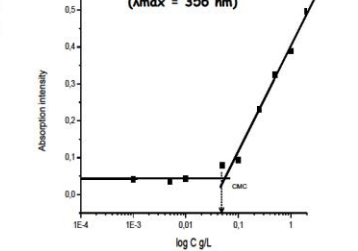
*Съгласно BASF



УВ абсорбционни спектри на DPH (0,4 μM) имобилизиран в смесените мицели във водна среда, регистрирани при температура 37°C

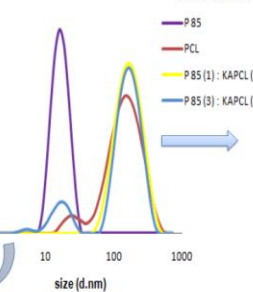


Интензитет на абсорбцията на DPH при различни полимерни концентрации при 37°C, определени 16 часа след разтварянето на багрилото в пробата (λ_{max} = 356 nm)



При концентрация на полимера, по-ниска от CMC, не се наблюдава абсорбция на DPH. След достигане на смес се формират мицели, което е придружено с рязко увеличение на абсорбцията на пробата при 37°C.

Определяне на размера на частиците, разпределението по размер и ζ-потенциала чрез динамично разсейване на светлина (DLS)



Съполимери	Молно съотношение	CMC g/L	Среден Размер (nm)	ζ-потенциал (mV)
Pluronic P 85	-	0.0341	17	-20
KaPCL	-	0.1028	25	-35
Pluronic P85 : KaPCL	1 : 3	0.081	176	-38
Pluronic P85 : KaPCL	3 : 1	0.061	174	-37

Изводи:

Успешно беше синтезиран амфифилен ПАК-ПКЛ-ПАК триблоков съполимер чрез радикалова полимеризация с пренос на атом и последваща хидролиза. Според данните от ЯМР и ГТХ, може да се заключи, че полимеризацията на двата външни блока е добре контролирана. Възможността за получаване на смесени мицели от два различни амфифилни блокови съполимери ПАК-ПКЛ-ПАК и PEO-PPG-PEO във водна среда беше потвърдено. Получените данни от DLS показват мономодално разпределение при Pluronic P85 : KaPCL в съотношение 1 : 3, което е индикация за формирането на смесени мицели, състоящи се от хидрофобно ППО/ПКЛ ядро и хидрофилна PEO/ПАК обвивка. Тези смесени полимерни мицели могат да бъдат използвани като носители на лекарствени вещества.

Данните от DLS показват мономодално разпределение при Pluronic P85 : KaPCL в молно съотношение 1 : 3, което показва формирането на смесени мицели

Cytotoxicity and cellular accumulation of cisplatin immobilized in a star-shaped polymer

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Cisplatin is the most widely used platinum-based antineoplastic agent yet characterized by severe toxicity side effects and short circulation period in the blood due to glomerular excretion. In order to reduce the side effects of the drug and to enhance its antineoplastic efficacy, it was immobilized in a star-shaped polymer carrier consisting of a hyperbranched core and arms made up from poly(acrylic acid), assigned as PSPA. Aiming to improve the performance of the therapeutic system, it was modified with PEG.

The present communication reports *in vitro* studies using a panel of tumor cell lines, carried out in order to define whether cisplatin loaded into the designed nanocarriers exerts cytotoxic effects and whether the polymeric carriers allow intracellular localization of the entrapped drug.

Synthesis of the PEGylating agent

Methoxy PEG succinate (2) was synthesized from PEG monomethylether (1) with a molecular mass 2000 g/mol and succinic anhydride (SuA). Then, PEG chains bearing a chelating carboxylate moiety at the polymer terminus were complexed with a drug molecule.

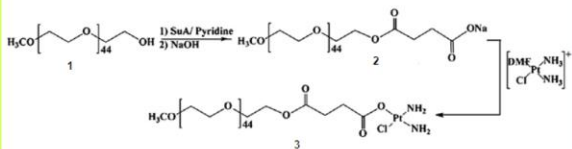


Figure 2. Synthesis of the PEGylating agent (3).

Loading of PSPA and PEGPSPA

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 8 and incubation time 24 hours.

Sample	Feeding ratio COO ⁻ : cisPt	Loading efficiency, %	Drug mass fraction in loaded particles	Drug mass fraction in original stars
PSPA*	3	80	45	45
PSPAPEG-Pt1	3	81	42	51
PSPAPEG-Pt2	2.5	79	46	55

*Data taken from Kowalczyk et al., 2011

AFM visualization of the nanoconjugates

Spherical in shape particles are observed. The dimensions of PSPA-Pt in horizontal and vertical direction calculated from the image are in the range 17-23 nm and <5 nm, respectively, and for PSPAPEG-Pt - 26-33 nm and 6 to 10 nm, respectively.

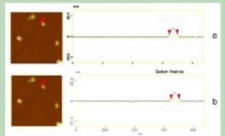


Figure 4. An AFM image of the nanoconjugates - (a) - PSPA-Pt and (b) - PSPAPEG-Pt.

