ДВАНАДЕСЕТА

НАУЧНА СЕСИЯ

„МЛАДИТЕ УЧЕНИ В СВЕТА НА ПОЛИМЕРИТЕ“

3 юни 2021 г.

Гр. София

Програма на научната сесия:

13:30-13:40 ч. Откриване

13:40 ч.-15:40 ч. Представяне на постери

15.40-15.50 ч. Награждаване на отличени постери

15.50-16.00 ч. Закриване

СПИСЪК НА УЧАСТНИЦИТЕ

Постер № 1

С. Захова, И. Цачева, К. Троев, В. Митова

Изследване процеса на гликолиза на отпадъчен ПЕТ в микровълнов реактор

Институт по полимери – БАН

Постер № 2

Б. Караманова , Л. Сосеров, Хр. Новаков, И. Димитров, А. Стоянова

Електрохимични и структурни изследвания на екологичен хибриден суперкондензатор с полимерно свързващо вещвство

Институт по електрохимия и енергийни системи, Българска академия на науките, София, България
Институт по полимери, Българска академия на науките, София, България

Постер № 3

N. Nachev, M. Spasova, N. Manolova, I. Rashkov, M.Naydenov

Polymer composite fibrous materials with imparted biological activity

Institute of Polymers, Bulgarian Academy of Sciences, Sofia, Bulgaria
Department of Microbiology, Agricultural University, Plovdiv, Bulgaria;

Постер № 4

М. Игнатова, Н. Начев, М. Спасова, Н. Манолова, И. Рашков, М. Найденов

Получаване, охарактеризиране и противогъбична активност на нови електроовлакнени материали от поли(3-хидроксибутират) и поливинилпиролидон, с включено производно на 8-хидроксихинолина

Институт по полимери, Българска академия на науките, София, България
Катедра „Микробиология и екологични биотехнологии“, Аграрен Университет, Пловдив, България

Постер № 5

M. Sabeva, R.Stancheva, E. Haladjova, S. Pispas, S. Rangelov

Effect of concentration on the physico-chemical properties and drug release profile of cationic polymer micelles

University of Chemical Technology and Metallurgy, Sofia, Bulgaria
Institute of Polymers, Bulgarian Academy of Sciences, Sofia, Bulgaria
Theoretical and Physical Chemistry Institute, National Hellenic Research Foundation, Athens, Greece

Постер № 6

R. Stancheva, E. Haladjova, T. Damyanova, T. Topouzova-Hristova, P. Petrov

Mixed polymeric micelles of different composition as vehicles for delivery of antibiotics

Institute of Polymers, Bulgarian Academy of Sciences, Sofia, Bulgaria
Faculty of Biology, Sofia University "St. Kliment Ohridski", Sofia, Bulgaria

Постер № 7

P. Dimitrova, Ts. Paunova-Krasteva, E. Haladjova, R. Stancheva, S. Stoitsova

Destruction of preformed bacterial biofilms bymixed polymeric micelles of different composition

Институт по микробиология „Стефан Ангелов", Българска академия на науките, София, България
Институт по полимери, Българска академия на науките, София, България

Постер № 8

С. Стоилова, Я. Данов, Б. Костова, П. Петров

Poly(N,N-dimethylacrylamide)/ß-cyclodextrin nanogel for drug delivery

Faculty of Pharmacy, Medical University of Sofia, Sofia, Bulgaria
Institute of Polymers, Bulgarian Academia of Science, Sofia, Bulgaria

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S. Dimova, K. Zaharieva, V. Hubenov, R. Eneva, F. Ublekov, I. Stambolova, D. Stoyanova, L. Dimitrov

Preparation, antibacterial and photocatalytic properties of Polylactide/Hydrozincite and Polylactide/Hydrozincite/Polyvinylpyrrolidone nanofilms

Институт по полимери, Българска академия на науките, София, България
Институт по катализ, Българска академия на науките, София, България
Институт по микробиология „Стефан Ангелов“, Българска академия на науките, София, България
Институт по обща и неорганична химия, Българска академия на науките, София, България
Институт по минералогия и кристалография “Акад. Иван Костов” , Българска академия на науките, София, България

