





**Институт по полимери, БАН**

**Петнадесета научна сесия**

**„МЛАДИТЕ УЧЕНИ В СВЕТА НА  
ПОЛИМЕРИТЕ“**



**6 юни, 2024г.**



## **Програма на научната сесия:**

**10:30-10:40 ч. Откриване**

**10:40-11:30 ч. Представяне на доклади**

**13:30-15:30 ч. Представяне на постери**

**15.30-15.50 ч. Награждаване на отличени  
постери и доклади**

**15.50-16.00 ч. Закриване**

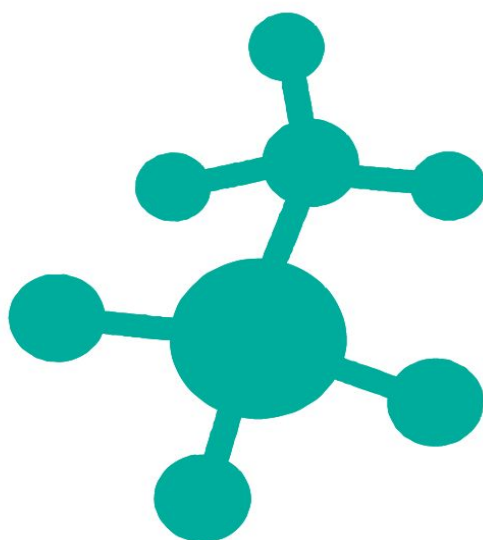


### **Място на провеждане**

**Заседателна зала и фоайе\* на Институт по полимери,  
БАН ул. Акад. Г. Бончев, бл. 103-В, гр. София**

**\*при подходящи метеорологични условия, постерната сесия ще се състои в  
откритото пространство пред Института по полимери**

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Румена Станчева<sup>1</sup>, Еми Халаджова<sup>1</sup>, Мария Петрова<sup>2</sup>, Ива Угринова<sup>2</sup>, Ивайло Димитров<sup>1</sup>, Станислав Рангелов<sup>1</sup>

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## Доклад № 2

**Дизайн на хибридни влакнести материали от поли(L-лактид-съ-D,L-лактид) за фотокаталитично пречистване на води**

Ина Анастасова, Петя Цекова, Милена Игнатова, Оля Стоилова

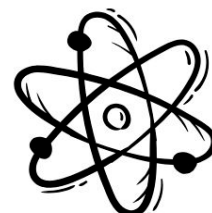
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Ерик Димитров, Сибела Долева, Наталия Тончева-Мончева, Станислав Рангелов

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Л. Радева, Й. Йорданов, В. Цанкова, К. Йончева

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Severina Semkova<sup>1</sup>, Radina Deneva<sup>1</sup>, Georgi Antov<sup>2</sup>, Donika Georgieva<sup>3-4</sup>, Zvezdelina Yaneva<sup>3</sup>, Biliana Nikolova<sup>1</sup>

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Denitsa Hristova<sup>1</sup>, Emi Haladjova<sup>1</sup>, Natalia Oleszko-Torbus<sup>2</sup>, Agnieszka Kowalczuk<sup>2</sup>, Stanislav Rangelov<sup>1</sup>

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Rumena Stancheva<sup>1</sup>, Tsvetozara Damyanova<sup>2</sup>, Dayana Borisova<sup>2</sup>, Ralitsa Veleva<sup>3</sup>, Petya Dimitrova<sup>2</sup>, Katya Kamenova-Stoyanova<sup>1</sup>, Tanya Topouzova-Hristova<sup>3</sup>, Tsvetelina Paunova-Krasteva<sup>2</sup>, Stoyanka Stoitsova<sup>2</sup>, Petar Petrov<sup>1</sup>, Emi Haladjova<sup>1</sup>

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Владимир Кръстев, Мария Спасова, Оля Стоилова

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Eftychia Gkalekou<sup>1-3</sup>, Emi Haladjova<sup>1</sup>, Antoaneta Trendafilova<sup>2</sup>, Viktoria Ivanova<sup>2</sup>, Ivaylo Dimitrov<sup>1</sup>, Stanislav Rangelov<sup>1</sup>

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A.Prancheva<sup>1</sup>, K. Kamenova<sup>1</sup>, L.Radeva<sup>2</sup>, S.Mitova<sup>3</sup>, K. Yoncheva<sup>2</sup>, P.Petrov<sup>1</sup>

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К. Каменова<sup>1</sup>, В. Гуглева<sup>2</sup>, Р. Михайлова<sup>3</sup>, Г. Момеков<sup>3</sup>, А. Форис<sup>4</sup>, Б. Тржебицка<sup>4</sup>, Д. Момекова<sup>3</sup>, П. Петров<sup>1</sup>

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Наско Начев, Мария Спасова, Оля Стоилова

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Mariela Alexandrova, Sijka Ivanova, Maya Staneva, Darinka Christova

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Борислава Младенова<sup>1</sup>, Мая Станева<sup>2</sup>, Галин Борисов<sup>1</sup>, Евелина Славчева<sup>1</sup>

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Sibela Doleva, Erik Dimitrov, Natalia Toncheva-Moncheva, Ch. Novakov, Stanislav Rangelov

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Niya Delcheva, Erik Dimitrov, Natalia Toncheva-Moncheva, Stanislav Rangelov

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Теодора Димитрова, Марин Симеонов, Елена Василева

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Савина Колева, Деница Николова, Елена Василева

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Крум Александров<sup>1</sup>, Ерик Димитров<sup>1</sup>, Наталия Тончева-Мончева<sup>1</sup>, Павлета Шестакова<sup>2</sup>, Станислав Рангелов<sup>1</sup>

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Dragomir Vassilev<sup>1,2</sup>, Vesela Stefanova<sup>3</sup>, Kostadin Zhekov<sup>3</sup>, Todor Petrov<sup>1</sup>, Lyubomir Stoychev<sup>1</sup>

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# Доклади



# Доклад 1

## ПОЛИМЕРНИ МИЦЕЛИ ОТ СМЕСЕН ТИП НА ОСНОВАТА НА ПОЛИПИПЕРАЗИНИ КАТО ВЕКТОРИ ЗА ПРЕНОС НА ГЕНИ

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Целта на настоящото изследване е дизайн на нови биосъвместими невирусни системи за пренос на гени на основата на смесени полимерни мицели (СПМ). В тази връзка бяха получени полимерни мицели от катионен поли(4-метил-пиперазин-1-ил)-пропенон-бл-полилактид и нейногенен поли(етилен оксид)-бл-поли(пропилен оксид)-бл-поли(етилен оксид) блокови съполимери. СПМ бяха използвани за получаване на мицелплекси с ДНК. Системите бяха охарактеризирани, като бяха определени техните размер, повърхностен потенциал, буферен капацитет и афинитет на свързване с ДНК. Беше изследвано влиянието на състава на СПМ върху свойствата и структурата на получените мицелплекси. Допълнително бяха симулирани условия, наподобяващи тези в ендолизозомите, за да се проследят промените на основните физико-химични параметри на системите. Беше оценена биосъвместимостта на получените СПМ и техните мицелплекси, като беше наблюдаван ефект от дължината на нейногенния компонент. Системите се характеризираха с добро клетъчно усвояване и способност да трансфектират плазмид, кодиращ зелен флуоресцентен протеин (pEGFP-N1).

### **Ключови думи:**

Мицелплекси, катионни съполимери, ДНК, трансфекция

### **Благодарности**

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# Доклад 2

## ДИЗАЙН НА ХИБРИДНИ ВЛАКНЕСТИ МАТЕРИАЛИ ОТ ПОЛИ(L-ЛАКТИД-СЪ-D,L-ЛАКТИД) ЗА ФОТОКАТАЛИТИЧНО ПРЕЧИСТВАНЕ НА ВОДИ

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Предложен е оригинален, лесен и ефективен подход за създаване на хибридни влакнести материали с подходящ дизайн за фотокаталитично пречистване на води от органични замърсители. Поли(L-лактид-съ-D,L-лактид)ът (PLDLLA) е избран като подходящ съполимер, тъй като е биоразградим и биосъвместим, аморфен е и се разгражда по-бързо от хомополимера. Като фотокатализатор е избран цинковият оксид (ZnO) поради своята биосъвместимост, ниска токсичност и добра антимикробна активност спрямо редица патогени. При това, ZnO се отличава с отлична УВ-абсорбция и фотокаталитична активност, която не зависи от рН на средата. Така, чрез комбиниране на свойствата на PLDLLA и на ZnO, са получени хибридни влакнести с насочен дизайн, като са приложени методите електроовлажняване и електроразпръскване. Морфологията на получените хибридни влакнести материали е наблюдавана със СЕМ, снабден с EDX и с ТЕМ, а кристалността и термичните им свойства са изследвани с XRD и с TGA. Чрез DPPH тест за свободни радикали е доказано, че включването на ZnO значително повишава антиоксидантната активност на хибридните материали. Нещо повече, те запазват своята фотокаталитична активност при облъчване с УВ-светлина спрямо моделния органичен замърсител метиленово синьо, дори и след 5-кратно използване. Тези предимства показват потенциала на новите материали като ефективни средства за пречистване на води от органични замърсители.

### **Ключови думи:**

електроовлажняване, електроразпръскване, поли(L-лактид-съ-D,L-лактид), ZnO, фотокаталитична активност

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# Доклад 3

## СИНТЕЗ НА СЪПОЛИМЕРИ НА ПОЛИ(2-ИЗОПРОПИЛ-2-ОКСАЗОЛИН) И ПОЛИЕТИЛЕНИМИН С ПОТЕНЦИАЛНИ ПРИЛОЖЕНИЯ ЗА ГЕННА ТЕРАПИЯ

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През последните години полимерите от класа на поли(2-алкил-2-оксазолините) привличат значително внимание, поради техните потенциални приложения във фармацията и медицината. Голяма част от тези полимери са хидрофилни, нетоксични и биосъвместими, което ги прави подходящи за доставка на лекарствени, биологично активни вещества и протеини. Друг широко употребяван полимер е полиетилениминът, известен още като „златния стандарт“ за генна трансфекция. Той има способността да формира стабилни полиелектролитни комплекси с нуклеиновите киселини, улеснявайки приема им от клетките чрез ендоцитоза. Въпреки това високата токсичност на полиетиленимина остава предизвикателство, ограничаващо възможностите му за приложение. За да бъде намален този ефект, бяха синтезирани блокови съполимери на полиетиленимин и поли(2-изопропил-2-оксазолин) чрез използване на различни подходи, включващи синтез на инициатори, катионна полимеризация с отваряне на пръстена на 2-алкил-2-оксазолини, функционализация на полимери и използването на високоефективни „клик“ химични реакции. Бяха проведени серия експерименти, целящи намиране на оптимални условия за селективна хидролиза на поли(2-етил-2-оксазолин)овия блок, като по този начин беше получен подобрен трансфектант с квази-блокова архитектура. Свойствата на получените блокови съполимери на поли(2-изопропил-2-оксазолин) и полиетиленимин както и възможностите за тяхното приложение във фармацията и медицината предстои да бъдат изследвани.

### Ключови думи:

полиетиленимин, генна трансфекция, поли(2-алкил-2-оксазолин)и, селективна хидролиза

### Благодарности

В тези изследвания е използвано оборудване на Разпределената научна инфраструктура ИНФРАМАТ, част от Националната пътна карта на България за научна инфраструктура, подкрепена финансово от Министерство на образованието и науката.

# Постери



## Стратегия за подобряване на ранозаздравяващото действие на ресвератрол чрез комплексообразуване с циклодекстрин и формулиране в хидрогел

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### Въведение

Ресвератролът е природен антиоксидант, който притежава потенциален ранозаздравяващ ефект. Разтворимостта му във вода обаче е много ограничена (0.05 mg/mL), което възпрепятства неговото приложение. Хидроксипропил-β-циклодекстринът е комплексообразувател с ниска токсичност и висока хидрофилност, което му дава възможност да повишава значително разтворимостта на хидрофобни вещества. Целта на настоящото проучване е оптимизиране на метод за получаване на комплекс между ресвератрол и хидроксипропил-β-циклодекстрин, изследване на възможността на системата за подобряване на ранозаздравяващия ефект на ресвератрол и последващото инкорпориране на комплексите в хидрогел за дермално приложение.

### Получаване на комплексите

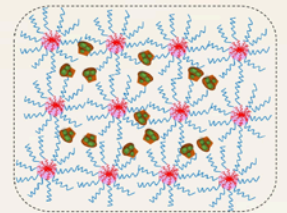
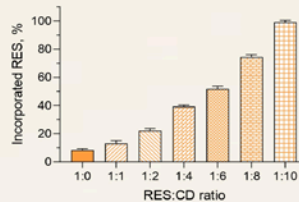


Комплексите са получени по метод на изпаряване на разтворителя. Проучени са възможностите за инкорпориране при различни съотношения между ресвератрол и хидроксипропил-β-циклодекстрин.

### Охарактеризиране на комплексите и формулиране в хидрогел

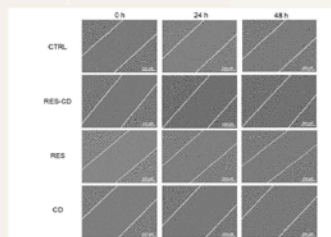
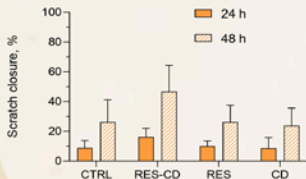
При съотношение на ресвератрол към циклодекстрин 1:10 (тг/тг) се наблюдава най-висок процент на инкорпориране на веществото в комплекса.

Комплексите са включени в хидрогел, формиран от Pluronic F127.



### Тест с надрасване на фибробласти

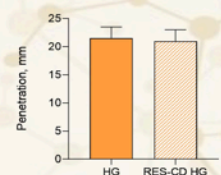
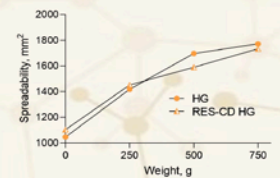
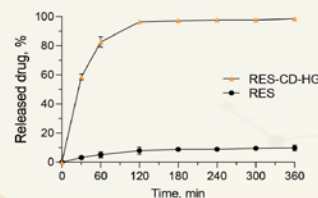
Резултатите от теста с надрасване показват тенденция за подобряване на ранозаздравяващото действие на ресвератрол след комплексообразуване.



### Охарактеризиране на хидрогела

Наблюдаваните стойности на разстилане и пенетрометрия са оптимални за дермално приложение.

Резултатите от *in vitro* тест за освобождаване показват постигане на повишена разтворимост на инкорпориания ресвератрол в сравнение с чистото вещество.



### Заклучение

Включването на ресвератрол в комплекси от хидроксипропил-β-циклодекстрин е подходяща стратегия за повишаване на разтворимостта му, което довежда и до потенциране на ранозаздравяващите му ефекти. Увеличаването на хидрофилността на веществото улеснява и последващото му формулиране в хидрогел. Получената хидрогелна форма показва подходящи за дермално приложение характеристики.

### Благодарности

Настоящата работа е разработена с финансова подкрепа по Договор № Д-212/03.08.2023 към СМН на Медицински Университет – София.

# New $\zeta$ -potential based procedure for separation of Lignin based micro-/nano-formulations for *in vitro* applications

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## Introduction

These days micro-/nano- polymer formulations are increasingly applied in both *in vitro* and *in vivo* drug research. Due to its natural origin, a highly branched biopolymer Lignin has a significant potential as a carrier.

The optimisation of the size of the micro-/nano-formulations is crucial for ensuring experimental consistency and to avoid negative influence on cell vitality. Achieving optimal size during manufacture is still a difficult task. Moreover, the concentration determination for *in vitro* application after purification procedures is an even greater challenge in case of biopolymer formulations, composed from units without spectral characteristics.

In this study we propose a novel procedure for size-dependent separation of Lignin based micro-/nano- formulations via using low-spin centrifugation and a new protocol for calculation of relative particles concentration.

Biopolymer Formulation's SIZE

CONCENTRATION (*in vitro* research)

## Results

Table 1. Change of size and  $\zeta$ -potential after centrifugation

Formulation's type	Size		$\zeta$ - potential	
	Before	After	Before	After
Lignin@	310.7 nm (74.66%)	79.88 nm (46.78%)	-31.48	-25.35
Lignin@Naringenin	488.7 nm (55.72%)	125.6 nm (46.39%)	-33.78	-19.37

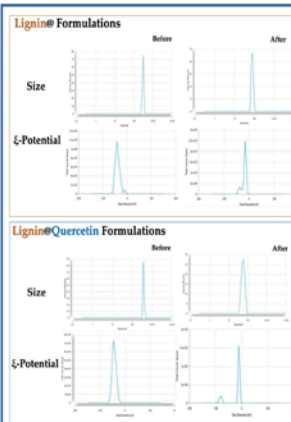


Figure 1. Size and  $\zeta$ -potential data from Zetasizer Nano ZS analyzer before and after centrifugation

Table 2. Change of concentrations after centrifugation

Calculations via DLS data by Formula:  $(U-Z)/(Y-Z) \cdot X$

Parameter	Formulation's type	
	Lignin@	Lignin@Naringenin
Y <sup>1</sup>	-31.48	-33.78
U <sup>2</sup>	-25.35	-19.37
X <sup>3</sup>	0.05 mg/mL	0.0247 mg/mL
Z <sup>4</sup>	-10.34 (d.f., 0)	
Calculated Relative concentrations after centrifugation	0.035 mg/mL	0.0247 mg/mL

## Materials and Methods

4 types of Lignin based biopolymer micro-/nano- formulations:

- Empty formulations
- loaded with Naringenin
- loaded with Quercetin
- loaded with Morine

- Zetasizer Nano ZS analyzer (Malvern Instruments, UK)
- Vivaspin™ centrifugal concentrators & Centrifuge
- Human breast cancer cell line (MDA-MB-231)
- Leica DMIL microscope
- Tecan Infinite F200 PRO™ (Tecan, Austria)

- Dynamic light scattering & electrophoretic light scattering techniques
- MTS-based cytotoxicity assay
- Microscopy

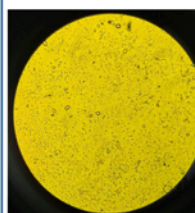


Figure 2. Microscopic images of formulations after centrifugation

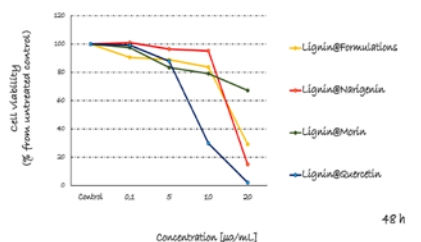
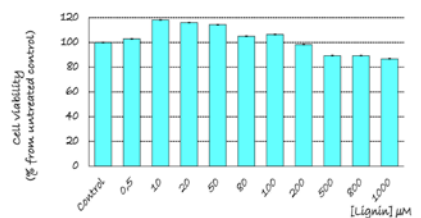


Figure 3. Cell viability of human breast cancer cell line MDA-MB-231 48 hours after treatment with Lignin monomer and size-separated micro-/nano- formulations

## Acknowledgements

This work was supported by the Bulgarian Scientific Fund under Contract № KP-06-N59/3. The authors thank the Bulgarian Ministry of Education and Science for the support provided via the "National Center for Biomedical Photonics" D01-352/2023 (Zetasizer Nano ZS analyzer), part of the Bulgarian National Roadmap for Scientific Infrastructures 2020-2027.