Growth inhibitory activity

Table 2. Efficative IC₅₀ values of cisplatin as free drug or as PEGylated nanoconjugates against three human tumor cell lines after 72 h or 120 h exposure.

Cell line	IC ₅₀ (μmol/L)							
	cisplatin		PSPA-Pt		PSPAPEG-Pt1		PSPAPEG-Pt2	
	72 h	120 h	72 h	120 h	72 h	120 h	72 h	120 h
K-562	9.2±2.1	3.5±1.8	15.4±2±2.2	66.7±2.3	136.4*±54.7	47.2*±4.1	110.1*±27.9	38.4*±2.3
HL-60	6.4±1.1	2.9±1.2	89.6±4.1	41.7±2.8	68.4*±3.4	28.8*±1.7	57.6*±2.9	24.1*±2.2
HUT-78	3.1±1.1	2.3±0.7	46.9±2.1	24.4±1.7	35.9*±1.4	13.3*±1.7	29.4*±2.1	17.0*±2.0

K-562 - chronic myeloid leukemia; HL-60 - acute myeloid leukemia; HUT-78 - T-cell lymphoma

The growth inhibitory activity of cisplatin-loaded nanoconjugates vs. the free drug was investigated in a panel of three human tumor cell lines. Cell viability was assessed using the MTT-dye reduction assay. As expected on the basis of the drug-release monitoring studies, the IC₅₀ values for the immobilized cisplatin were higher compared to those of the free drug. PEGylation did not compromise the pharmacological effect of the system, just the opposite: the IC₅₀ values determined for the PEGylated conjugates were invariably lower than those for the nonPEGylated system.

Conclusions

A core-shell type star-shaped polymer was synthesized as a delivery vehicle for cisplatin. PEGylation of the carrier prevented crosslinking of the stars during loading and also increased the percentage of the released drug. The observed sustained manner of platinum(II) complexes from carrier is crucial for passive targeting of solid tumors. The PEGylated drug conjugates exerted enhanced growth inhibitory activity compared to the nonPEGylated system which can be attributed to the higher drug payload and improved drug release profile. Both of the nanoconjugates proved the ability to accumulate effectively within the tumor cells. On this basis it can be inferred that this new PEGylated polymer carrier represents a promising system for cisplatin delivery.

Acknowledgement
The support by the POLINNOVA project (GA 316086) is highly acknowledged

Synthetic route to the star polymers

The synthesis of the star macromolecules involved yielding a precursor star polymer with a branched polystyrene core and poly(tert-butyl acrylate) arms. Following an acidic hydrolysis of the linear arms of precursors to polyacids, polymers with branched hydrophobic interior and hydrophilic shell from poly(acrylic acid) chains were obtained.

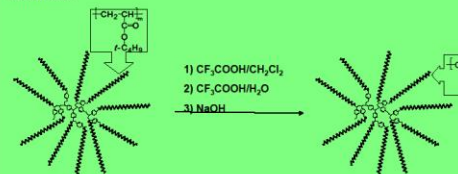


Figure 1. The route to star polymers with poly(acrylic acid) arms and branched polystyrene interior.

PEGylation of PSPA

PEGylation of the core-shell star polymer was performed in an aqueous solution applying the PEGylating agent (3). A hyperbranched structure was obtained with arms consisting of poly(sodium acrylate) and methoxy PEG succinate chains linked by a platinum(II) bridge. The obtained product was assigned as PSPAPEG.

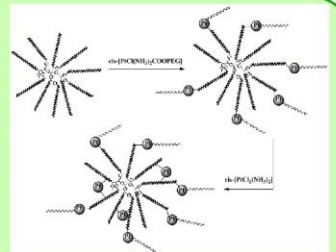


Figure 3. The route to PEGylated star polymer-cisplatin conjugates.

Release of platinum(II) complexes in physiological saline

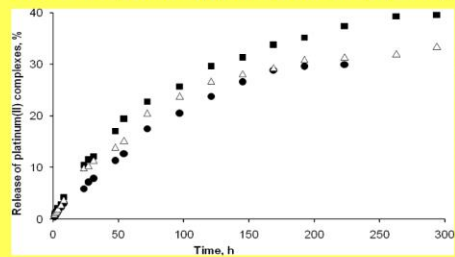


Figure 5. Release of Pt(II) complexes from drug loaded star copolymers in phosphate buffered saline (pH 7.4, 0.14 M NaCl) at 37°C: (●) PSPA-Pt (data taken from Kowalczyk et al., 2011); (○) PSPAPEG-Pt1; (■) PSPAPEG-Pt2).

Cellular uptake

In order to define whether polymer-bound cisplatin retains its ability to accumulate in cells, two tumor cell lines were exposed to cisplatin as free drug and macromolecular conjugates PSPA-Pt and PSPAPEG-Pt1 for 3 h and 24 h. Although the free drug was more rapidly and completely internalized by both cell lines, after the 24-hour-long exposition of the cells to PSPAPEG-Pt1 the intracellular levels of Pt were comparable to those, obtained after their treatment with free cisplatin. Moreover, the level of platinum uptake was not compatible with the established slow rate of drug release, especially having in consideration the short incubation periods. Hence, the measured cellular accumulation of cisplatin can be ascribed to the uptake of both pre-released complexes and endocytosed drug conjugates.