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M. Alexandrova , S. Ivanova, N. Minev , V. Marinova , D. Christova

Poly(vinyl acetals) from aromatic aldehydes for nanocomposite aqueous graphene dispersions and thin films

Institute of Polymers, Bulgarian Academy of Sciences, Sofia, Bulgaria
Institute of Optical Materials and Technologies “Acad. J. Malinowski”, Bulgarian Academy of Sciences, Sofia, Bulgaria

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Й. Тупарова, Д. Николова, К. Русева, М. Симеонов, Л. Христов, Х. Цачев, Е. Василева

Нови лекарствени носители за модифицирано лекарствено доставяне на тимолол малеат на базата на поли(сулфобетаин метакрилат) и хитозан

Факултет по химия и фармация, СУ „Св. Климент Охридски“, София България

Постер № 12

З. Тодорова, А. Бакалова, Д. Динева, Я. Петрова, Н. Косева

Получаване на синтетичен полимерен слой с потенциално антибактериално действие

Институт по полимери, Българска академия на науките, София, България

Постер № 13

K. Kamenova, V. Kortenova, G. Grancharov, P. Petrov

Shell-crosslinked mixed micelles for intracellular drug release

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

Постер № 14

D. Petkova, E. Haladjova, S. Rangelov

New strategy for preparation of Spherical Nucleic Acids with hybrid lipid/polymer cores

University of Chemical Technology and Metallurgy, Sofia, Bulgaria
Institute of Polymers, Bulgarian Academy of Sciences, Sofia, Bulgaria

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S. Bozhilova, K. Lazarova, S. Ivanova, Ts. Babeva, D. Christova

Colloidal dispersions of methyl acrylate grafted poly(vinyl alcohol)s: synthesis and application for optical sensing of acetone

Institute of Polymers, Bulgarian Academy of Sciences, Sofia, Bulgaria
Institute of Optical Materials and Technologies “Acad. J. Malinowski”, Bulgarian Academy of Sciences, Sofia, Bulgaria

Постер № 16

A. Danailova, S. Stoichev, D. Manga, I. Iliev, S. Taneva, T Andreeva

Effect of grapheme oxide incorporation on the biocompatibility of natural polyelectrolyte multilayers

Institute of Biophysics and Biomedical Engineering, Bulgarian Academy of Sciences, Sofia, Bulgaria,
Institute of Experimental Morphology, Pathology and Anthropology with Museum, Bulgarian Academy of Sciences, Sofia, Bulgaria

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V. Uzunova, A.-R. Tsiapla, E. Myrovali, I. Georgieva, M. Popova, T. Stoyanova, M. Angelakeris, O. Kalogirou, R. Tzoneva

Magnetic hyperthermia and magnetomechanical treatment on breast cancer cells

Institute of Biophysics & Biomedical Engineering, Bulgarian Academy of Sciences, Sofia, Bulgaria
Department of Physics, Aristotle University of Thessaloniki, Thessaloniki, Greece

Постер № 18

G. Borisov, H. Penchev, M. Staneva, D. Bodurova, F. Ublekov, E. Slavcheva

Highly advanced aem water electrolyzer with composite Polybenzimidazole/Zif-8 based polymer electrolyte membrane

Institute of Electrochemistry and Energy Systems “Acad. Evgeni Budevski”, Bulgarian Academy of Sciences, Sofia, Bulgaria
Institute of Polymers, Bulgarian Academy of Sciences, Sofia, Bulgaria

Постер № 19

N. Borisov, G. Borisov, E. Slavcheva

AEM water electrolyzer in stack mode with PBI-membrane

Institute of Electrochemistry and Energy Systems “Acad. Evgeni Budevski”, Bulgarian Academy of Sciences, Sofia, Bulgaria