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## Conclusions

By using this novel procedure, we successfully purified the initial Lignin based formulations, separated particles by size and proposed the methodology for calculation of their relative concentration. Additionally, we concluded that these formulations are suitable for *in vitro* experiments after applying this new optimised protocol.



## Physicochemical Properties of Gene Delivery Vector Systems Based on Functionalized Polyoxazolines: Influence of Various Environmental Conditions

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<sup>2</sup> Centre of Carbon and Polymer Materials, Polish Academy of Sciences, Marii Curie-Skłodowskiej 34 41-819 Zabrze, Poland



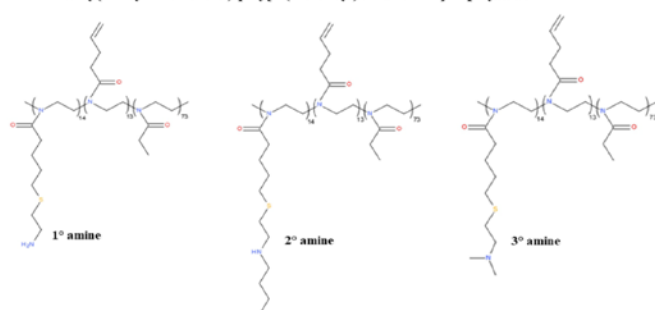
### INTRODUCTION

The exogenous DNA delivery in the human body is of great importance since it enables the development of modern therapeutic drugs and treatment strategies. In the current research, the potential of poly(2-ethyl-2-oxazoline)-poly[2-(3-butenyl)-2-oxazoline] copolymers functionalized with primary, secondary or tertiary amino groups as gene vectors was investigated.

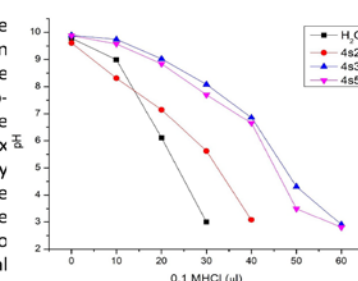
### POLYMER STRUCTURES AND MOLECULAR CHARACTERISTICS

The type and the ratio of amino functionalities in the macromolecules are essential for their complexation ability, release properties and biocompatibility. Here we used three identical copolymers differing in the type of amino functional groups to follow their influence on the polyplexes properties.

Poly(2-ethyl-2-oxazoline)-poly[2-(3-butenyl)-2-oxazoline] copolymers

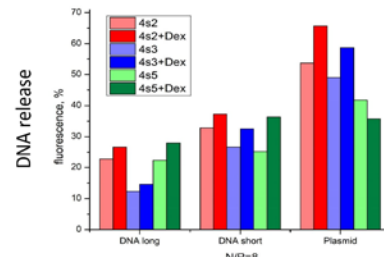
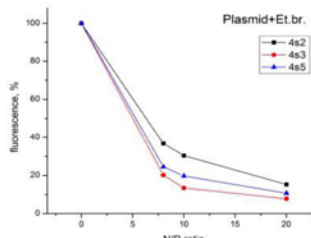
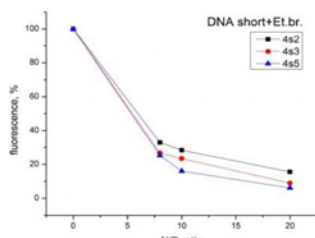
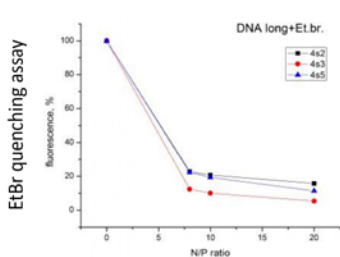


The buffering capacity of the (co)polymers is related to the proton sponge effect and together they are considered responsible for endo-lysosomal escape of polyplexes. The buffering capacity of the PEtOx-PBtOx copolymers was estimated by standard acid-base titration. Despite the low content of amino groups the copolymers showed capacity to escape the endo-lysosomal compartment.



### COMPLEXATION WITH DNA

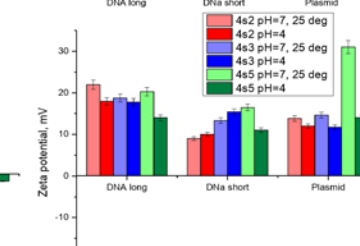
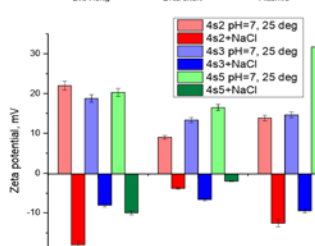
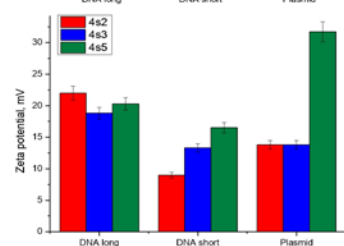
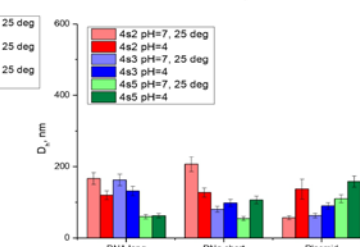
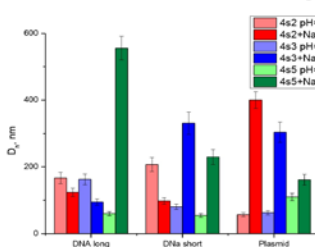
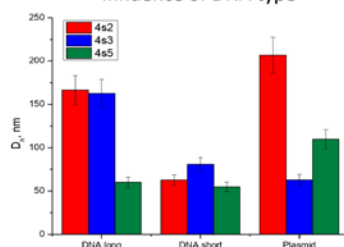
The PEtOx-PBtOx copolymers were used to compact DNA. The complexation ability of the copolymers was studied by the ethidium bromide quenching assay. Then, polyplex particles at an amino-to-phosphate group (N/P) ratio of 8 were prepared with short (115 bp), long (2000 bp), and plasmid (4730 bp) DNA. Their physicochemical parameters (hydrodynamic diameter and  $\zeta$ -potential) were determined by dynamic and electrophoretic light scattering. The behavior of complexes at various environmental conditions such as low pH, presence of salts were studied. The release properties of the copolymers were determined.



Influence of DNA type

Influence of ionic strength

Influence of pH



### CONCLUSIONS

The investigated PEtOx-PBtOx copolymers were able to interact with short, long and plasmid DNA forming polyplexes. The size of complexes ranged from 50 to 210 nm depending on the amino functionality (1°, 2° or 3°) and DNA type. The surface potential of the vector systems was mostly positive. The copolymers were characterized by prominent buffering capacity. They exhibited ability to release DNA molecules. Effects of the amino functionality as well as the type of DNA on the physicochemical and release properties were found. Therefore, we could conclude that by fine tuning of these parameters we could obtain biocompatible and effective gene delivery platforms.

## Drug-loaded Mixed Polymeric Micelles: Effects of Carriers' Composition, Concentration and Type of Loaded Antibiotic on the Biocompatibility and Antibiofilm Properties

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<sup>1</sup>Institute of Polymers, Bulgarian Academy of Sciences;

<sup>2</sup>The Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences;

<sup>3</sup>Faculty of Biology, Sofia University "St. Kliment Ohridski"

### Introduction

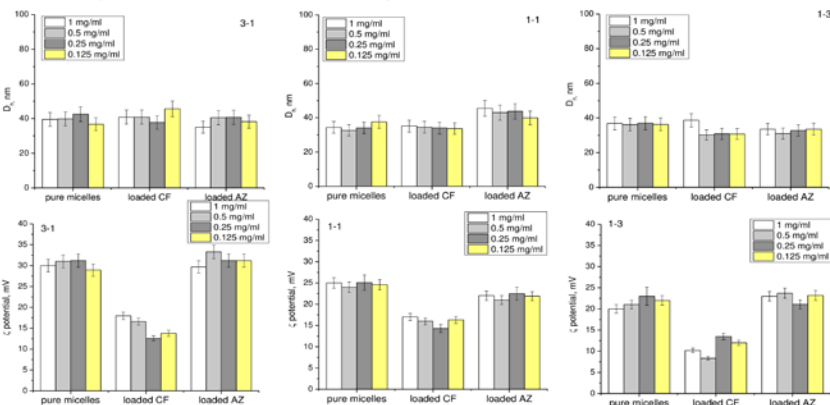
Polymeric micelles have been extensively studied as drug delivery carriers. In recent years, various micellar systems carrying a positive charge have been found to exhibit strong antibacterial and antibiofilm activity. Since the polycations are usually associated with pronounced cytotoxicity, mixed polymeric micelles bearing non-ionic moieties might be a good alternative for the development of novel biocompatible anti-biofilm agents.

In this work, mixed polymeric micelles (MPMs) based on two amphiphilic block copolymers - cationic poly(2-(dimethylamino)ethyl methacrylate)-b-poly( $\epsilon$ -caprolactone)-b-poly(2-(dimethylamino)ethyl methacrylate) (PDMAEMA-PCL) and non-ionic poly(ethylene oxide)-b-poly(propylene oxide)-b-poly(ethylene oxide) (PEO-PPO-PEO, known as Pluronic F127) were prepared. The resulting MPMs possess a mixed hydrophobic PCL/PPO core and a mixed hydrophilic PDMAEMA/PEO shell. The preparation of MPMs carrying both cationic and nonionic moieties is aimed at the development of biocompatible systems with strong antibacterial properties able to deliver antibiotics and combat bacterial biofilms.

### Formation of mixed polymeric micelles and their loading with antibiotics

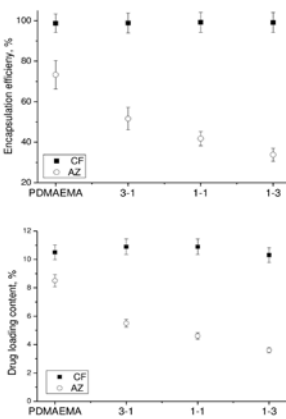
MPMs were formed by dropwise addition of copolymer organic solution to aqueous media followed by dialysis against water. Three different molar ratios (3/1, 1/1 and 1/3) were used. All dispersions were prepared at a concentration of 1 mg/ml, then they were diluted, giving concentrations in the range of 1 to 0.125 mg/ml.

The particles were characterized by small size ranging from 31 to 45 nm and a positive  $\zeta$ -potential dependent on their composition. Their physicochemical characteristics were not influenced by the concentration of the micellar dispersions.



All systems were successfully loaded with two different types of antibiotics. Both ciprofloxacin (CF) and azithromycin (AZ) were selected since they are wide spectrum antibiotics approved by the FDA against various bacterial infections.

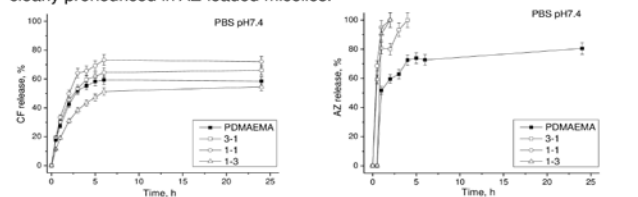
The encapsulation efficiency (EE) and drug loading content (DLC) of the systems were determined by HPLC analysis. An effect of the antibiotic nature on the EE and DLC was observed. CF exhibited high values of EE and DLC due to its localization in both the micellar core and the micellar shell. In contrast, AZ was accommodated only in the micellar core as its loading was strongly influenced by the micellar composition.



### Release profiles

The antibiotic release from MPMs was investigated in phosphate buffer (pH 7.4) at physiological temperature. The amount of released drugs was determined by HPLC.

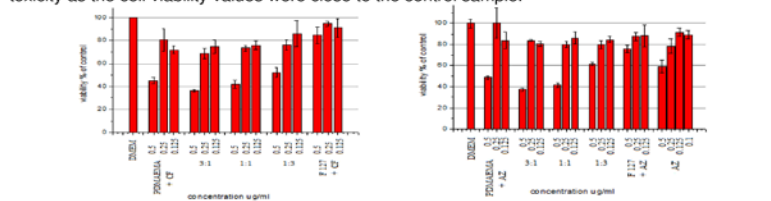
Generally, the CF-loaded systems displayed a prolonged release profile, while the AZ-loaded MPMs exhibited a burst release. The effect of the micellar composition was only slightly expressed in CF-loaded particles and was more clearly pronounced in AZ-loaded micelles.



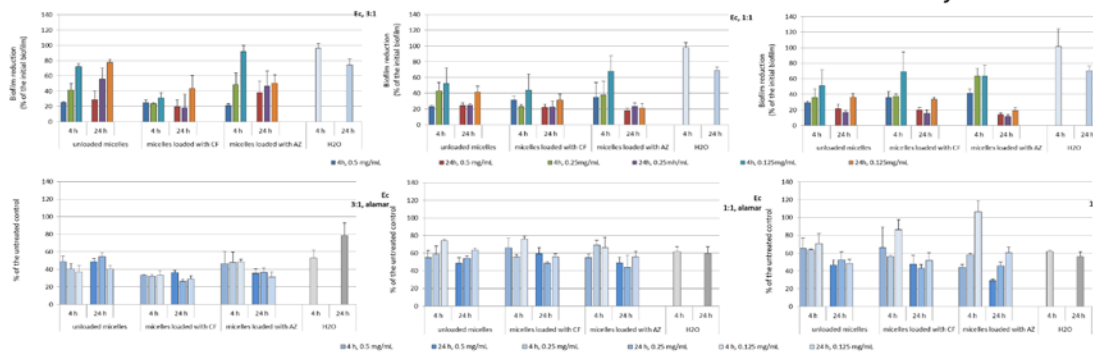
### Cytotoxicity

The cytotoxicity of the resulting micellar systems was determined by the standard MTT method. Normal diploid human skin fibroblasts (HSF) were used for this study.

A strong composition dependent cell viability was observed. As expected, the cytotoxicity decreased with the lower cationic content in the micelles. An effect of the concentration on cell viability was also observed. The AZ-loaded systems were mostly less toxic than CF-loaded MPMs. However, at lower concentrations (0.25 and 0.125 mg/ml), all systems demonstrated a lack of toxicity as the cell viability values were close to the control sample.



### Biofilm biomass reduction and metabolic activity



Biofilm biomass reduction was estimated by a crystal violet assay. For evaluation of the metabolic activity of the biofilm bacteria, the redox indicator Alamar blue was used. The bacterial strain *E. coli* 25922 (ATCC) was selected for these experiments.

All micellar systems could detach pre-formed bacterial biofilms, reducing their biomass by more than 70%. The metabolic activity of the biofilm was strongly suppressed by the antibiotic-loaded micelles, indicating successful drug delivery and release.

### Conclusions

MPMs of different compositions were prepared. They were in the nanoscale range with a hydrodynamic diameter around 40 nm, while the  $\zeta$ -potential value was dependent on their composition. The physicochemical parameters of the mixed systems were not influenced by their concentration. The MPMs were effectively loaded with two wide spectrum antibiotics - CF and AZ. A strong effect of the antibiotic nature on the EE and DLC was observed. The CF-loaded systems were characterized by delayed release profile while AZ-loaded micelles exhibited burst release. In vitro cytotoxicity trials evidenced lack of cytotoxicity of the MPMs at lower concentrations. The systems were able to detach preformed bacterial biofilms formed from *E. coli* 25922. They successfully suppressed the metabolic activity of the rest of the biofilm, indicating the effective delivery of antibiotics. Therefore, we can conclude that the designed systems based on mixed polymeric micelles have great potential as effective and biocompatible antibacterial agents.

**Acknowledgement:** This work was funded by the National Science Fund of Bulgaria, Project № KP-06-H41/8. Research equipment from Distributed Research Infrastructure INFRAMAT, which is part of Bulgarian National Roadmap for Research Infrastructures, supported by Bulgarian Ministry of Education and Science was used in this investigation.