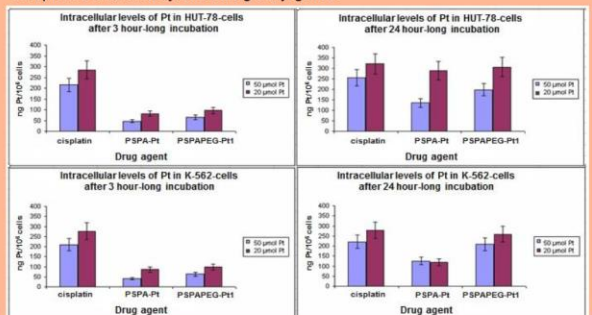


Figure 6. Intracellular levels of platinum after 3-hour and 24-hour-long exposure of tumor cells to free and immobilized cisplatin.



Получаване на нетъкан текстил при използване на усъвършенствана апаратура за електроовлажняване в центробежно поле

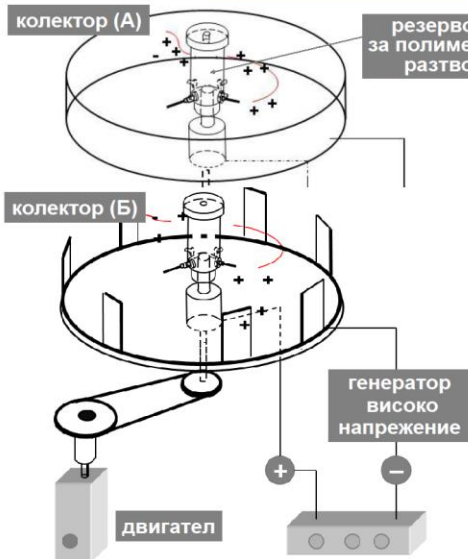


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ЦЕЛ

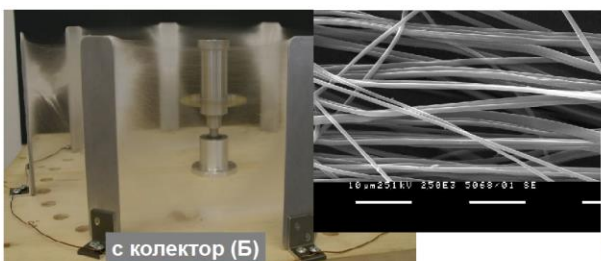
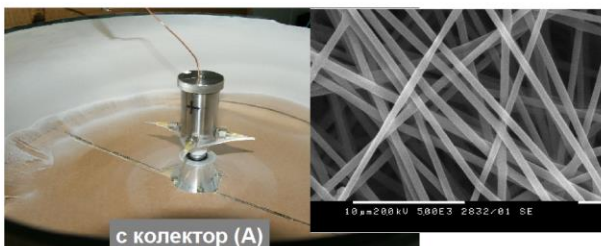
Получаване на нетъкан текстил с голяма площ чрез електроовлажняване в центробежно поле върху стационарни колектори с голям диаметър (45 см и повече) и различен дизайн. Използване на по-голям брой дюзи с цел съкращаване на времето за получаване на влакнестите материали. Изследване влиянието на якостните характеристики на получените матове.

Апаратура за електроовлажняване в центробежно поле

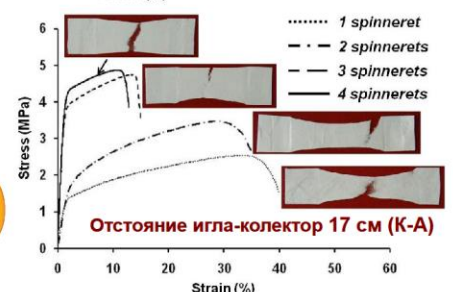
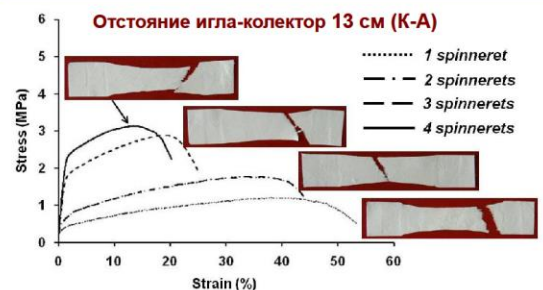


Апаратура за електроовлажняване в центробежно поле позволява да бъдат получени тъкани с голяма площ (2200 cm²) за кратко време. Специалната конструкция на резервоара осигурява неговия минимален мъртъв обем и максимално оползотворяване на пределия разтвор. Дюзите могат лесно да бъдат подменяни или да се варира отстоянието от дюзите до колекторите