Постер № 20

К. Младенова, Е. Димитров, Н. Тончева-Мончева, П. Бакърджиев, С. Петрова, П. Видев, В. Москова-Думанова, Й. Думанов, С. Рангелов

ДНАзна и липазна активност върху липозомни сферични нуклеинови киселини

Биологически факултет, Софийски Университет „Св. Климент Охридски“, София, България
Институт по Полимери, Българска академия на науките, София, България

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E. Dimitrov, N. Toncheva-Moncheva, P. Bakardzhiev, K. Mladenova, S. Petrova, P. Videv, V. Moskova-Doumanova, J. Doumanov, B. Trzebicka, A. Forys, S. Rangelov

Synthesis and characterization of liposomal spherical nucleic acids via incorporation of an original nucleolipid

Institute of Polymers, Bulgarian Academy of Sciences, Sofia, Bulgaria
Faculty of Biology, Sofia University “, Sofia, Bulgaria
Centre of Polymer and Carbon Materials, Polish Academy of Sciences, Zabrze, Poland

Постер № 22

E. Dimitrov, E. Vlassi, N. Toncheva-Moncheva, K. Mladenova, J. Doumanov, S. Pispas, S. Rangelov

Development of spherical nucleic acids from novel poly(chloromethylstyrene)-oligonucleotide conjugates via rapid and initiator-free click chemistry

Institute of Polymers, Bulgarian Academy of Sciences, Sofia, Bulgaria
Faculty of Biology, Sofia University, Sofia, Bulgaria
Theoretical and Physical Chemistry Institute, National Hellenic Research Foundation, Athens, Greece

Постер № 23

D. Yordanova, E. Dimitrov, N. Toncheva-Moncheva, D. Momekova, P. Petrov, G. Grancharov, S. Rangelov

Novel amphiphilic polyglycidol/poly(ε-caprolactone) and polyglycidol/poly(α-cinnamyl-ε-caprolactone) copolymers as highly effective cannabidiol-loaded nanocarriers

Institute of Polymers, Bulgarian Academy of Sciences, Sofia, Bulgaria
Faculty of Pharmacy, Medical University of Sofia, Sofia, Bulgaria

Постер №24

C. A. C. da Silva, N. Koseva

Glycolysis of Polyethylene Terephthalate (PET) - Literature Search

Faculty of Chemistry and Pharmacy, Sofia University “St. Kliment Ohridski”, Sofia, Bulgaria
Institute of Polymers, Bulgarian Academy of Sciences, Sofia, Bulgaria

Постер №25

Х. Манов, Д. Станева, С. Стоянов, И. Грабчев

Фоточувствителни дендримери като добра алтернатива на антимикробна фотодинамична терапия срещу Грам отрицателни бактерии с противотуморна активност

Факултет по химия и фармация, СУ“Св.Кл.Охридски“, София, България

Химикотехнологичен и металургичен университет, София, България
Медицински факултет, СУ“Св. Кл.Охридски“, София, България