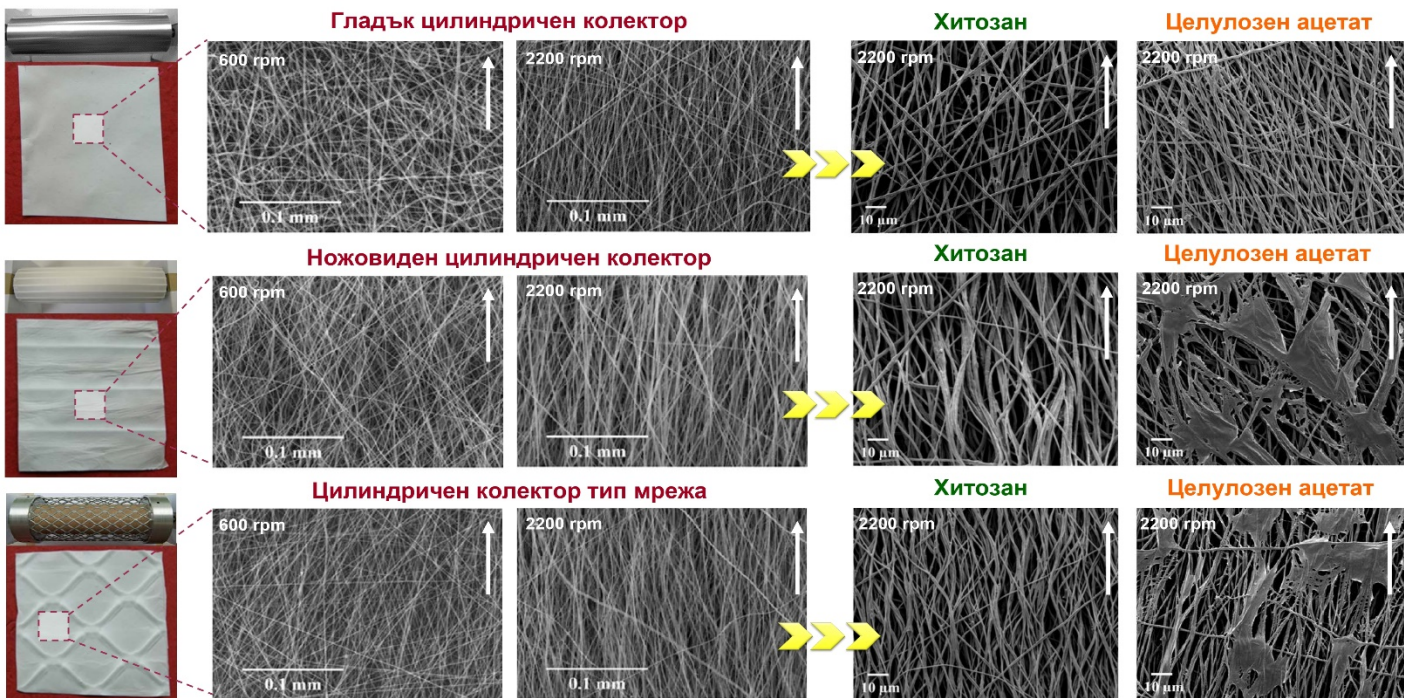
## ПОДХОДИ ЗА ПОЛУЧАВАНЕ НА ЕЛЕКТРООВЛАКНЕНИ МАТЕРИАЛИ ОТ ПОЛИ(3-ХИДРОКСИБУТИРАТ) С ПОДОБРЕНИ ФИЗИКОМЕХАНИЧНИ СВОЙСТВА

Владимир Кръстев, Мария Спасова, Оля Стоилова

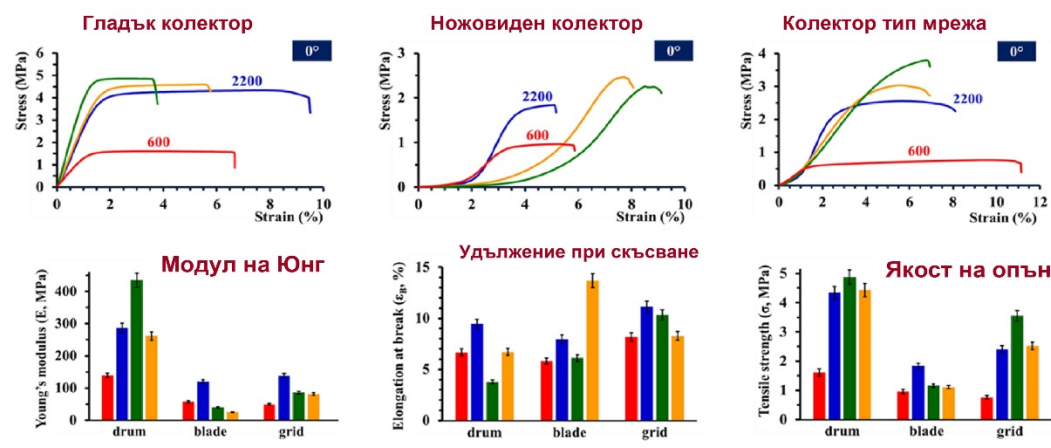
Лаборатория Биологично активни полимери, Институт по полимери-БАН, ул. Акад. Г. Бончев, бл. 103-А

Поли(3-хидроксибутират)ът (PHB) е многообещаващ хидрофобен и термопластичен полимер с физични свойства, подобни с тези на PP, но се получава от възобновяеми източници и е напълно биосъвместим и биоразградим. Основен проблем при обработката му обаче, са лошите му физикомеханични свойства, дължащи се на високата му степен на кристалност, водеща до крехкост на получените от него материали. Фокусът на настоящето изследване е насочен към изследване на възможностите за подобряване на физикомеханичните свойства на влакнести материали от PHB, получени чрез електроовлакняване.

Влияние на геометрията на колектора, на скоростта на въртене на колектора и на нанасянето на покритие



### Физикомеханични свойства



### ИЗВОДИ

- Използването на колектори с различна геометрия оказва влияние върху подреждането на влакната от PHB;
- Повишаването на скоростта на въртене на колектора води до по-голяма подреденост на PHB;
- Нанасянето на покритие от хитозан и целулозен ацетат подобрява физикомеханичните свойства на PHB матовете



## ANTIBACTERIAL AND PHOTOCATALYTIC ABILITY OF meta-PBI STABILIZED CARBON NANOTUBES /PLANT EXTRACT SYNTHESIZED ZINC OXIDE HYBRID MATERIALS

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Green synthesis of hybrid materials is an alternative method to physical and conventional chemical methods, which is cost-effective and environmentally friendly. The hybrid materials combine the advantages of the polymeric substrate scaffold such as low-cost, mechanical stability, high durability and flexibility and combining the photocatalyst property the inorganic parts. This study focuses on the preparation of multi-walled carbon nanotubes (MWCNTs) and nanostructured zinc oxide nanocomposites from natural extracts and meta-polybenzimidazole (m-PBI) surface wrapped hybrid dispersion of multi-walled carbon nanotubes (m-PBI@MWCNTs) was prepared from organic solvent. The ZnO nanoparticle powders were prepared by green synthesis using plant extract of *Vaccinium vitis-idaea L.* Direct re-dispersion of the surface modified ZnO powder in m-PBI@MWCNTs hybrid dispersion lead to preparation of mixed photocatalyst hybrid dispersion of m-PBI@ZnO/MWCNTs with variable content. The resultant hybrid dispersions were used for surface impregnation onto microfibrillar cellulosic substrate. The prepared composites were characterized using powder X-ray diffraction and SEM analysis. The antibacterial activity of ZnO NPs was evaluated with *Escherichia coli* ATCC 25922 as a test microorganism. The photocatalytic efficiency of m-PBI@ZnO/MWCNTs composite and the ZnO were also investigated in the photocatalytic degradation of Methylene Blue dye in aqueous media.

### HYBRIDS PREPARATION:

Schematic representation of m-PBI@ZnO/MWCNTs hybrid

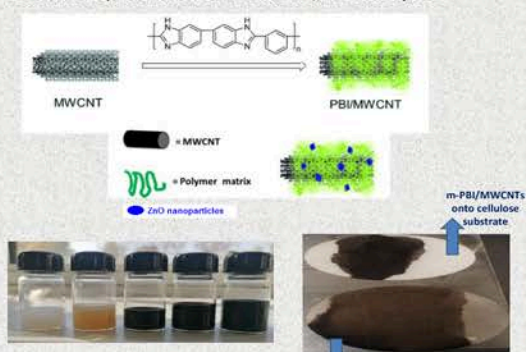


Fig. 1. Hybrid dispersions from left to right: ZnO NPs; m-PBI@ZnO; m-PBI@MWCNTs; m-PBI@ZnO/MWCNTs 1:1 and m-PBI@ZnO/MWCNTs 3:1.

### CHARACTERIZATION

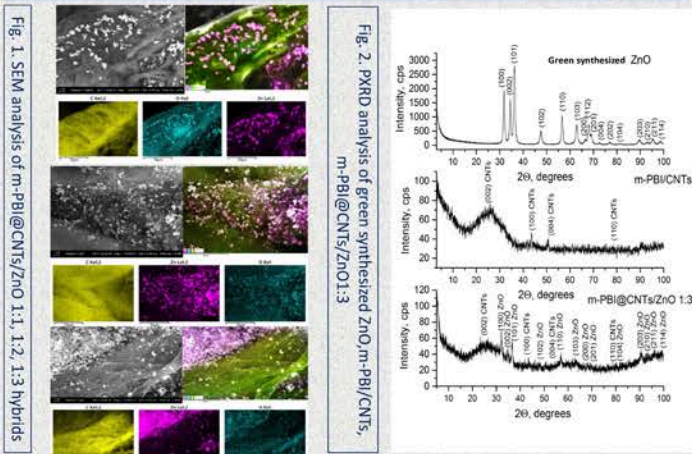


Fig. 1. SEM analysis of m-PBI@CNTs/ZnO 1:1, 1:2, 1:3 hybrids

Fig. 2. PXRD analysis of green synthesized ZnO, m-PBI/CNTs, m-PBI@CNTs/ZnO 1:3

### ANTIBACTERIAL ACTIVITY

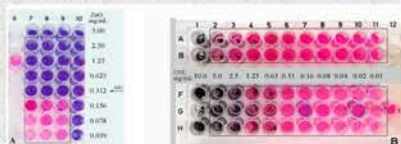


Fig. 3. Resazurin based Microtitre Dilution Assay (RMDA) method for evaluation of MIC in 96-well plate. Wells in the rectangles are inoculated with bacterial culture of  $5 \times 10^5$  CFU/mL. Pink wells indicate cell growth.

A) Minimum inhibitory concentration (MIC) of ZnO nanoparticles, column 6; positive control, column 10; control wells of resazurin dye for each ZnO concentration. The MIC of the ZnO nanoparticles was 0.312 mg/mL (Fig. 3A). B) MIC of CNT nanoparticles, lines A, B: a sector from 96-well plate kept in static condition. Lines F-H: a sector from another 96-well plate incubated on a wrist-shaker. Legend between B and F lines shows the concentration of CNT in each column of wells. Well G12 – positive control.

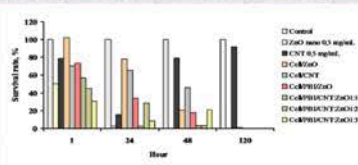


Fig. 4. Antibacterial activity of the hybrid materials. The results are presented as percentage of the control sample for each hour of testing. The combination of cellulose and CNT in dynamic contact with the bacteria also showed antimicrobial properties.



Fig. 5. Photocatalytic antibacterial test. Left: scheme of the experiment. Right: results, A) effect of the tested materials after UV-irradiation; B) effect of the tested materials without irradiation. The photocatalytic antimicrobial effect of the materials was observed for a short irradiation interval – 10 minutes.

### PHOTOCATALYTIC ACTIVITY

### CONCLUSIONS

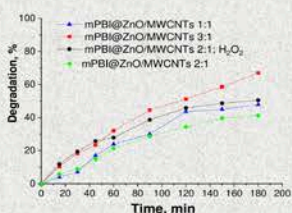


Fig. 6. Photocatalytic degradation of Methylene Blue dye (MB) as model contaminant in aqueous solution (5 ppm) under UV irradiation.

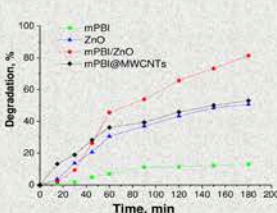
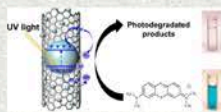


Fig. 7. The degree of degradation of the MB dye in aqueous solution with time under UV irradiation using prepared hybrid materials as photocatalysts.

- Novel hybrid materials based on PBI stabilized ZnO and/or MWCNTs dispersions were prepared and deposited on microfibrillar cellulose substrate.
- The addition of ZnO NPs greatly improve the impregnation efficiency/spread ability of MWCNT dispersion onto cellulosic substrate.
- Combinations of inert carrier, stabilizing agent, and two types of nanoparticles showed significant antibacterial activity, which was primarily due to ZnO. Its ability to induce the release of ROS is increased many times upon irradiation with UV light and greatly reduces time required to achieve a bactericidal effect.



## POLYMERIC MICELLES LOADED WITH INORGANIC NANOPARTICLES AS PLATFORMS FOR DELIVERY OF BIOACTIVE SESQUITERPENE LACTONES FROM INULA HELENIUM

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<sup>3</sup> University of Chemical Technology and Metallurgy, Bul. Kliment Ohridski №8, 1756, Sofia, Bulgaria

### Introduction

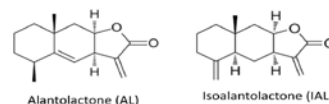
Plants possess substantial quantities of non-nutrient secondary metabolites with bioactive properties, commonly referred to as phytochemicals. They are interesting sources of active substances with capability to combat bacterial infections. Polymeric micelles, PMs, are nanoscopic core/shell structures formed by amphiphilic block copolymers. The properties of polymeric micelles make them particularly well suited for drug delivery purposes. They could serve as vehicles giving shield to phytochemicals against oxidation in vitro and in vivo.

The aim of this work is the design of polymeric nanoscopic antibacterial agents of plant extracts. Therefore, polymeric micelles based on amphiphilic poly(4-methyl-piperazin-1-yl)-propenone)-b-poly lactide block copolymer (PMPP-PLA), were prepared. The micelles were used as carriers for sesquiterpene lactones from *Inula helenium*. Additionally, the loaded polymeric micelles were decorated with silver nanoparticles to strengthen the antibacterial properties of the resulting systems.

### Inula helenium



The extract of *Inula helenium* root has a prominent potential as antiinflammatory, antioxidant, antibacterial, antifungal, anthelmintic, antiproliferative and cytotoxic activity. Most of these biological activities are due to the presence of the sesquiterpene lactones (alantolactone, AL, and isoalantolactone, IAL)

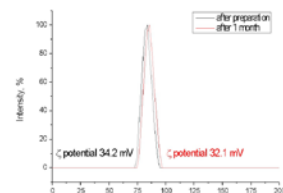
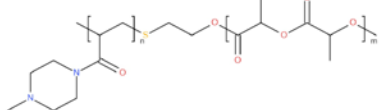


The extraction of plant material was carried out as an air-dried and ground *Inula helenium* roots were extracted with chloroform at room temperature. The crude extract was obtained after filtration and concentration under reduced pressure. HPLC analysis, was used for quantification of both AL and IAL.

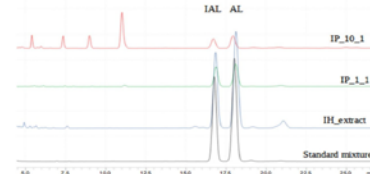
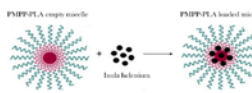
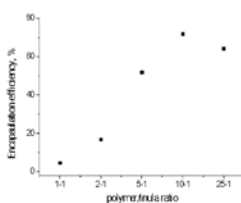
### Preparation of PMPP micelles

PMs were formed by dropwise addition of a copolymer organic solution to aqueous media followed by dialysis against water. The final concentration of micellar dispersion was 0.5 mg/ml. The micelles were composed of hydrophobic PLA core and hydrophilic PMPP shell. They were of small size at about 80 nm and positive  $\zeta$ -potential. The micelles are characterized by good colloidal stability as their physicochemical parameters remain unchanged for 1 month.

poly(4-methyl-piperazin-1-yl)-propenone)-b-poly lactide,



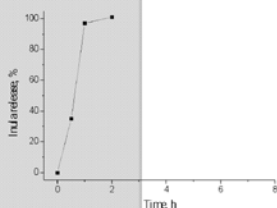
### Loading of polymeric micelles with Inula helenium



Polymer/Inula ratio	Dn, nm		$\zeta$ -potential	
	After preparation	After 1 month	After preparation	After 1 month
1-1	103.8	-	15.8	-
2-1	92.6	94.0	15.0	6.6
3-1	69.6	66.3	18.8	9.4
10-1	66.4	69.2	24.4	12.3
25-1	69.8	85.5	22.4	9.0

Loading of *Inula helenium* was performed by addition of the plant extract to the micellar dispersions to obtain polymer-to-extract weight ratio in the range of 1/1 to 25/1. The mixtures were first sonicated for 1 h at 60 °C and then filtered. The filter was washed with methanol to collect the unloaded extract. The encapsulation efficiency (EE) was determined by HPLC. It was found to depend on polymer-to-plant weight ratio as the optimum values were observed above 10-1. The size and  $\zeta$ -potential of loaded micelles were also influenced by the same ratio.