Охарактеризиране



Якостни характеристики



Заклучение

Получен е нетъкан текстил от полиакрилонитрил с площ около 2200 cm² и с по-значителна дебелина при използване на колектор-А, както и текстил с подредени влакна в пространството между пластините - при използване на колектор-Б. Наблюдавано беше съществено съкращаване на времето за получаване на нетъкания текстил, както и пълно оползотворяване на разтвора. При използване на 4 дюзи времето за получаване на тъкан с площ около 2200 cm² е по-малко от 50 мин. Якостните характеристики при разстояние дюза/колектор - 13 и 17 см показаха, че с увеличаване броя на използваните дюзи тъканите стават по-здрави и се късат при по-малка деформация. С увеличаване на разстоянието дюза/колектор се увеличава здравината на получените матове. С апаратурата е възможно електроовлажняването на разтвори на различни полимери, например полистирен, полиетиленов окис, полиметилметакрилат, поливинилов алкохол и др.

DSC and WAXS studies on cold crystallization of PLLA/Montmorillonite nanocomposites

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INTRODUCTION

Poly(L-lactic acid) (PLLA) is biodegradable aliphatic polyester derived from renewable resources that has gained much interest in recent years. PLLA could become a competitive alternative to traditional commodity plastics for everyday applications from an environmental standpoint. The development of commercial applications from PLLA requires improvement of its mechanical properties, crystallization and processing behaviour. The mechanical properties and degradation rates of PLLA depend on their morphology and crystallinity. The aim of this work is thus to analyze the crystallization behaviour of PLLA/montmorillonite nanocomposites.

MATERIALS AND EXPERIMENTAL PROCEDURE

Granulated PLA has been a commercial product of the Biomer. Cloisite 30B is organically modified montmorillonite (MMT), were chosen as the clay for the nanocomposites. The organoclay and PLLA were dry under vacuum at 80°C for 12 h. To study the effect of organophilic clay concentration on the crystallization, the PLLA/MMT nanocomposites were prepared by mixing PLLA with various amounts of MMT. After melt-blending at 190°C, the samples were rapidly cooled to room temperature at a rate of -20°C min⁻¹.

RESULTS AND DISCUSSION

DSC measurements were carried out in order to study the influence of the clay load on the thermal properties of the PLLA/MMT nanocomposites. Selected thermograms are presented in Fig.1. All DSC data obtained is given in Tabs. 1 and 2. Heat of cold crystallization ΔH_{cc} decreases with increasing MMT concentration due to reduced mobility of PLLA chains, resulting in retarded cold crystallization. Glass transition temperature T_g is slightly higher for neat PLLA, which indicates that its chains are more closely packed in the glassy state; however, after crossing T_g , their mobility becomes higher (higher ΔH_{cc}). There is no trend in peak temperature of cold crystallization T_{cc} . Melting endotherms of the PLLA/MMT samples show some secondary maxima, pointing to multimodal distribution of lamellae.

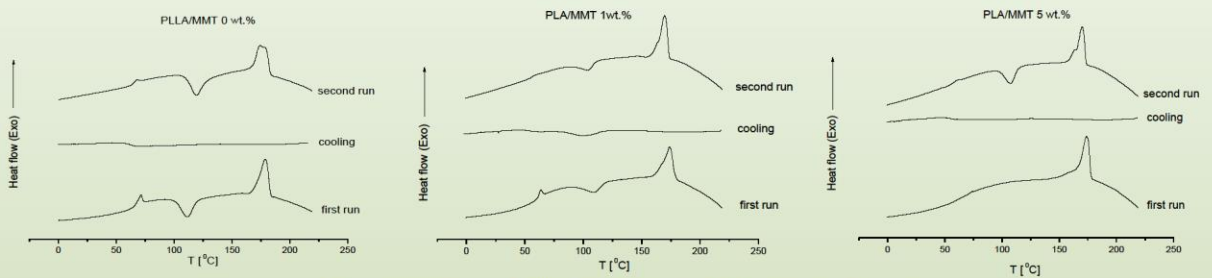


Figure 1. Selected DSC thermograms of PLLA and PLLA/MMT composites (first, second heating runs and cooling)

Sample	1st heating run			Cooling	2nd heating run		
	ΔH_{cc} [J/g]	ΔH_m [J/g]	Δ^*		ΔH_{cc} [J/g]	ΔH_m [J/g]	Δ^*
PLA0M	-25.3	35.0	9.7	0	-33.9	34.5	0.6
PLA1M	-17.9	37.5	19.6	-14.3	-12.6	43.5	16.6
PLA3M	-15.2	38.8	23.6	-1.7	-25.5	36.4	9.2
PLA5M	0	49.5	49.5	-2.4	-22.5	39.3	14.4
PLA7M	0	42.1	42.1	-1.2	-23.1	36.4	12.1
PLA9M	0	38.9	38.9	-3.4	-27.7	37.3	6.2

Table 1. Thermal properties of PLLA/MMT composites with different MMT load (calculated from DSC data). $\Delta^* = \Delta H_{cc} + \Delta H_m$