ПОСТЕРИ

Постер 1

ДВАНАДЕСЕТА НАУЧНА СЕСИЯ „МЛАДИТЕ УЧЕНИ В СВЕТА НА ПОЛИМЕРИТЕ“

3 юни 2021 година, ИП-БАН, гр София, ул. Академик Георги Бончев 103

ИЗСЛЕДВАНЕ ПРОЦЕСА НА ГЛИКОЛИЗА НА ОТПАДЪЧЕН ПЕТ В МИКРОВЪЛНОВ РЕАКТОР

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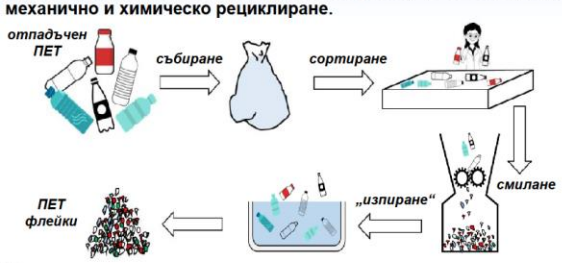
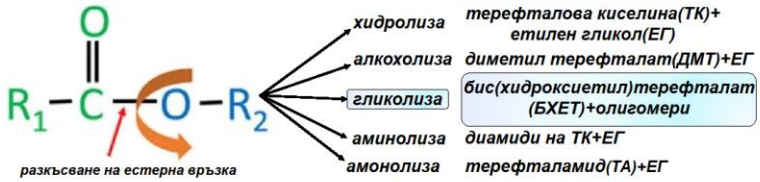
Полиестерите са едни от най-често използваните полимери в нашето съвремие. Получават се чрез реакция на поликондензация между диол или диалкохол с дикиселина. Сред тях полиетиелен терефталатът (ПЕТ) е предпочитан за употреба, като опаковъчен материал за храни и напитки. Най-важните му характеристики са висока механична устойчивост, термична стабилност, отлични бариерни свойства, ниска производствена цена. Не на последно място, полимерът е напълно рециклируем. Според проучване на Greenpeace във Великобритания 245 милиона тона пластмаса се използват всяка година, от тях опаковките са една четвърт, като само 14% се рециклират. ПЕТ бутилките са втората по големина категория пластмасови опаковки, а тяхното производство расте непрекъснато. Това се дължи на факта, че ПЕТ може да замени стъклото. Два са основните метода за рециклиране на отпадъчен ПЕТ материал – механично и химическо рециклиране.



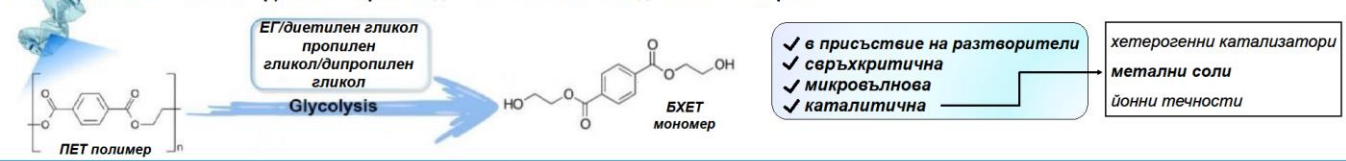
Методът се отнася до механичното смилане и получаване на различни изделия при повторна преработка на материала.



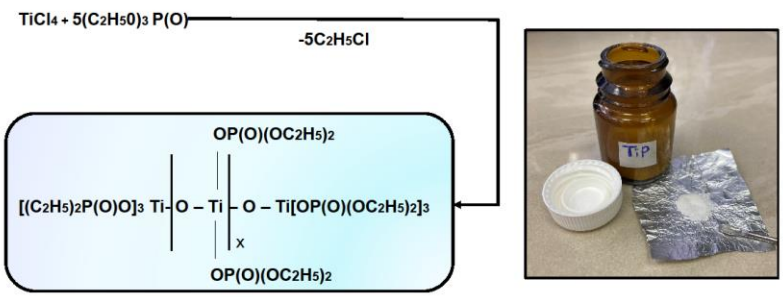
Методите на химическо рециклиране са по-добра алтернатива за оползотворяването на ПЕТ отпадъците, тъй като представляват начин за възстановяване на основните му мономери. Гликолизата и свързаните с нея процеси, допринасят за по-устойчива ПЕТ икономика, въпреки високите енергийни разходи за поддържане на температури и дълги реакционни времена, необходими за ефективна деполимеризация.