### Release of Inula helenium from polymeric micelles

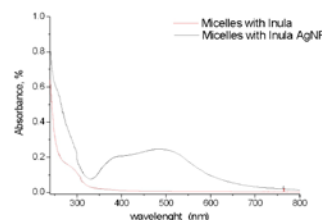
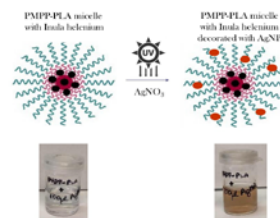
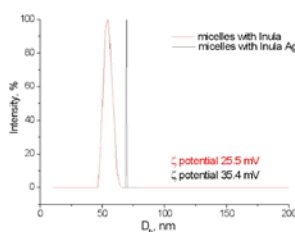


*Inula helenium* release from the micellar systems was investigated in a phosphate buffer (pH=7.4) at physiological temperature. PMs loaded at a polymer-to-extract weight ratio of 10/1 were used. The amount of released drug was determined by HPLC. A burst release profile was observed.

### Conclusions

- ✓ Polymeric micelles based on poly(4-methyl-piperazin-1-yl)-propenone)-b-poly lactide block copolymer were prepared.
- ✓ The micelles were successfully loaded with sesquiterpene lactones from *Inula helenium* root extract.
- ✓ The polymeric carriers exhibited burst release profile of the plant extract.
- ✓ The systems were decorated with AgNPs for strengthening their antibacterial efficiency.
- ✓ The results imply that the systems are promising to be used as antibacterial agents.

### Decoration of Inula helenium loaded micelles with AgNP



The *Inula helenium* loaded micelles were decorated with silver nanoparticles (AgNPs), prepared by in-situ reduction of AgNO<sub>3</sub> on the polycationic micellar corona under UV irradiation. The successful formation of AgNPs into cationic micellar corona was proved by UV spectroscopy and light scattering measurements.

### Acknowledgements:

The support by the Operational Program "Research, Innovation and Digitalization for Smart Transformation", PRIDST 2021-2027, funded by EU and Bulgarian Government, (Project Centre of Competence "Sustainable Utilization of Bio Resources and Waste of Medicinal and Aromatic Plants for Innovative Bioactive Products") is gratefully acknowledged. Research equipment from Distributed Research Infrastructure INFRAMAT, which is part of Bulgarian National Roadmap for Research Infrastructures, supported by Bulgarian Ministry of Education and Science was used in this investigation.

## Preparation and characterization of serratiopeptidase-loaded polymeric micelles

Anna Prancheva<sup>1</sup>, Katya Kamenova<sup>1</sup>, Lyubomira Radeva<sup>2</sup>, Simona Miteva<sup>3</sup>, Krassimira Yoncheva<sup>2</sup>, Petar Petrov<sup>1</sup>

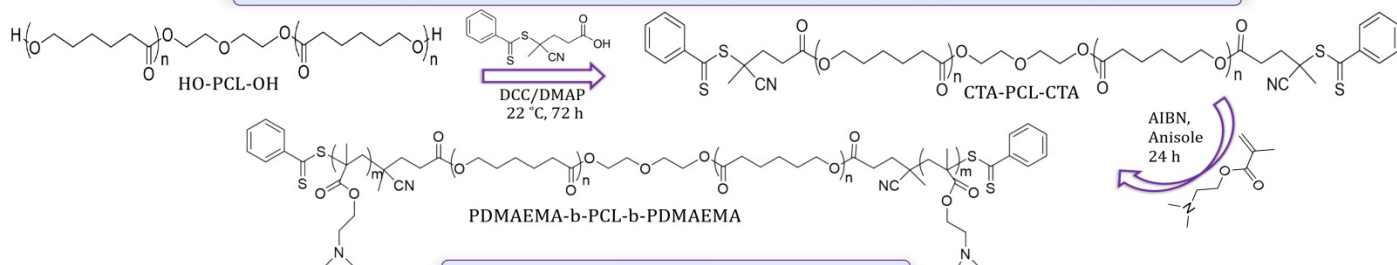
<sup>1</sup>Institute of Polymers, Bulgarian Academy of Sciences, Akad. G. Bonchev St. 103-A 1113, Sofia, Bulgaria

<sup>2</sup>Faculty of pharmacy, Medical University-Sofia 1000, Sofia, Bulgaria

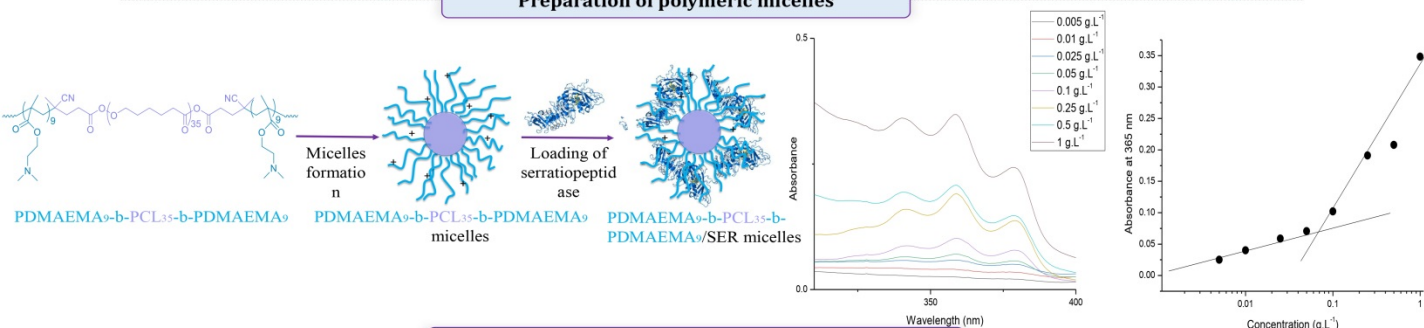
<sup>3</sup>Institute of Microbiology "Stephan Angeloff", Bulgarian academy of sciences, Acad. Georgi Bonchev Street, blok. 26, Sofia, zip 1113

Serratiopeptidase is a proteolytic enzyme defined as a "super enzyme" with proven powerful anti-inflammatory activity. Clinical use of the enzyme has been reported for many diseases such as arthritis, sinusitis, inflammatory bowel disease, fibrocystic breast disease, chronic bronchitis, post-operative swelling and pain, atherosclerosis, etc. The critical problem in enzyme therapy arises from the large size of the protein molecule, susceptibility to denaturation and degradation, short half-life, and poor bioavailability. One of the promising strategies to solve these problems is the use of polymeric nanocarriers which have several advantages as drug delivery systems, including biocompatibility, biodegradability, stability, high loading capacity, and controlled release into target cells. In recent years, polymeric micelles have been widely investigated in preclinical studies for the delivery of several bioactive substances, including therapeutic proteins, DNA, and RNA.

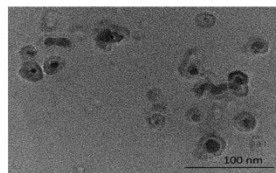
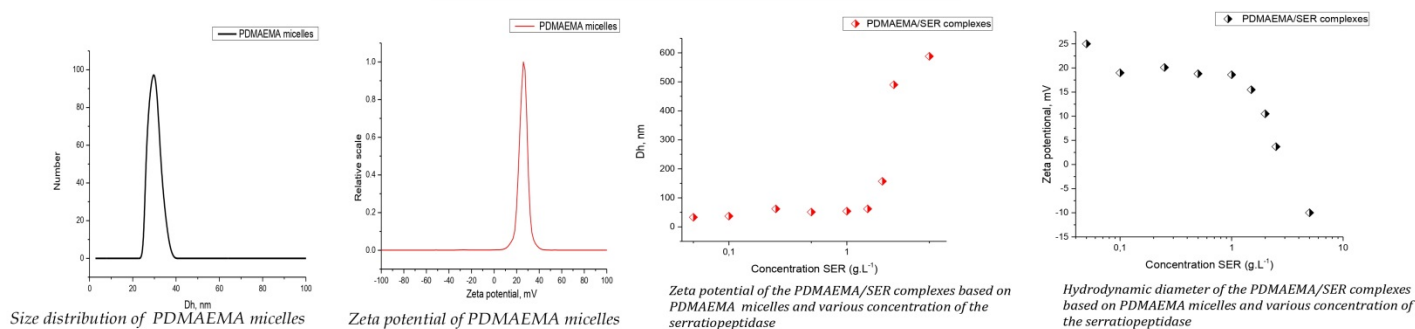
### Synthesis of amphiphilic PDMAEMA<sub>9</sub>-b-PCL<sub>35</sub>-b-PDMAEMA<sub>9</sub> triblock copolymer by RAFT polymerization



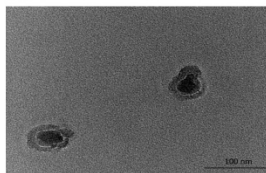
### Preparation of polymeric micelles



### Preparation of PDMAEMA micelles/SER complexes



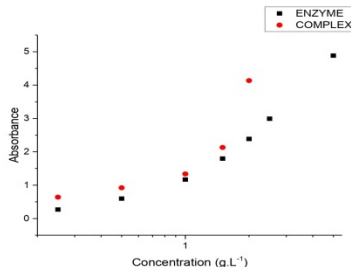
TEM image of PDMAEMA/SER complexes with concentration of enzyme 0.25 mg/ml



TEM image of PDMAEMA/SER complexes with concentration of enzyme 1.5 mg/ml

Enzyme activity

	C [mg/ml]	U/ml	U/g
0.1		1,31	26267
0.1 complex		1,98	19793
0.05		1,59	31718
0,05 complex		1,69	33798



UV-vis spectra of SER and PDMAEMA/SER complexes at different enzyme concentrations (from 0.1 to 5 mg/ml) at 25 °C.

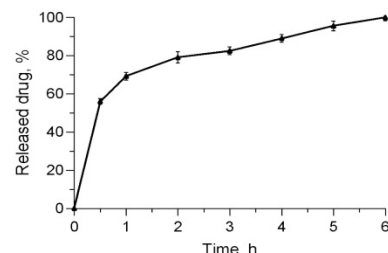


Figure. In vitro release test of serratiopeptidase loaded into the nanomicelles in phosphate buffer with pH=6.8.

**Conclusions:** An amphiphilic PDMAEMA-b-PCL-b-PDMAEMA triblock copolymer was successfully synthesized via RAFT polymerization. Nanosized micellar carriers, comprising a PCL core and a PDMAEMA shell, were prepared by self-assembly in aqueous media. The resulting particles have a small size of 29 nm and a positive zeta potential of 29 mV. Serratiopeptidase was loaded into cationic micellar nanocarriers by electrostatic interactions between negatively charged protein molecules and positively charged PDMAEMA segments at different mass ratio polymer/enzyme (from 1:0.1 to 1:10). At the highest concentration of SER was observed significant increase in particle size due to the formation of copolymer-protein aggregates.

**Acknowledgments:** This research was funded by the Bulgarian National Science Fund (Grant KP-06-M-69/3). The authors thank the INFRAMAT project for the research equipment that was used in this investigation.



## Получаване на полимер-модифицирани pH-чувствителни ниозоми за контролирано доставяне на лекарствени вещества

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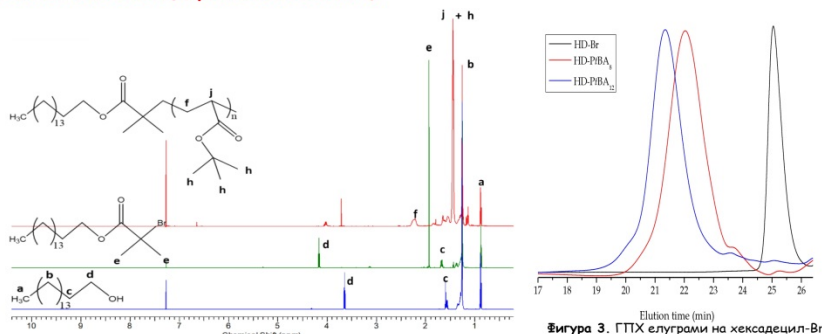
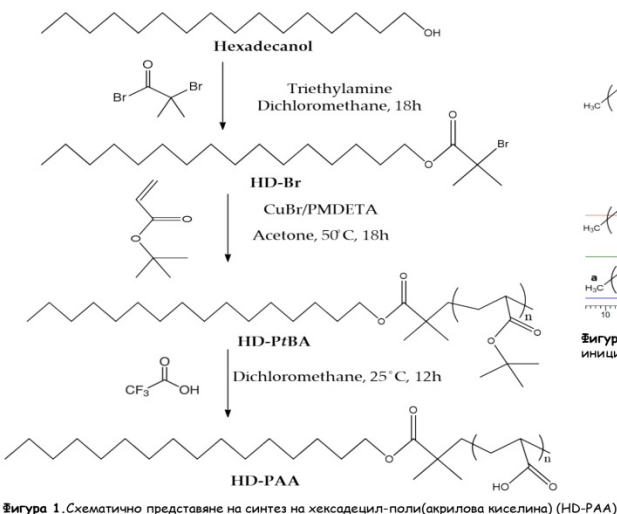
<sup>4</sup>Център по полимерни и въглеродни материали, Полска академия на науките, ул. М. Кюри - Складовска 34, Забже, Полша



**Въведение:** Ниозомите са везикуларни наноносители, образувани от амфифилни нейногенни повърхностноактивни вещества и холестерол, които самоасоциират във водна среда и образуват затворени двуслойни структури. Тяхната уникална структура позволява да бъдат натоварени както с хидрофобни вещества в липидната си част, така и с хидрофилни вещества вътре в хидрофилното ядро. Структурната модификация на ниозомалната мембрана с различни полимери може да придаде допълнителни функции и да подобри техните физикохимични и биофармацевтични характеристики.

**Цел:** Целта на настоящото изследване е разработване на pH-чувствителни наноносители за доставяне на биоактивни вещества чрез мембранна модификация на конвенционални ниозоми с pH-чувствителни съполимери на основата на хексадецил-поли(акрилова киселина).

### Синтез на pH-чувствителни полимери на основата на хексадецил-поли(акрилова киселина)



Фигура 2. <sup>1</sup>H ЯМР спектри на хексадеканол (син цвят), хексадецил-Br ATRP инициатор (зелен цвят) и хексадецил(терт-бутил акрилат)<sub>6</sub> (червен цвят), хексадецил(терт-бутил акрилат)<sub>12</sub> (червен цвят) в CDCl<sub>3</sub>.

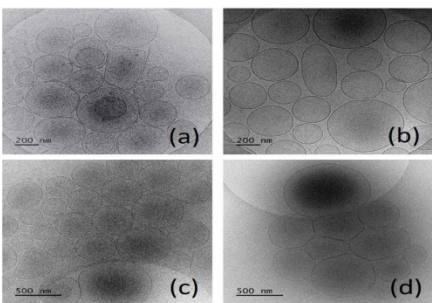
Състав и молекулни характеристики на HD-Br, HD-PtBA и HD-PAA	M <sub>n</sub> <sup>GPC</sup> g mol <sup>-1</sup>	M <sub>w</sub> <sup>GPC</sup> g mol <sup>-1</sup>	M <sub>w</sub> /M <sub>n</sub>
HD-Br	390	510	1.01
HD-PtBA <sub>6</sub>	1415	1850	1.10
HD-PtBA <sub>12</sub>	820	-	-
HD-PtBA <sub>12</sub>	1930	3100	1.17
HD-PtBA <sub>12</sub>	1100	-	-
HD-PtBA <sub>17</sub>	2600	3200	1.20
HD-PAA <sub>17</sub>	1470	-	-

Фигура 1. Схематично представяне на синтез на хексадецил-поли(акрилова киселина) (HD-PAA)

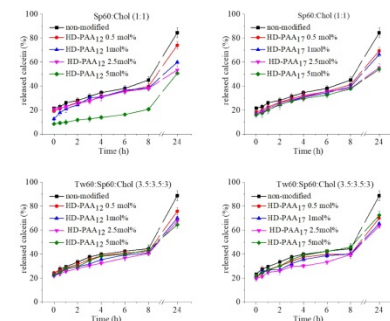
### Получаване и охарактеризиране на pH-чувствителни ниозоми, натоварени с куркумин

Състав, физикохимични характеристики и ефективност на натоварване на ниозоми (конвенционални и модифицирани) приготвени по метода на хидратиране на липиден филм

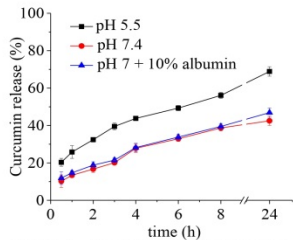
Sample	SF:Chol (mol:mol)	Polymer (mol %)	D <sub>v</sub> (nm) ± SD	PDI ± SD	ζ potential (mV) ± SD	EE (%)	Curc	DL (%)
Conventional niosomes								
S1	Sp60:Chol 1:1 (blanc)	-	573 ± 5.2	0.45 ± 0.03	-8.7 ± 0.4	-	-	-
S2	Sp60:Chol 1:1	-	389 ± 5.2	0.321 ± 5.2	-5.7 ± 0.4	27 ± 1.6	1.23	-
S3	Tw60:Sp60:Chol 3.5:3.5:3 (blanc)	-	489.1 ± 4.8	0.34 ± 0.06	-12.3 ± 2.3	-	-	-
S4	Tw60:Sp60:Chol 3.5:3.5:3	-	379 ± 3.3	0.32 ± 0.02	-12.2 ± 2.1	80 ± 1.8	2.03	-
Niosomes modified with HD-PAA <sub>12</sub>								
S6	Sp60:Chol 1:1	2.5	330 ± 4.2	0.25 ± 0.05	-21.2 ± 1.1	32 ± 1.6	1.47	-
S7	Tw60:Sp60:Chol 3.5:3.5:3	2.5	324 ± 3.3	0.38 ± 0.03	-22.1 ± 1.4	83 ± 1.3	2.12	-
Niosomes modified with HD-PAA <sub>17</sub>								
S8	Sp60:Chol 1:1	2.5	563 ± 4.6	0.36 ± 0.04	-23.8 ± 1.2	30 ± 3.4	1.38	-
S9	Tw60:Sp60:Chol 3.5:3.5:3	2.5	302 ± 6.6	0.34 ± 0.02	-21.1 ± 1.7	83 ± 2.8	2.12	-



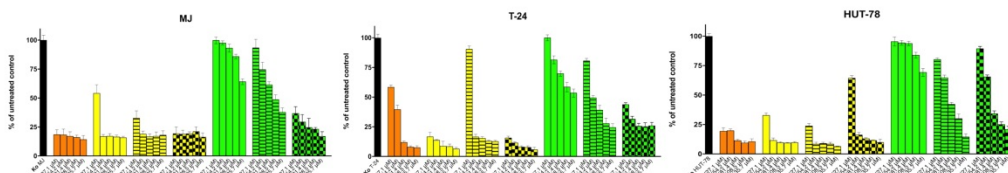
Фигура 4. Cryo-TEM снимки на ниозоми: (a) Sp60:Chol (1:1); (b) Tw60:Sp60:Chol (3.5:3.5:3); (c) Sp60:Chol:HD-PAA<sub>12</sub> (2.5 mol %); (d) Tw60:Sp60:Chol:HD-PAA<sub>12</sub> (2.5 mol %).