Sample	1st run				Cooling		2nd run					
	T_g [°C]	T_{cc} [°C]	T_m [°C]		T_g [°C]	T_{mc} [°C]	T_d [°C]	T_{cc} [°C]	T_m [°C]			
PLA0M	65.9	111.4	-	-	178.7	-	61.5	-	64.4	119.4	175.5	178.0
PLA1M	60.4	109.7	166.0	174.0	-	-	54.3	100.1	56.3	103.9	163.0	169.7
PLA3M	61.7	110.0	-	173.5	178.6	-	58.4	96.5	59.5	112.2	166.2	172.5
PLA5M	63.8	-	157.0	174.0	-	-	55.7	100.3	56.5	107.6	163.5	170.1
PLA7M	62.2	-	158.4	173.6	178.0	193.7	57.3	97.5	59.6	107.0	165.0	171.6
PLA9M	61.6	-	157.0	173.0	-	-	53.8	97.4	57.3	106.0	163.5	171.8

Table 2. Values temperatures of PLLA/MMT composites with different weight ratio of MMT collected from DSC thermograms.

CONCLUSIONS

In the present study, we investigated the effects of organophilic MMT (Cloisite® 30B) upon non-isothermal crystallization of PLLA. Thermal measurements reveal that in neat PLLA, PLLA 1wt.% MMT and PLLA 3 wt.% MMT nanocomposites, cold crystallization takes place. In nanocomposites with 5, 7 and 9 wt.% clay loading the heat of cold crystallization disappears. This phenomenon has to be attributed to hindered PLLA chains movement in the clay galleries. On melting during the first run, PLLA chains are released from the organized composite structure and subsequently undergo melt and cold crystallization during cooling and reheating. This significant alteration of the PLLA crystallization behavior has to be definitely attributed to the presence of Cloisite® 30B organophilic clay in the system.

ACKNOWLEDGMENT

This work is supported by Bulgarian Ministry of Education, Youth and Science and Institute of Polymers, Bulgarian Academy of sciences.

Similarly to the first runs, the highest heat of cold crystallization ΔH_{cc} was found for neat PLA. However, unlike the first runs, intensive cold crystallization was also detected for all PLA-MMT samples. Melting endotherms of all samples in the second run show two peaks indicating bimodal distribution of lamellae. Both peaks of neat PLA are found at significantly higher temperatures, which suggests higher perfection of the crystallites.

The WAXS patterns of neat PLLA and PLLA/MMT. It can be clearly seen that the sample PLA0M, PLA1M and PLA3M is completely amorphous. In contrast, the PLA5M, PLA7M and PLA9M composites are highly crystalline. The WAXS patterns of these samples show many diffraction peaks and agrees well with the orthorhombic crystal structure, which has been assigned as α -form. The parameters of the calculated unit cell are: $a = 10.55 \text{ \AA}$, $b = 5.91 \text{ \AA}$, $c = 9.42 \text{ \AA}$.

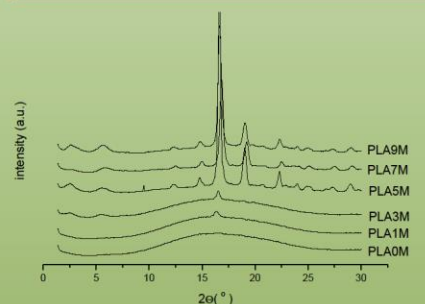


Figure 2. WAXS patterns of PLLA and PLLA/MMT composites with different weight ratio.



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Абстракт: Това изследване е насочено към търсене на възможности за подобряване на работните условия и повишаване на енергийната ефективност на пречиствателни станции за пречистване на битови отпадъчни води, прилагачи процесите на автотермално термофилно аеробно разграждане на утайките (Autothermal Thermophilic Aerobic Digestion – ATAD), при което се получава биотор. Идеята за това идва от системни наблюдения върху такъв тип системи, при които е било установено, че постъпването на всяка нова порция отпадъчни води до причиняване на термичен шок за термофилните микроорганизми, което се дължи на рязкото спадане на температурите в първите реакторни стъпала и колебания в температурите в цялата система. Това от своя страна удължава времето, необходимо за достигане на нормалните работни условия на системата и увеличава разходите за енергия за разбъркване и аериране на биореакторите. Проблемът за редуциране на термичния шок може да бъде решен чрез прилагане на енергийна интеграция на процесите в системата. За тази цел, обаче е необходимо да се преодолеят несигурностите в параметрите на входящите сурови утайки, за да се гарантират по-устойчиви работни условия на пречиствателните съоръжения.

Автотермално Термофилно Аеробно Разграждане

ATAD процесът

- използва аеробни термофилни микроорганизми с екзотермичен метаболизъм за биохимично окисление на органични вещества в битови отпадъчни води;
- е автотермален – отделената топлина служи за разграждане на утайките и пастьоризация на патогените в отпадъчните води;
- има висока реакционна скорост и използва биореактори с малки размери.



Конвенционални индустриални ATAD системи

- паралелни серии от два последователно свързани биореактора с аерация и разбъркване



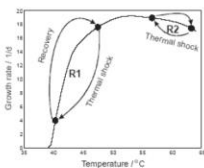
Спирален аератор Централен аератор

Условия на работа на ATAD системите:

- един път на ден обработваните утайки се зауват като "продукт" – биотор и системата се захранва с нова порция отпадъчни води. Хидравличното време на задържане е ~ 6-7 дни;
- обработване на утайките при различни температури:
 - ❖ необходими работни температури за биореакторите от първия етап ~ 55°C – оптимална за бактериалния растеж;
 - ❖ необходима работна температура за биореакторите от втория етап ~65°C – най-добра за пастьоризация.

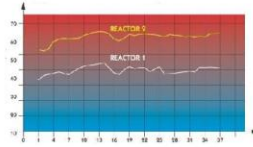
Основни проблеми при индустриалните ATAD системи

•термичен шок на микроорганизмите;



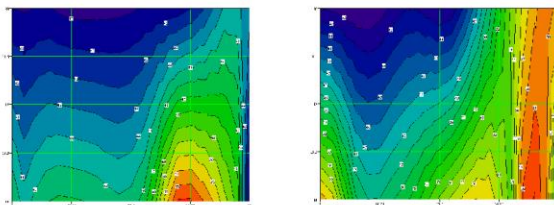
Темп на растеж на термофилите като функция на температурата.

•температурни колебания в двата биореактора;



Температури в конвекционална двуреакторна ATAD система

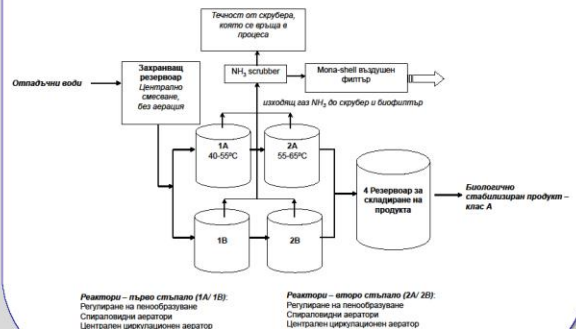
•наличие на ежедневни несигурности в параметрите на постъпващите отпадъчни води;



Фиг.1

Фиг.2

Въздействие на несигурностите в хидравличното натоварване и температурата на заредената сурова утайка, върху пада на температурата (фиг. 1) и температурата в края на процеса (фиг.2) в първият реактор.



Пътища за контрол върху температурата

- подаване на по-разредени утайки - води до намаляване на капацитета на системата.
- промяна на продължителността на цикъла чрез подаване на по-малки количества утайка - увеличава се хидравличното време на задържане.
- рекулерация на наличната топлина в системата - ще ограничи температурните колебания в реакторите от първия етап и потенциално ще допринесе за по-кратко време на задържане и увеличаване на производителността на системата.

Енергийна интеграция при ATAD системи. Проблеми.

- процесите са периодични и кандидат-потоците за топлинна интеграция са изместени във времето.
- несигурностите в оценките на температурите на кандидат-потоците участващи в задачите за топлинната интеграция.
- проблемът за енергийната интеграция трябва да се разглежда като проблем на стохастичната оптимизация.



БЛАГОДАРНОСТИ

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Novel Amalgam Mediated Synthesis of Metal, Alloy and Metal Oxide Nanoparticles

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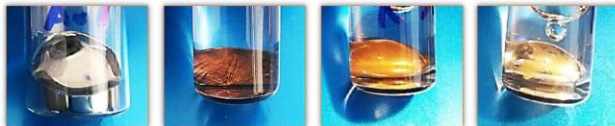
Hg + Au in THF

INTRODUCTION

- A simple and novel method for synthesis of **Metal and Metal Oxide** nanoparticles are presented hereby
- The technique may be extended to all metals that form amalgams (exceptions are iron, platinum, tungsten and tantalum) and their corresponding binary or higher **Alloys** to synthesize custom nanoparticles with design properties.
- At low concentrations, most metals readily dissolve in mercury liquid at room temperature and above. Driven by thermodynamics and possible relativistic effects dissolved metal is extracted into organic solvent at mercury-solvent interface in form of nanoparticles (NP).

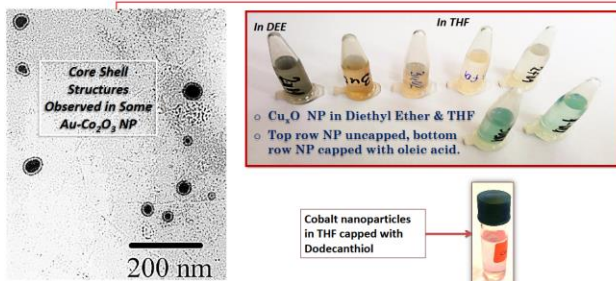
THE SYNTHESIS

- Mercury is the only liquid (and thus amorphous) metal at room temperature exhibiting weak metallic bonding and exceptionally high surface free energy.
- At low concentrations, a crystalline solid metal at room temperature, dissolves in liquid mercury and stay as weakly bound clusters.
- At mercury-organic solvent interface the dissolved metal is in metastable amorphous state weakly bound to mercury. Fluctuations can release the interfacial metals atoms in form of crystalline nanoparticles with lower free energy.
- The NPs can then be stabilized by standard sensitizing capping reagents.
- Solution is filtered by 450nm cartridge.