Фигура 5. Освобождане на куркумин във фосфатен буфер с pH 7.4 при 37°C с различна концентрация на съполимерите



Фигура 6. Освобождане на куркумин от HD-PAA<sub>17</sub> модифицирани ниозоми на основата на Sp60:Tw60:Chol (3.5:3.5:3 mol:mol)



Фигура 7. Цитотоксичен ефект на свободен и натоварен в конвенционални и pH-чувствителни ниозоми куркумин срещу панел от човешки злокачествени клетъчни линии, определени чрез анализ на редукция на МТТ-багрило след 72 часа.

**Заклучение:** Успешно бяха синтезирани pH-чувствителни съполимери, включващи хексадецил хидрофобен сегмент и хидрофилен блок от поли(акрилова киселина) чрез радикална полимеризация с пренос на атом на терт-бутил акрилат последвана от селективна хидролиза за превръщане на блоковете от поли(терт-бутил акрилат) в поли(акрилова киселина). Съполимерите и полимерните прекурсори са охарактеризирани с протонен ядрено-магнитен резонанс и геловпропираща хроматография. Натоварените с куркумин pH-чувствителни ниозоми бяха успешно разработени чрез модификация на мембраната с HD-PAA12 и HD-PAA17. Всички съполимерно модифицирани ниозоми показват pH-зависимо освобождаване на натовареното лекарствено вещество, с по-висока скорост на освобождаване в кисела среда, което може да се използва като възможен подход за насочване при противотуморна терапия.

Благодарности: Тава изследване е финансово подкрепено от Фонд научни изследвания (Договор КП-06-Н43/3 от 2020г.). Авторите изказват своята благодарност към проект Инф рамаг за изследователското оборудване, използвано в това изследване и за научното сътрудничество между Българската академия на науките и Полската академия на науките (проект IC-PL/12/2024-2025).



## Деалкохолизация на червено вино – Мавруд чрез нанофилтрация посредством полиестерна мембрана Alfa Laval NF99HF



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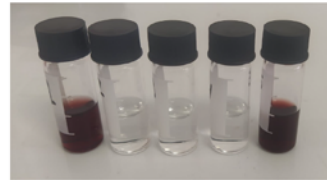
Виктор Проданов<sup>1</sup>, Юлия Генова<sup>1</sup>, Мария Денчева-Заркова<sup>1</sup>, Драгомир  
Василев<sup>1</sup>, Ирен Цибранска<sup>2</sup>, Апостол Апостолов<sup>2</sup>, Драгомир Янков<sup>2</sup>

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### Абстракт

Нанофилтрацията е ефективен метод на мембранно задържане/концентриране на етанол и биоактивни вещества в реални системи. Настоящата работа е фокусирана върху серия експерименти по нанофилтрация на червено сухо вино Мавруд с Мембранна филтрационна система MaxiMem - PS Prozesstechnik GmbH, оборудвана с полиестерна мембрана Alfa Laval NF99HF (MWCO 200 Da). Експериментите са проведени при периодичен режим на работа на апарата – концентриране, в режим на охлаждане посредством Термостатна охлаждаща вана Lauda Alpha RA8, с поддържане на работна температура 17-19°C. Работните параметри на мембранното разделяне са както следва: трансмембранно налягане 10, 20, 30, 40, 50 бара и тангенциална скорост 1.2 л/мин. Изследвано е влиянието на работните параметри (налягане и температура) върху съдържанието на алкохол и биоактивни вещества (полифеноли, антоцианини, антиоксидантна активност) във виното. Определени са оптималните условия и параметри на нанофилтрация. В допълнение е проведено и експериментално изследване на промените в обемната морфология на полимерната мембрана, настъпили в резултат на нанофилтрацията.

### Мембранна филтрационна система MaxiMem и охлаждаща вана Lauda Alpha RA 8



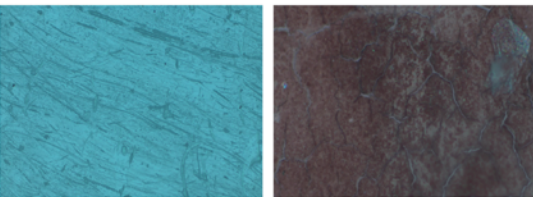
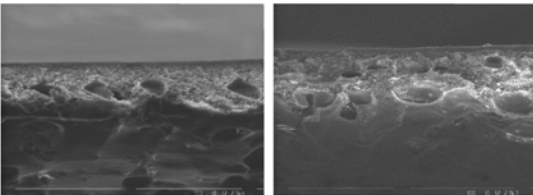
Проби: вино, пермеат, средна пермеат и средна ретенат

### Газов хроматограф Agilent 8890 G3540A

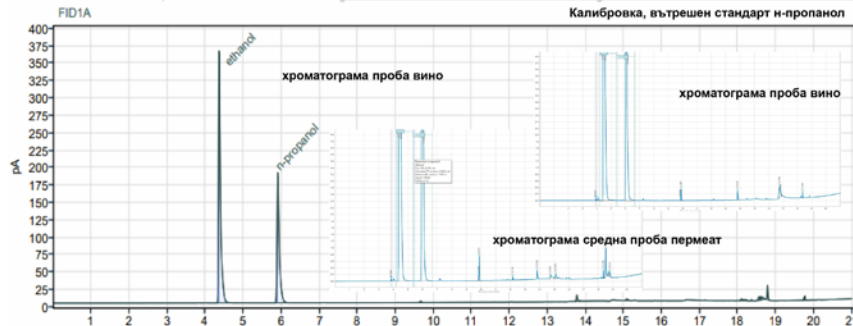
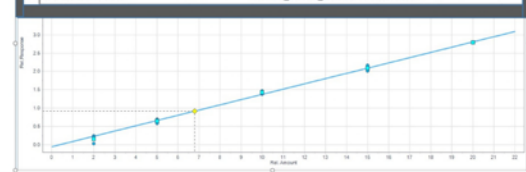


### Резултати:

СЕМ на мембраната преди и след филтрацията, получени със сканиращ електронен  
микроскоп JEOL SEM T-200 в SEI режим



Изображения на мембраната преди и след нанофилтрация, получени с микроскоп  
Zeiss LSM 900, увеличени x100



### Резултати биоактивни вещества

Проба	Антоцианини, мг/л	Полифеноли, мг/л	Антиоксидантна активност, $\mu\text{mol/l}$
1 – вино 2 – 180мл пермеат 3 – 300 мл пермеат 4 – средна пермеат 5 – средна ретенат	27.4	2681.8 ± 80.5	69894.6 ± 1383.1
10 бара	27.4	23.9 ± 0.3	1118.3 ± 11.9
2	-	81.3 ± 0.3	1369.4 ± 37.1
3	-	58.9 ± 4.2	1697.0 ± 23.1
4	46.8	4395.4 ± 145.0	107743.3 ± 1835.0
5	22.4	2549.2 ± 54.8	48355.8 ± 602.3
20 бара	27.4	23.9 ± 0.3	693.8 ± 25.0
2	-	38.0 ± 4.2	819.8 ± 39.1
3	-	24.4 ± 0.3	1255.9 ± 11.8
4	41.7	4523.9 ± 38.7	97051.1 ± 706.4
5	27.4	2640.3 ± 22.6	53787.5 ± 1173.5
2	-	24.4 ± 0.3	1342.4 ± 25.0
3	-	28.5 ± 1.6	1317.7 ± 38.8
4	38.7	214 ± 0.6	1552.2 ± 35.8
5	44.1	4219.1 ± 58.0	109299.4 ± 1788.3
40 бара	28.1	2715.5 ± 19.3	85445.5 ± 852.8
2	-	22.3 ± 0.6	1432.4 ± 65.5
3	-	33.7 ± 0.6	1837.1 ± 47.6
4	44.1	33.0 ± 2.9	1901.5 ± 31.9
5	44.1	4795.4 ± 80.5	121310.3 ± 485.9
50 бара	29.1	2731.5 ± 9.7	87879.2 ± 1049.3
2	-	28.5 ± 0.3	1167.1 ± 10.7
3	-	23.9 ± 1.0	1291.2 ± 76.3
4	44.1	29.6 ± 1.9	1655.8 ± 61.3
5	51.1	4927.6 ± 9.7	130034.9 ± 1641.4

### Резултати алкохолно съдържание

Alfa Laval NF99HF	10 бара	20 бара	30 бара	30 бара 17°C	40 бара	40 бара 17°C	50 бара
Обемна концентрация на етанол, об. %	1	11,160	13,303	13,843	12,323	11,626	12,838
Чисто вино	2	10,094	12,056	9,479	9,806	10,142	9,316
	3	9,366	11,959	9,908	10,378	10,998	10,384
180 мл пермеат	4	10,366	10,902	9,547	10,027	9,780	9,530
	5	10,507	12,240	10,990	12,230	12,142	11,145
360 мл пермеат	1	0,94	0,82	0,69	0,83	0,84	0,77
	2	0,94	0,82	0,69	0,83	0,84	0,77
Средна проба пермеат	0,94	0,82	0,69	0,83	0,84	0,77	0,78
Средна проба ретенат	0,94	0,82	0,69	0,83	0,84	0,77	0,78
Средна проба пермеат/вино	0,94	0,82	0,69	0,83	0,84	0,77	0,78

### Заклучение:

Резултатите от изследванията показват, че мембраната Alfa Laval NF99HF е подходяща за деалкохолизация на вино, като задържането на етанол е около 3 об.%, при относително запазване на ценните биоактивни вещества в състава на виното. Установени са оптималните параметри за деалкохолизация: 40 бара налягане и температура от 17 °C. Показано е, че в следствие на нанофилтрацията се наблюдават промени в морфологията на мембраната - разширяване и деформация на порите.

**Благодарности:** Авторите изказват своята благодарност за финансовата подкрепа от Фонд „Научни изследвания“, Министерство на образованието и науката по Договор № КП-06-H47/1/26.11.2020 г.



15<sup>th</sup> Conference "The Young Scientists in the World of Polymers" - 06.06.2024

# Polymer membrane nanofiltration of Bulgarian red wine. Determination of ethanol content by liquid chromatography.

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**Introduction** This work presents results on determination of the ethanol content in samples obtained after nanofiltration of certified Bulgarian red wine (Mavrud). The process of nanofiltration is carried through a polymer membrane — polyether sulfone. The membrane is a commercial product — NADIR NP030P MWCO. The information for the amount of EtOH was obtained by instrumental method of analysis — High-Performance Liquid Chromatography (HPLC) with Refractive Index Detector (RID). The results could improve the selectivity of the process carried through a conventional or modified polymer membranes regarding the water-alcohol system as part of the composition of the wine.

## Method development

## Experiments and results

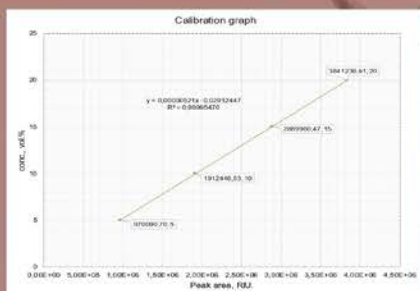


Figure 1: Calibration plot for method development.

### Object of research



Figure 4: Mavrud wine certificate.

### Experimental setup



Figure 5: Laboratory membrane filtration unit.



Figure 5a: Cooling thermostat.



Figure 2: Analytical equipment - Agilent 1260 Infinity II - RID+DAD.

### Nanofiltration membrane

NADIR NP030P MWCO 500D - nanofiltration membrane made from polyether sulfone backed with polypropylene. Exhibits nanofiltration characteristics when exposed to high pressure. Examination of the morphological changes in the polymer membrane - SEM pictures.

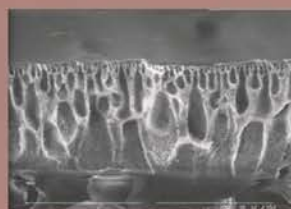


Figure 6: Membrane before filtration

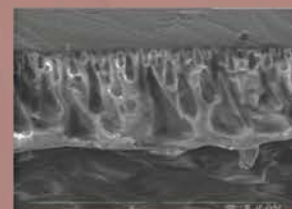


Figure 7: Membrane after filtration

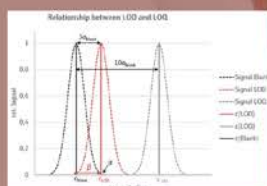


Figure 3: Relationship between LoD and LoQ.

Method accuracy:

Limit of detection (LoD): 0,1822 %/L of EtOH

Limit of quantitation (LoQ): 0,5521 %/L of EtOH

### Obtained results after analysis

Pressure	30 bar	40 bar	50 bar
Sample	Conc. EtOH vol. %		
Wine	11,46	11,82	11,54
90 ml of permeate	9,4	9,32	9,03
180 ml of permeate	9,6	9,62	9,14
Avg. permeate	8,99	8,97	8,8
Retentate	10,76	11,13	10,97

**Conclusions** As seen from the results obtained after the process of wine nanofiltration, the polyethersulfone membrane can retain 2-2,5% EtOH. Furthermore, the pressure applied on the membrane and the possible influence of the wine components leads to changes in the morphology of the polymer membrane.

### Acknowledgments

The authors gratefully acknowledge the Bulgarian National Science Fund for its financial support via the contract for project КП-06-ПН47/1



### Additional information

Joint science project - Valorization of valuable bioactive substances and ethanol from grape products through innovative nano- and ultrafiltration membrane processes.  
 Head of project - prof. Darinka Hristova, PhD - Institute of Polymers, acad. G. Bonchev str., Bl.103,  
 \*Apostol Apostolov - Ph.D. student, chemical engineer, assistant - Institute of Chemical Engineering;  
 \*Contact info: a\_apostolov@iche.bas.bg,  
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## Дизайн на иновативни полимерни материали като агенти за биоконтрол с приложение в екоземеделието

**Наско Начев, Мария Спасова, Оля Стоилова**

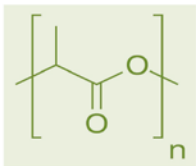
**Лаборатория Биологично активни полимери, Институт по полимери – БАН**

Болестите по културните растения са световен проблем, който всяка година причинява огромни щети върху земеделската реколта. Основни причинители на заболяванията са различни фитопатогени, най-широко разпространените сред които са гъби от рода *Fusarium*, *Phaeoaniella*, *Verticillium*, *Botrytis* и *Rhizoctonia*. Към момента, за борба с болестите по растенията, широко се прилагат химически пестициди, които в дългосрочен план водят до замърсяване на почвите, водата и въздуха, вреди на насекоми, птици и бозайници, и са опасни за човешкото здраве. Иновативните агенти за биоконтрол могат да ускорят процеса за намаляване на зависимостта от пестициди и така да осигурят устойчиво екоземеделие, безопасно за околната среда.

**Целта** на изследването е да се създадат иновативни полимерни материали с различен дизайн като агенти за биоконтрол с приложение в екоземеделието чрез прилагане на класически и на „зелени“ методи за включване на полезни микроорганизми, които стимулират растежа на растенията или се прилагат като агенти за биоконтрол на фитопатогенни микроорганизми.