I. (Au + Co) in Hg II. THF is Added III. Surfactant is Added IV. Gently Shaken

SOME TYPICAL EXAMPLES

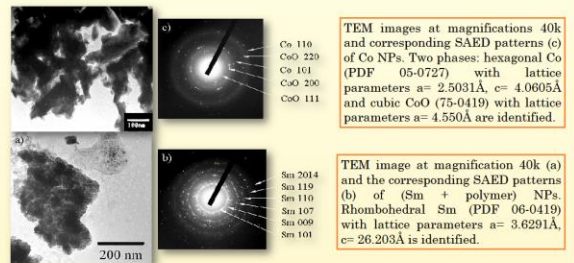


CONCLUSIONS

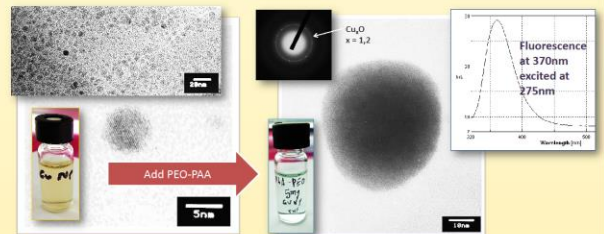
- Novel syntheses for metal, alloy & oxide nanoparticles is presented.
- The technique is purely physical and simple.
- Designer alloy nanoparticles for optoelectronics, medicine, sensors, etc.
- Morphology, crystallinity, color, oxidation state and size distribution varies with temperature and with capping agents.
- No control on nanoparticle size, dispersion mode & morphology.
- Both core sheath & single phase alloy nanoparticles have been observed.
- Process involves Mercury and appropriate caution has to be exercised.
- Mercury has not been detected in the nano particles.
- Spectroscopic techniques are used to characterize and differentiate between various nanoparticles and their compositions.
- Migration of metal atoms to Hg-THF interface is yet to be understood.

RESULTS

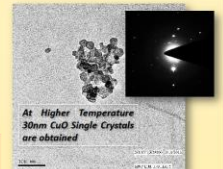
Metal Nanoparticles in PEO-PAA



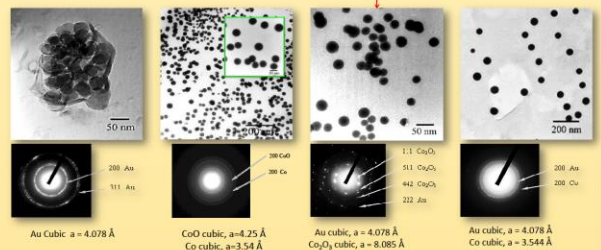
Copper Oxide Quantum Dots



On addition of Polyethylene oxide-co-acrylic acid surfactant the CuO NPs aggregate into larger polymer spherical enclosures. The color of the solution is changed from yellow to blue due to surface complexation.



Binary Alloy Nanoparticles (Au + Co)



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ucalneel

Physicochemical and toxicological properties of polyglycidol-grafted liposomes

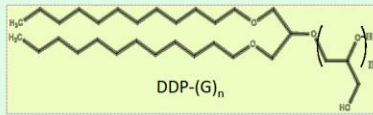
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Following the growing needs of improvement the chemotherapy in the oncology field, researchers are paying more attention to new or optimized drug delivery systems as well as to synthesis of new drug molecules. Interesting objects, used as vehiculum, are liposomes. Consisting of phospholipid molecules, self-assembled in bilayer structure, which encloses large hydrophilic cargo volume, liposomes can be loaded with both hydrophilic and hydrophobic drugs. However, plain liposomes are characterized by short life-time, when applied *in vivo*, due to fast recognition by the mononuclear phagocyte system cells and burst leakage of the loaded therapeutic agent. Introduction of small amounts of polyethylene glycol (PEG) derivatized lipids in the liposomal membrane leads to stabilization and prolongation of their life time *in vivo*. Shortcomings, associated with the presence of carbamate linkage and lack of functional groups to be conjugated with bioactive molecules (vitamins, monoclonal antibodies etc.) in order to provide target action of the liposomes have been frequently reported.

The aim of this study is to evaluate the potential of linear polyglycidols conjugated to lipid-mimetic residue (1,3-didodecyloxypropane-2-ol, DDP) to provide steric stabilization of liposomes based on dipalmitoylphosphatidylcholine and to investigate the physicochemical properties of resulting liposomes. The cytotoxicity of the polyglycidol-grafted liposomes is investigated as well.