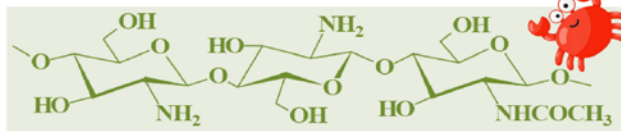
### Материали

**полимлечна киселина**



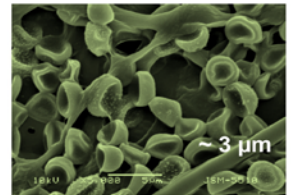
PLLA 259 000 g/mol

**хитозан**



COS 3-5 kDa; LMW 50-200 kDa; HMW 600 kDa

**спори на *T. asperellum***

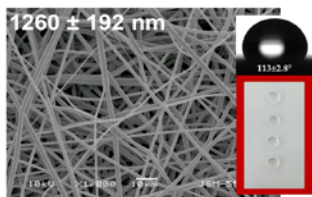


~ 3 µm

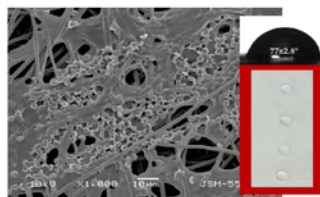
**нетоксични, биосъвместими, биоразградими полимери**

### Морфология и ъгъл на омокряне

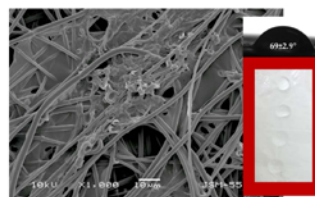
**PLLA**



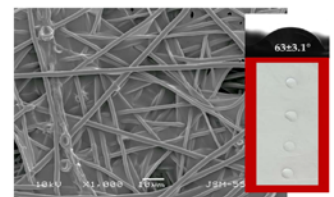
**PLLA / COS / *T. asp.***



**PLLA / LMW / *T. asp.***

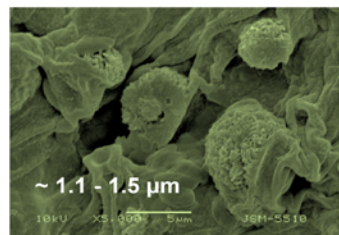


**PLLA / HMW / *T. asp.***



### Противогъбична активност

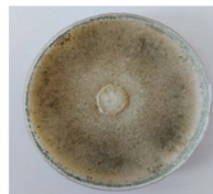
***Phaeoacremonium aleophilum***



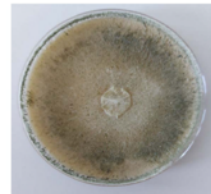
~ 1.1 - 1.5 µm



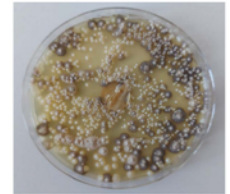
PLLA



PLLA/COS/*T. asp.*

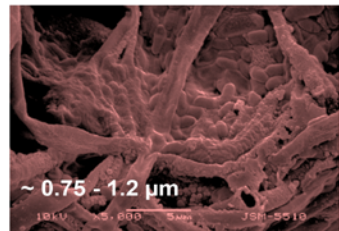


PLLA/LMW/*T. asp.*

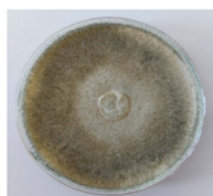


PLLA/HMW/*T. asp.*

***Phaeoaniella chlamydospora***



~ 0.75 - 1.2 µm



**Заключение:** Успешно са получени иновативни хибридни биоматериали от PLLA, хитозан и *T. asperellum*. Разработеният полимерен носител играе активна роля за осигуряване жизнеспособността на биологичния агент по време на съхранение, а поставен в контакт с влага осигурява нормалното му развитие. Проведените микробиологични изследвания показват, че получените хибридни влакнести биоматериали възпрепятстват растежа на фитопатогенни гъби, което ги прави изключително обещаващи кандидати за създаването на нови биоконтролни агенти за защита на растенията.

**БЛАГОДАРНОСТ:** В изследванията е използвано оборудване на Разпределената научна инфраструктура ИНФРАМАТ, част от Националната пътна карта на България за научна инфраструктура, подкрепена финансово от МОН.



# MODIFICATION OF NANOFILTRATION MEMBRANE SURFACE PROPERTIES VIA UV-ASSISTED GRAFTING OF HYDROPHILIC MONOMERS

**Mariela Alexandrova, Sijka Ivanova, Maya Staneva, Darinka Christova**  
*Institute of Polymers, Bulgarian Academy of Sciences*

With the development of macromolecular surface science, surface grafting polymers, also known as polymer brushes, have become an important approach to modify or functionalize the surface of materials. Graft polymerization induced by UV irradiation is a commonly used polymer membrane surface treatment method due to its high efficiency, simplicity, and distribution of grafted chains near the surface without damaging the bulk membrane structure. In this work, nanofiltration polyethersulfone membrane properties were modified by UV-assisted grafting of different hydrophilic monomers, including N-isopropylacrylamide (NIPAAm) and dimethylacrylamide (DMAAm), when using benzophenone as photoinitiator.

## MATERIALS AND METHODS

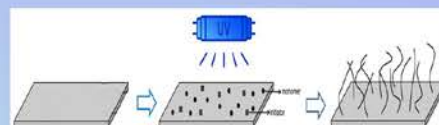
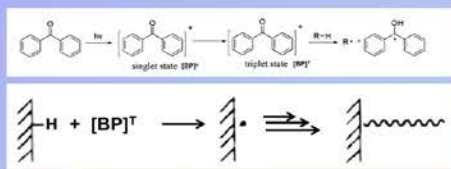
### Original membrane

Commercial *Microdyn Nadir™ NP030P* flat sheet nanofiltration membrane of following characteristics was used as a basic membrane:

Characteristic parameters	
Thickness	210-250 μm
Polymer	Polyethersulfone
Backing	PE / PP
Pore size / MWCO	~ 500 Da

### Surface grafting

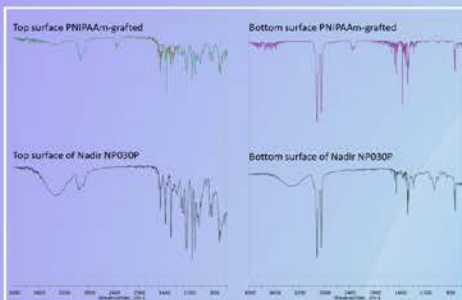
When UV irradiated, benzophenone (BP) molecules are excited to a singlet state and then jump to a triplet state by intersystem crossing. BP in a triplet state undergo hydrogen-abstrating reactions from substrates, consequently providing surface radicals (R•) capable of initiating surface graft polymerization [Ref.1-2].



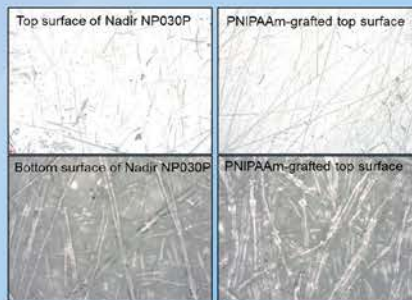
Ref.1. Pan D., Vasanthakumari K., et al. *J. Polym. Sci.: Part A: Polym. Chem.* 2004, 42, 1853.  
 Ref.2. Yang W.T., Rånby B. *Macromolecules* 1998, 29, 3308.

## PNIPAAm-modified membranes

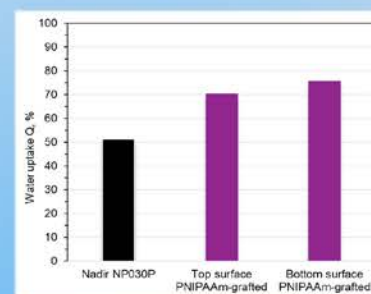
### FTIR spectroscopy



### Optical microscopy (10x)

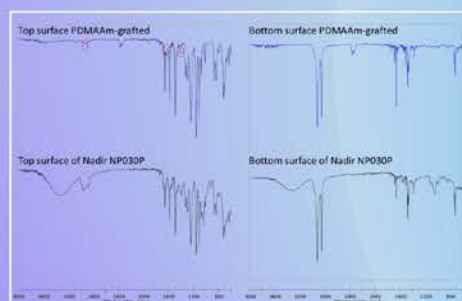


### Water uptake (20°C)

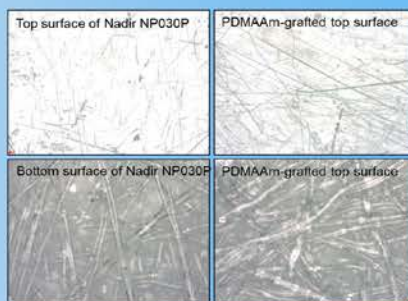


## PDMAAm-modified membranes

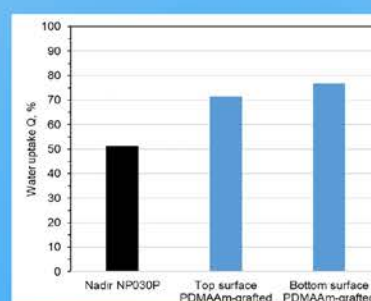
### FTIR spectroscopy



### Optical microscopy (10x)



### Water uptake (20°C)



The water uptake measurements of modified membranes confirmed that grafting of thermoresponsive PNIPAAm and hydrophilic PDMAAm chain on PES membrane surface (top or bottom) result in considerable increase in the membrane hydrophilicity. Contact angle measurements as well as AFM and SEM analyses are in progress in order to evaluate the impact of chemical structure and composition of the modified layers on the membrane properties. Further, permeation and separation properties of modified membranes will be investigated towards water and water-ethanol mixtures.

### ACKNOWLEDGEMENTS:

This work is supported by the Bulgarian National Science Fund under the grant agreement # KII-06-H47/1 from 26.11.2020



## Водороден електрохимичен компресор с полимерна електролитна мембрана – възможност за работа при ниска влажност и диференциално налягане

Борислава Младенова<sup>1</sup>, Мая Станева<sup>2</sup>, Галин Борисов<sup>1</sup>, Евелина Славчева<sup>1</sup>

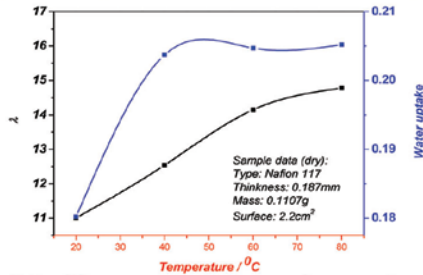
<sup>1</sup>Институт по електрохимия и енергийни системи „Акад. Евгени Будевски“ – БАН, София 1113, ул. Акад. Георги Бончев, бл. 10

<sup>2</sup>Институт по полимери – БАН, София 1113, ул. Акад. Георги Бончев, бл. 103, вх. А

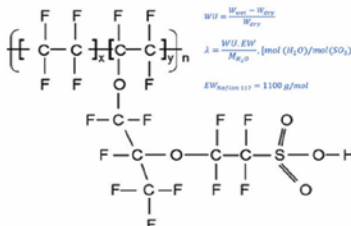
### Въведение:

Водородният електрохимичен помпа/компресор (ВЕП/ВЕК) притежава редица предимства в сравнение с комерсиално предлаганите механични компресори, в това число висока енергийна ефективност, неподвижни механични части, възможност за работа при високи работни налягания без необходимост от допълнително третиране (пред компресия) на подавания реагент. Основно предизвикателство пред тази нова технология за пречистване и компресиране на водород е влагосъдържанието в полимерната електролитна мембрана, която определя скоростта на електрохимичното преобразуване и диференциалното налягане между двата газодифузионни електрода.

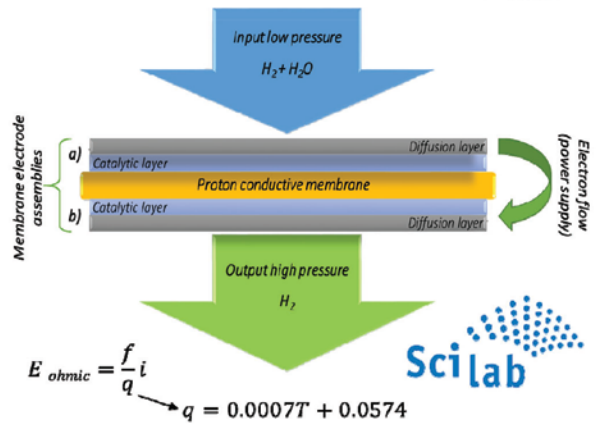
### Полимерна електролитна мембрана:



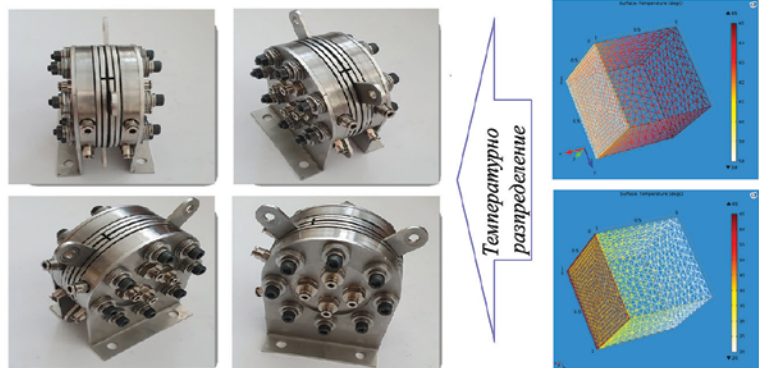
Nafion 117 е композитен материал, който може да се използва като полимерна електролитна мембрана за вграждане във ВЕП/ВЕК.



$$E_{\text{Nernst}} = E_0 + \frac{RT}{2F} \ln \left( \frac{P_{\text{cathode}}}{P_{\text{anode}}} \right)$$

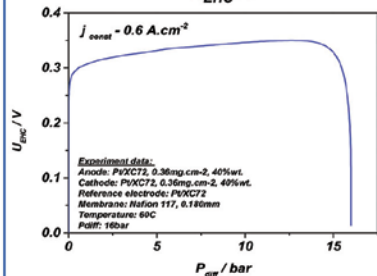
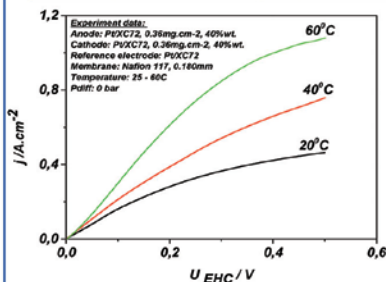


### Прототип на ВЕП/ВЕК



Температурно разпределение

### Електрохимични резултати:



### Изводи:

Nafion 117 може да поглъща вода в широк температурен диапазон като максималната му стойност достига до около 0.2.

Температурното разпределение в пилотното устройство е равномерно, както в областта на полимерните уплътнения, така и в областта на компресия.

Разработената водородна електрохимична помпа може успешно да работи в широк температурен диапазон от 20°C до 60°C като максималното работно налягане може да достигне до 16 bar.



## SYNTHESIS AND CHARACTERIZATION OF NOVEL AMPHIPHILIC POLYGLYCIDOL/POLY(ALLYL GLYCIDYL ETHER)/POLY(ε-CAPROLACTONE) BASED BLOCK COPOLYMERS

Sibela Doleva<sup>1</sup>, Erik Dimitrov<sup>1</sup>, Natalia Toncheva-Moncheva<sup>1</sup>, Ch. Novakov<sup>1</sup>, Stanislav Rangelov<sup>1</sup>

<sup>1</sup>Institute of Polymers, Bulgarian Academy of Sciences, ul. "Akad. Georgi Bonchev" 103, 1113 Geo Milev, Sofia, Bulgaria,

Inframat

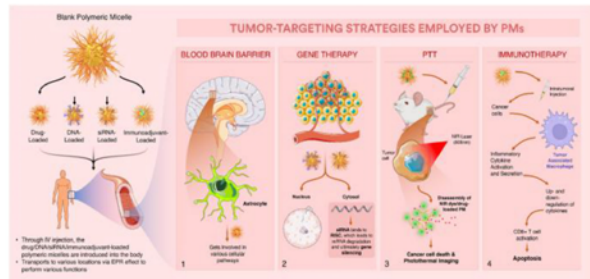
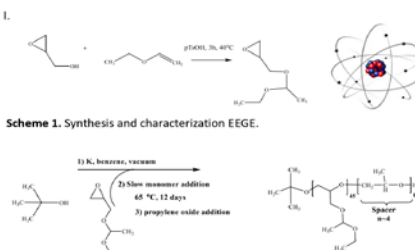


Figure 1. Schematic representation of polymeric micelles (PMs) as multifunctional nanoparticles and their applications as nanocarriers in a wide range of scientific fields.



**ABSTRACT:** Nanotechnology is emerging as a powerful tool and rapidly growing field with a wide range of applications in drug delivery and manufacturing new materials at a nanoscale level. The targeted drug delivery and gene therapy through polymeric nanoparticles (NPs) is an area of major interest in the field of nanotechnology and pharmaceuticals. The present study is aimed at synthesis and characterization of novel amphiphilic copolymers based on linear polyglycidol-b-poly(allyl glycidyl ether)-b-poly(ε-caprolactone)-b-poly(allyl glycidyl ether)-b-polyglycidol (PG-PAGE-PCL-PAGE-PG) which can act as vehicles for drug encapsulation, co-delivery of lipophilic/water insoluble and hydrophilic compounds and/or as carriers of nucleic acids.



Scheme 1. Synthesis and characterization EEGE.

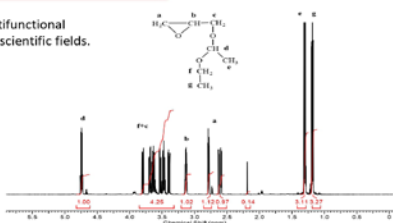


Figure 1. <sup>1</sup>H NMR spectrum of EEGE monomer in CD<sub>3</sub>OD at 600MHz.

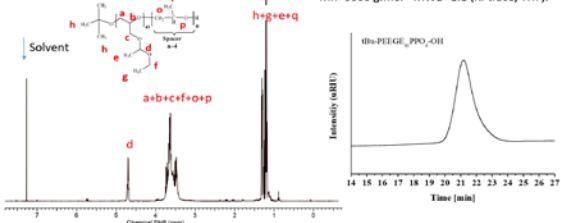
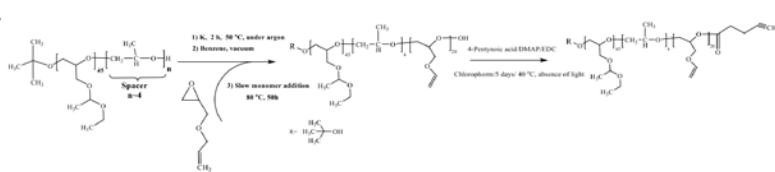
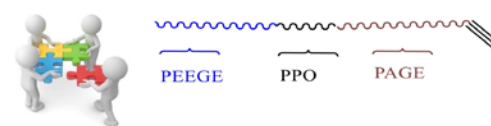


Figure 2. <sup>1</sup>H NMR spectrum (PEEGE<sub>43</sub>PPO<sub>4</sub>OH) macroagent in CDCl<sub>3</sub> at 400MHz.

Scheme 2. Synthesis and characterization of mono-hydroxyl terminated poly(ethoxyethyl glycidyl ether), (PEEGE<sub>43</sub>PPO<sub>4</sub>OH) macroagent.



Scheme 3. Synthesis and characterization of mono-alkyne terminated PEEGE<sub>43</sub>PPO<sub>4</sub>PAGE<sub>20</sub>-Alkyne macroagent.



III. Mn=2000 g/mol, Mw/Mn=1.1, N<sub>2</sub> PCL N<sub>2</sub>

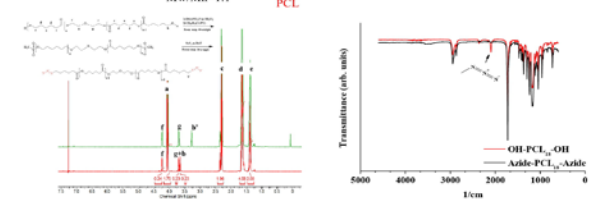
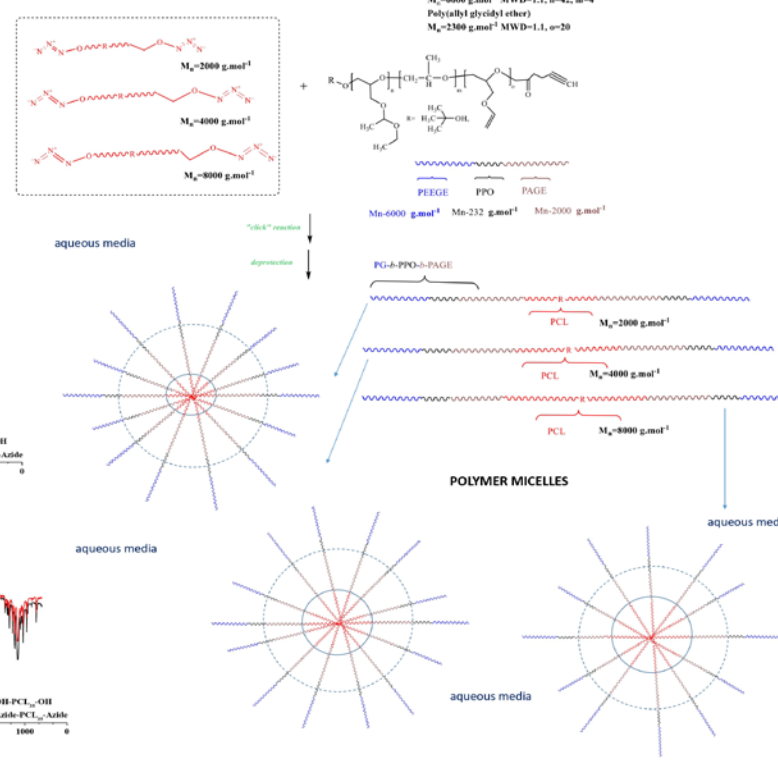
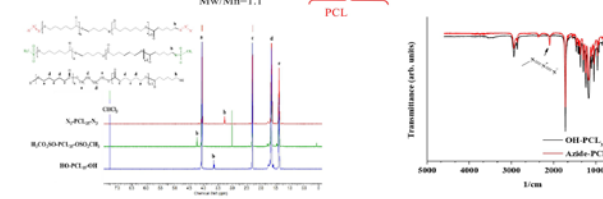
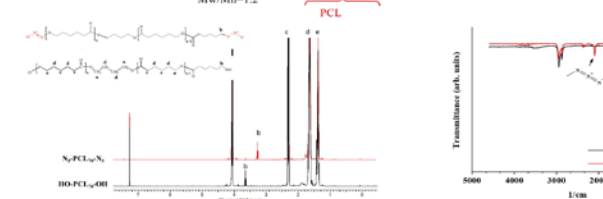


Figure 3. GPC chromatogram of tBu-PEGGE<sub>43</sub>PPO<sub>4</sub>OH, Mn=6000 g.mol<sup>-1</sup> MWD=1.1 (RI trace, THF).

Mn=4000 g/mol, Mw/Mn=1.1, N<sub>2</sub> PCL N<sub>2</sub>



Mn=8000 g/mol, Mw/Mn=1.2, N<sub>2</sub> PCL N<sub>2</sub>



**Funding:** The support by the Operational Program "Research, Innovation and Digitalization for Smart Transformation", PRIDST 2021-2027, funded by EU and Bulgarian Government, (Project Centre of Competence "Sustainable Utilization of Bio Resources and Waste of Medicinal and Aromatic Plants for Innovative Bioactive Products") is gratefully acknowledged. The authors thank the INFRAMAT project (part of the Bulgarian National Roadmap for Research Infrastructures, supported by the Bulgarian Ministry of Education and Science) for the research equipment that was used in this investigation.



## NOVEL DELIVERY SYSTEMS BASED ON POLY( $\epsilon$ -CAPROLACTONE)/POLYGLYCIDOL BASED BLOCK AND STAR COPOLYMERS

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<sup>1</sup>Institute of Polymers, Bulgarian Academy of Sciences, Bulgaria



### Abstract:

Recently, one of the fastest growing areas in the modern pharmaceutical science and technology is targeted drug delivery. The practical realization of this concept is possible thanks to recent advances in nanotechnology. In the field of nanoscale drug carriers, polymer micelles are attracting increasing scientific interest as promising drug delivery systems. They are based on amphiphilic copolymers and offer several advantages as vehicles for drug encapsulation, co-delivery of lipophilic/water insoluble and hydrophilic compounds, biocompatibility, low-immunogenicity, stability (physical, chemical and osmotic), controlled release and targeting properties. In this regard, a series of linear block and star copolymers based on poly( $\epsilon$ -caprolactone)/polyglycidol were synthesized and characterized in detail using the "click" chemistry reactions. The aqueous solution properties of the carriers were also investigated.

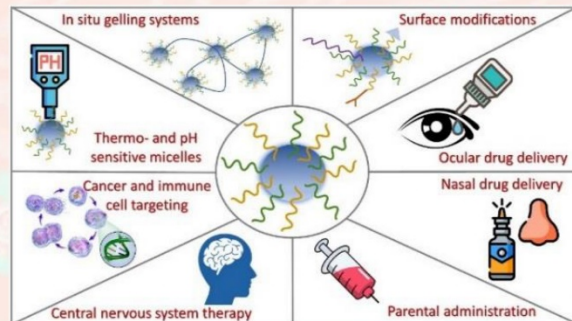
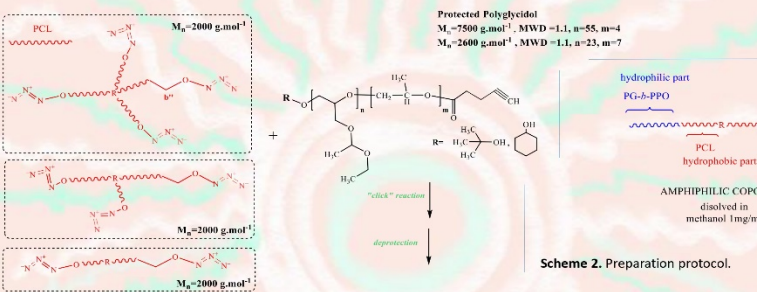
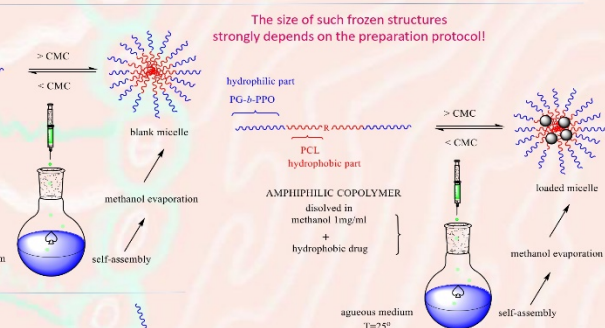


Figure 1. Polymer micelles for enhanced bioavailability and targeted drug delivery.

**Scheme 1.** Schematic Representation of the synthesis of amphiphilic linear and star-like copolymers by copper-catalyzed "click" coupling reaction and subsequent hydrolysis.



Scheme 2. Preparation protocol.



**Table 1.** Composition and molecular characteristics of amphiphilic poly( $\epsilon$ -caprolactone) (PCL) and polyglycidol (PG)-based copolymers with linear and star-shaped architectures.

Topology	Copolymer Composition <sup>d,e</sup>	Abbreviation	$M_n^a$ (g/mol)	$M_w^b$ (g/mol)	$M_w/M_n^c$
Linear	R[(CL) <sub>1</sub> (PO) <sub>1</sub> (EEGE) <sub>2</sub> ] <sub>2</sub>	2F-3K	9600	13200	1.20
Linear	R[(CL) <sub>1</sub> (PO) <sub>1</sub> (G) <sub>1</sub> ] <sub>2</sub>	2F-3K	5900	-	-
Star-like, 3-armed	R[(CL) <sub>1</sub> (PO) <sub>1</sub> (EEGE) <sub>2</sub> ] <sub>3</sub>	3F-3K	13400	17700	1.22
Star-like, 3-armed	R[(CL) <sub>1</sub> (PO) <sub>1</sub> (G) <sub>1</sub> ] <sub>3</sub>	3F-3K	8300	-	-
Star-like, 4-armed	R[(CL) <sub>1</sub> (PO) <sub>1</sub> (EEGE) <sub>2</sub> ] <sub>4</sub>	4F-3K	17200	14100	1.17
Star-like, 4-armed	R[(CL) <sub>1</sub> (PO) <sub>1</sub> (G) <sub>1</sub> ] <sub>4</sub>	4F-3K	10400	-	-
Linear	R[(CL) <sub>1</sub> (PO) <sub>1</sub> (EEGE) <sub>2</sub> ] <sub>2</sub>	2F-8K	18500	16000	1.16
Linear	R[(CL) <sub>1</sub> (PO) <sub>1</sub> (G) <sub>1</sub> ] <sub>2</sub>	2F-8K	9600	-	-
Star-like, 3-armed	R[(CL) <sub>1</sub> (PO) <sub>1</sub> (EEGE) <sub>2</sub> ] <sub>3</sub>	3F-8K	26500	30316	1.19
Star-like, 3-armed	R[(CL) <sub>1</sub> (PO) <sub>1</sub> (G) <sub>1</sub> ] <sub>3</sub>	3F-8K	13500	-	-
Star-like, 4-armed	R[(CL) <sub>1</sub> (PO) <sub>1</sub> (EEGE) <sub>2</sub> ] <sub>4</sub>	4F-8K	34700	40100	1.20
Star-like, 4-armed	R[(CL) <sub>1</sub> (PO) <sub>1</sub> (G) <sub>1</sub> ] <sub>4</sub>	4F-8K	16700	-	-

<sup>a</sup> number-averaged molar mass from <sup>1</sup>H NMR; <sup>b</sup> weight-averaged molar mass from SEC; <sup>c</sup>  $M_w/M_n$  molar mass distribution from SEC; <sup>d</sup> obtained from <sup>1</sup>H NMR; <sup>e</sup> CL, PO, EE, GE, and G denote molar ratio of poly( $\epsilon$ -caprolactone), polyglycidol, ethylene glycol, poly(ethylene glycol) diols, and polyglycidol, respectively. \* R represents a diol unit or tetraol core.

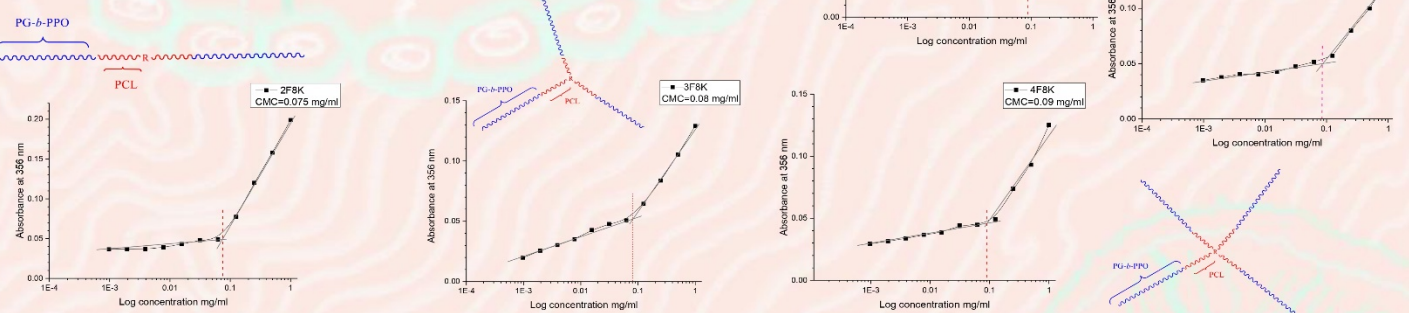


Figure 2. Determination of CMC of the synthesized copolymers using the DPH absorbance at 356 nm in aqueous media at 37 °C.

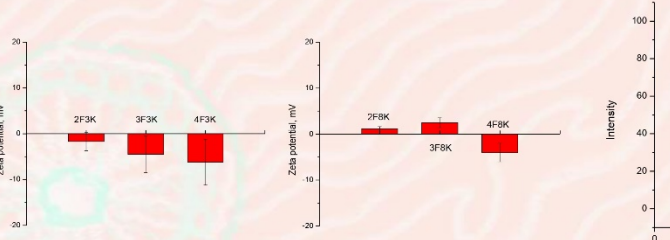


Figure 3. Zeta potential of synthesized copolymers (Error bars in the graph represent standard deviations (n = 3)).

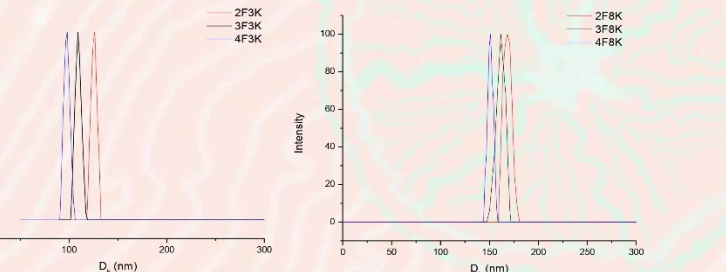
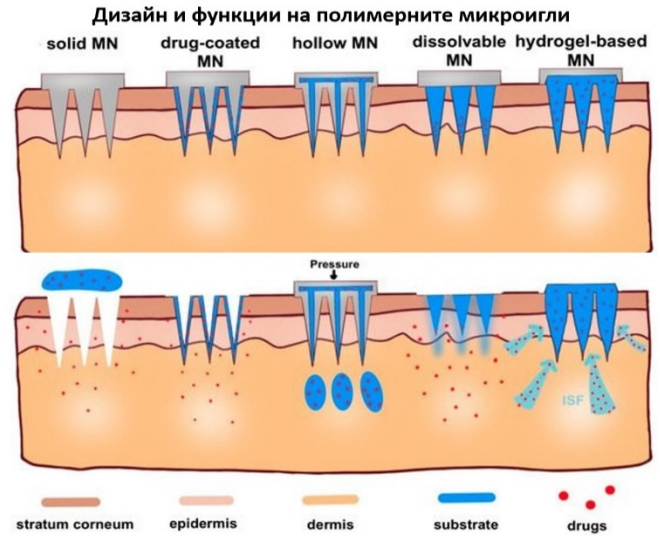
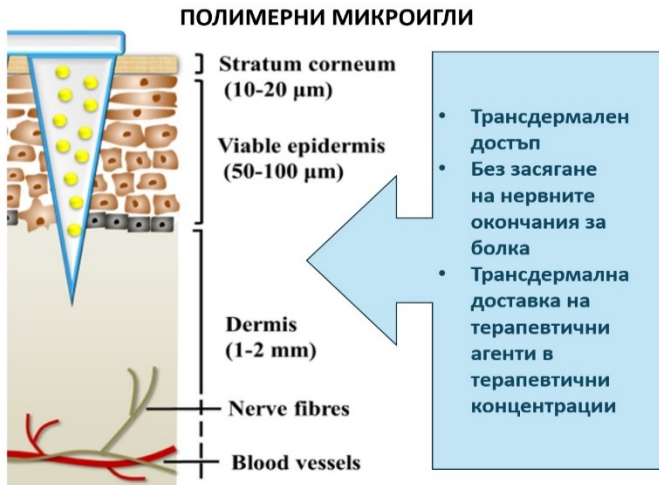


Figure 4. Size distributions from DLS of aggregates obtained from synthesized copolymers.

**Funding:** The support by the Operational Program "Research, Innovation and Digitalization for Smart Transformation", PRIDST 2021-2027, funded by EU and Bulgarian Government, (Project Centre of Competence "Sustainable Utilization of Bio Resources and Waste of Medicinal and Aromatic Plants for Innovative Bioactive Products") is gratefully acknowledged. The authors thank the INFRAMAT project (part of the Bulgarian National Roadmap for Research Infrastructures, supported by the Bulgarian Ministry of Education and Science) for the research equipment that was used in this investigation.