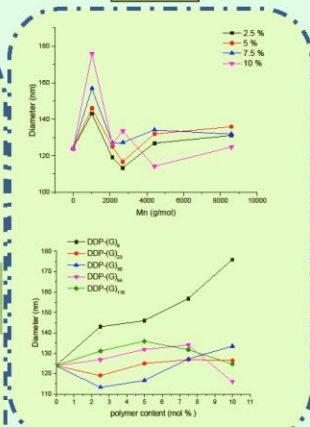
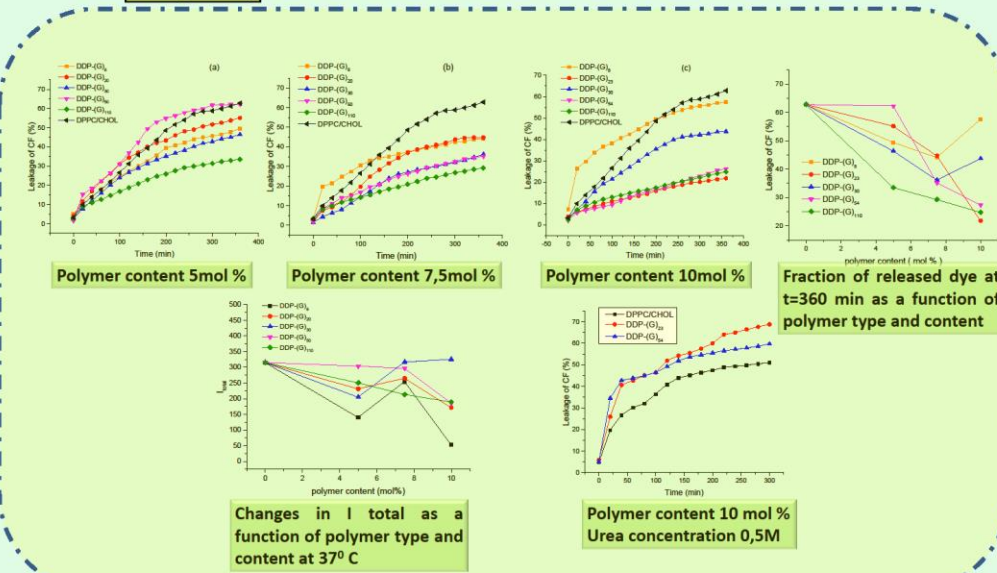


DDP-polyglycidol	Mn(nmr)	PDI (GPC)
n = 8 DDP-(G) ₈	1020	1.44
n = 23 DDP-(G) ₂₃	2130	1.35
n = 30 DDP-(G) ₃₀	2700	1.39
n = 54 DDP-(G) ₅₄	4420	1.26
n = 110 DDP-(G) ₁₁₀	8570	1.36

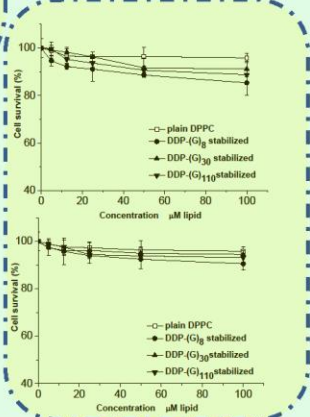
Leakage assay

Physicochemical characterization of DPPC/CHOL liposomes

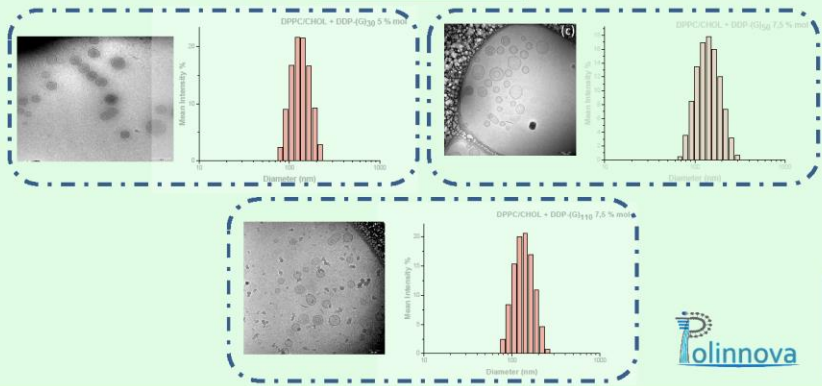
DLS data



Cytotoxicity



Cryo TEM micrographs



Cytotoxicity of DPPC:CHOL liposomes, plain or grafted with 10 mol% DDP-(G)₈, DDP-(G)₃₀ and DDP-(G)₁₁₀ against EJ (up) and OPM (down) cell lines

DPPC/CHOL liposomes containing different (2.5 – 10 mol %) amounts of DDP-polyglycidol conjugates were successfully prepared. The experimental data, obtained from the *in vitro* leakage assays clearly indicate a stabilization effect of the polymers. Additional experiments in urea containing media revealed the role of intermolecular hydrogen bonding in the polyglycidol layer around the liposomes in reducing the membrane permeability. The liposomes, sizing 112 - 180 nm, were intact and well-separated, judging by cryo-TEM images. Disc-like micelles at high polymer contents were observed. Toxicology tests indicate lack of cytotoxicity against EJ and OPM cells.

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