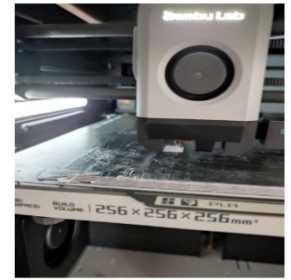
## 3D ПРИНТИРАНЕ НА ПОЛИМЕРНИ МИКРОИГЛИ



### 3D печат с MSLA и FDM 3D принтери

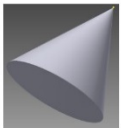


Стереолитографски 3D принтер MSLA

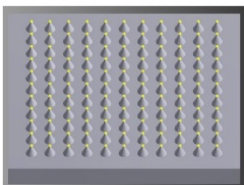


Екструзионен 3D принтер FDM

### Дигитален дизайн: CAD program AutoDesk Inventor



Най-прост модел: прав кръгов конус

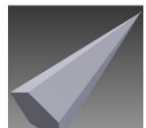


Пач с масив от конусовидни микроигли

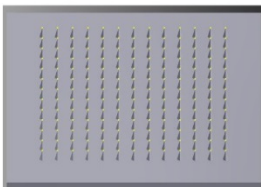
- Фотополимерни смоли
- Специфична работна  $\lambda_{UV}$ , nm
- Специфичен долен праг на работна разделителна способност - z axis: 5  $\mu\text{m}$

- Термопластични полимери
- Специфичен долен праг на работна разделителна способност - z axis: 80  $\mu\text{m}$

### Реални 3D модели на полимерни микроигли

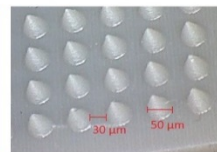


Усложнен модел: Пет-стенна пирамида

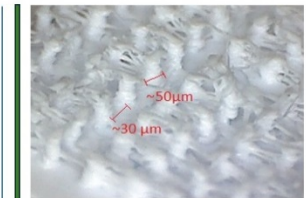
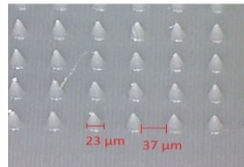


Пач с масив от пирамидални микроигли

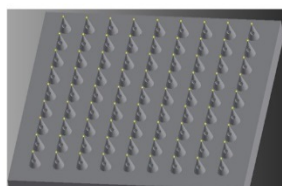
- Най-прост модел: прав кръгов конус



- Усложнен модел: пет-стенна пирамида

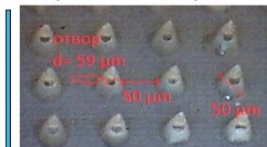


Усложнен модел: Кух конус със страничен отвор



Пач с масив от кухи конусовидни микроигли със странични отвори

- Усложнен модел: кухи конусовидни микроигли със странични отвори



Представя: Теодора Димитрова, бакалавър Инж. химия и съвременни материали, 3 курс.

С подкрепата на проф. Елена Василева. Ръководен от гл. ас. Марин Симеонов

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Благодарности: Това изследване е реализирано с финансовата подкрепа на Министерство на образованието и науката, програма Европейски научни мрежи, проект EXTREME, D01-76/30.03.202.





## Synthesis of Polymer Amphiphiles for Niosome Surface Modification

Krum Aleksandrov<sup>1</sup>, Erik Dimitrov<sup>1</sup>, Natalia Toncheva-Moncheva<sup>1</sup>, Pavleta Shestakova<sup>1</sup>, Stanislav Rangelov<sup>1</sup>

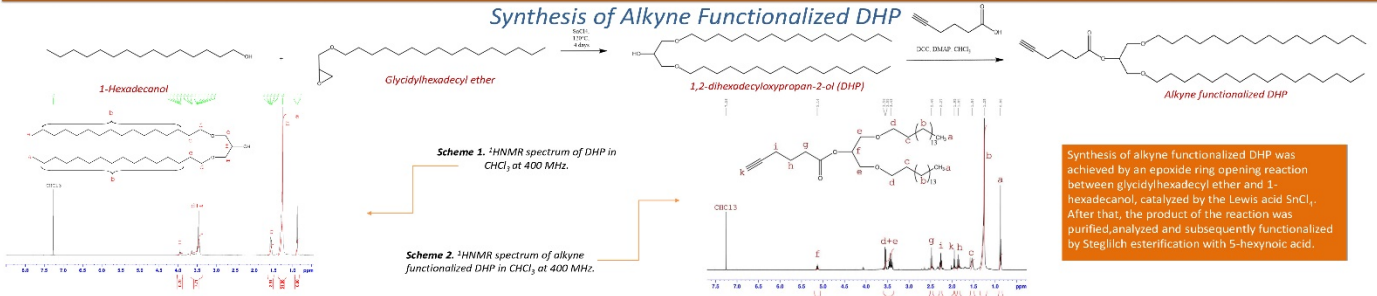
<sup>1</sup>Institute of Polymers, Bulgarian Academy of Sciences, Akad. G. Bonchev St., block 103-A, BG - 1113 Sofia, Bulgaria

<sup>2</sup>Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences, Acad. G. Bonchev str., bl. 9, 1113 Sofia, Bulgaria

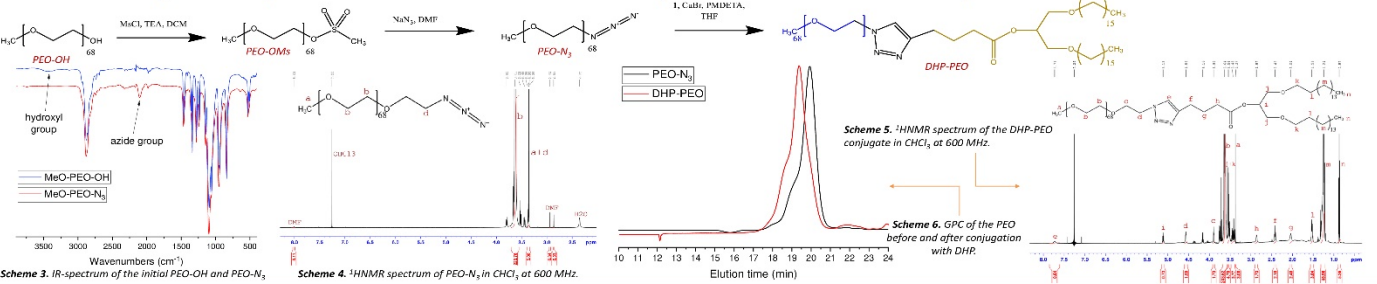


Targeted drug delivery is rapidly becoming a focal point in contemporary pharmaceutical science and technology. This concept has been brought to life due to the latest breakthroughs in nanotechnology. Niosomes, which are nanoscale drug carriers, are garnering significant scientific attention as potential drug delivery systems. These are made up of nonionic surfactants and cholesterol, and they present numerous benefits as vesicles for drug encapsulation, including co-delivery of lipophilic/water-insoluble and hydrophilic compounds, biocompatibility, low immunogenicity, stability (physical, chemical, and osmotic), and properties of controlled release and targeting. The niosome membranes can be altered by incorporating suitably designed polymers. This approach opens up multiple opportunities for constructing highly efficient carriers that can also control the release of the encapsulated drugs. In this context, a variety of polymer amphiphiles based on a series of non-phospholipid conjugates of polyethylene oxide, polyacrylic acid, poly(2-isopropyl-2-oxazoline), and poly(ethyltriethyleneglycolacrylate) were synthesized and thoroughly characterized using "click" chemistry reactions. New niosome formulations using various surfactants and the polymer amphiphile are set to be developed and characterized in terms of size, size distribution, and morphology.

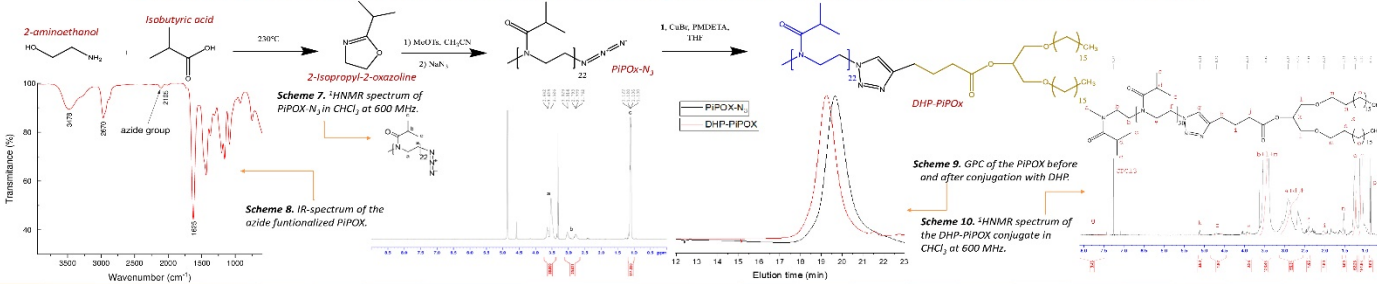
### Synthesis of Alkyne Functionalized DHP



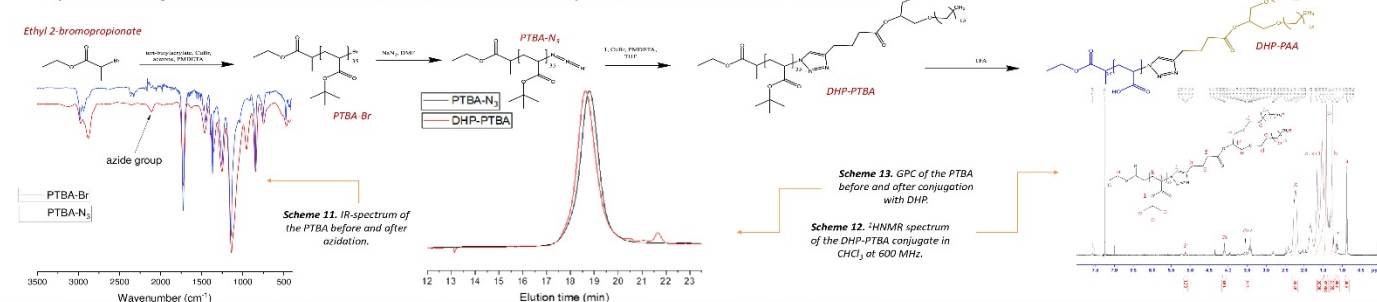
### Synthesis of Azide Functionalized PEO and Subsequent Click Reaction with Alkyne Functionalized DHP



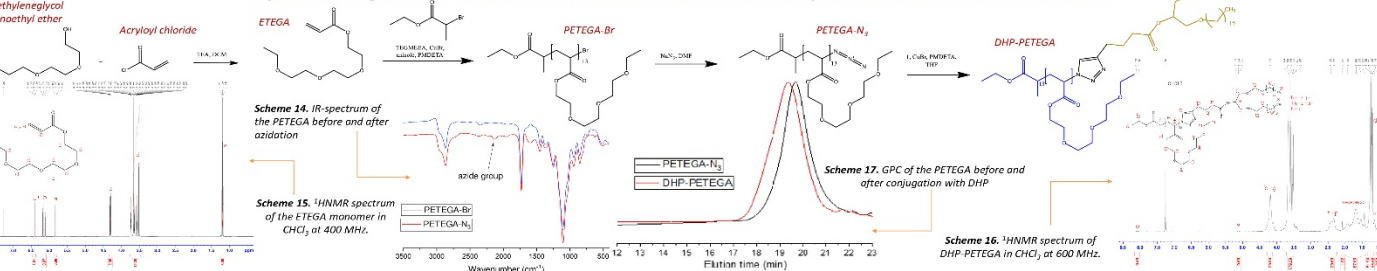
### Synthesis of Azide Functionalized PIPOx and Subsequent Click Reaction with Alkyne Functionalized DHP



### Synthesis of Azide Functionalized PTBA and Subsequent Click Reaction with DHP



### Synthesis of Azide Functionalized PETEGA and Subsequent Click Reaction with DHP





## Dental composite polymer surface treated by Femtosecond laser

**Dragomir Vassilev<sup>1,2\*</sup>, Vesela Stefanova<sup>3</sup>, Kostadin Zhekov<sup>3</sup>, Todor Petrov<sup>1</sup>, Lyubomir Stoychev<sup>1</sup>**

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### Introduction

Composite fillings are made up of silica, or glass bounded with polymer resins; polymer resins are commonly filled with glass fillers (35%–85%), and methacrylic acid is the main monomer unit. Today, composite fillings are widely used for dental fillings because they can mimic the original color and texture of the patient's tooth by the addition of different fillers. Bis-GMA is the potential dental resin material that is widely used for dental applications along with TEGDMA, which acts as a diluent, CQ, which acts as the photoinitiator, and EDMAB or DMAEMA.

### Aim

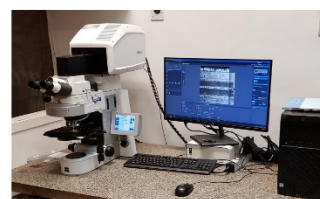
To study the interactions of femtosecond laser radiation with dental composite polymer.



Laser - Pharos model Ph2-10-1000-02-H0-B



Polymer treated with laser light



Confocal microscope ZEISS LSM 9006

### Materials and methods

Clearfil Majesty Esthetic opaque OA3 (Kuraray Noritake Dental Inc., Japan) a dental commercial composite polymer was used for this research. A sample with dimensions 8x11x1 mm (width/length/thickness) light cured with standard clinical light source at wavelength 450 nm for 60 seconds was studied.

Laser - Pharos model Ph2-10-1000-02-H0-B (Light Conversion UAB, Lithuania), with an automated harmonic generator, operating at three wavelengths - 1030 nm, 515 nm and 343 nm, with maximum output powers of 10 W, 5.9 W and 2.8 W respectively was used as a laser source. In the present study we used the fundamental wavelength at 1030 nm with pulse width of 170 fs as there are plenty of commercial lasers working at this wavelength.

The output powers of the laser radiation at all wavelengths is finely attenuated by internal power control, giving possibility to set the appropriate value of power densities on the treated areas.

The effects of the treatment were observed with the help of a confocal microscope ZEISS LSM 900 with Airyscan 2, resolution - lateral (XY) down to 120 nm, axial (Z) 350 nm. Digital images of x10 magnification were obtained as well as 3D profiles by using the z-stack feature of the microscope.

### Results

The composite polymer sample was treated with the 1030 nm laser wavelength at 100 kHz repetition rate. We processed an areas of 0.5 x 0.5 mm using a scanner intelliSCAN se 14 (SCANLAB GmbH), equipped with an F-Theta lens with focal length of 150 mm, at different setting - number of cycles drawn, number of hatches in a cycle and step (distance between the hatches), - at different laser pulse energies: 2 μJ, 4 μJ, 6 μJ, 8 μJ, 10 μJ, 15 μJ, 20 μJ. The step determines the distance between the lines that the laser executes to fill the object. By increasing the number of cycles, we increase the number of times we repeat the processing of the object at the given settings. Interaction is first occurring at 4μJ or 6 μJ laser energy at the given laser settings - λ=1030 nm, 100 kHz, 10 W, 100 μJ. As can be seen from the results of depth measurements of the processed areas, presented in the table the removed material increases proportionally with the applied energy and the number of hatches.

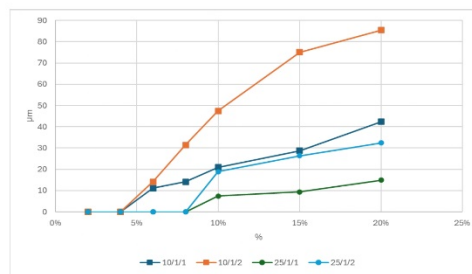
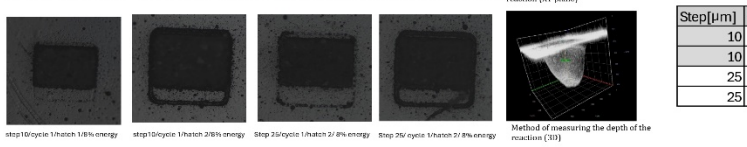
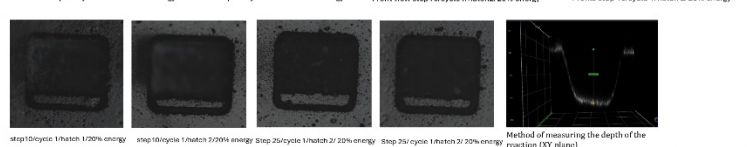
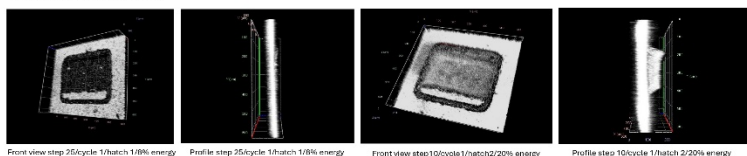


Figure 1: Graph of the received experimental data from Figure 1

Step[μm]	Cycle[N]	Hatch[N]	2%	4%	6%	8%	10%	15%	20%
10	1	1	0	0	11,092	14,168	20,963	28,783	42,335
10	1	2	0	x	14,128	31,449	47,436	75,07	85,393
25	1	1	0	0	x	x	7,447	9,387	14,908
25	1	2	0	x	x	x	18,939	26,409	32,41

Figure 2: Depth of the processed Clearfil polymer, treated with laser light with different operation parameters

### Conclusion

From the obtained results it is visible that for rough treatment the higher energies are more appropriate, while for precise removal of material lower energies (6μJ – 8 μJ) should be applied. Further studies of different regimes of the scanner settings will be performed in order to better understand the optimal parameters for processing of dental polymer, as well as other polymers with application in dental medicine. The effects of treatment of the Clearfil dental polymer with other laser wavelengths will be done to find the most suitable for processing.

### Acknowledgments

This work was financially supported by the Bulgarian National Science Fund under project Grant No: KP-06-N78/8 (14.12.2023) and ELI "Extreme Light" (Extreme Light Infrastructure BG) D01-401 (18.12.2020) BG05M2OP001-1.001-0008.

# Организационен КОМИТЕТ

**Председател**

**Доц. д-р Еми Халаджова**

**Членове**

**Гл. ас. д-р Катя Каменова-Стоянова**

**Гл. ас. д-р Велмира Димитрова**

София, 2024г.