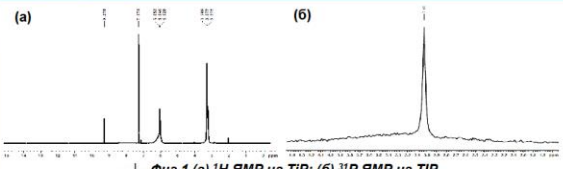
ПЕТ гликолиза

Гликолизата без катализатор е много бавен процес. Не може да се постигне пълна деполимеризация на ПЕТ до БХЕТ. Добивът съдържа значително количество олигомери, което затруднява възстановяването на желания мономер. Изследователските усилия се насочват към увеличаване добива на БХЕТ чрез разработване на високоефективни катализатори и оптимизиране на други техники и реакционни условия (температура, време, съотношение ПЕТ/ЕГ, съотношение ПЕТ /катализатор). Има четири метода за гликолиза на отпадъчен ПЕТ материал:

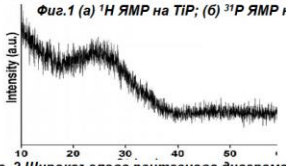


Получаване на титанов(IV)фосфат (TiP)





Фиг.1 (а) ^{1}H ЯМР на TiP; (б) ^{31}P ЯМР на TIP



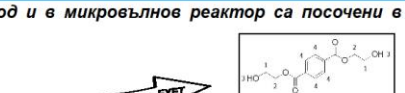
Фиг. 2 Широкоъглова рентгенова диаграма на TiP

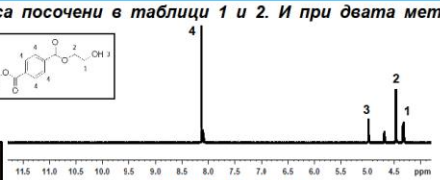
Гликолиза на ПЕТ/TiP

Условията за провеждане на гликолиза чрез конвенционален метод и в микровълнов реактор са посочени в таблици 1 и 2. И при двата метода молното отношението ПЕТ/ЕГ е 1:2,77.

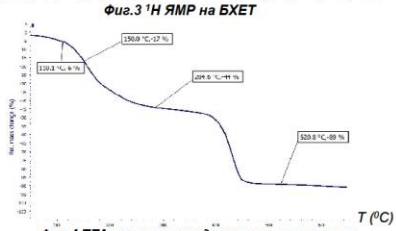
Таблица 1. Конвенционална гликолиза

код проба	TiP (тег %)	T (^{0}C)	време за разграждане (мин)	БХЕТ (%)
1	-	190-200	540	59,13
2	0,05	190-200	175	63,90
3	0,1	190-200	155	66,37
4	0,2	190-200	130	64,66
5	0,3	190-200	120	67,11
6	0,5	190-200	125	65,26





Фиг.3 ^{1}H ЯМР на БХЕТ



Фиг.4 ТГА крива на продукта на гликолизата

Таблица 2. Гликолиза в микровълнов реактор „RotoSynth“

код проба	TiP (тег %)	T (^{0}C)	мощност (W)	време за разграждане (мин)	БХЕТ (%)
MW1	-	217-220	450	260	44,28
MW2	-	217-220	450	320	49,20
MW3	-	217-220	500	225	48,09
MW4	0,05	217-220	450	65	57,50
MW5	0,1	217-220	450	50	58,95
MW6	***0,2***	***217-220***	***450***	***45***	***61,71***
MW7	0,2	217-220	500	41	53,83
MW8	0,2	217-220	600	38	56,03
MW9	0,3	217-220	450	42	55,09
MW10	0,5	217-220	450	45	56,41

Изводи:

- **Получен е катализатор, който ефективно разгражда ПЕТ до високо чист мономер при сравнително меки условия, което оптимизира процесите на рециклиране.**
- **При конвенционален метод на гликолиза, най-добро разграждане се получава при 0,3% катализатор, за време 120 мин и добив на БХЕТ-67,11%.**
- **При гликолиза в микровълнов реактор, най-добро разграждане се получава при 0,2% катализатор с време на разграждане 45 мин и добив на БХЕТ-61,71%.**

Постер 2

Електрохимични и структурни изследвания на екологичен хибриден суперкондензатор с полимерно свързващо вещество

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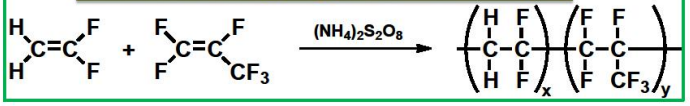
Хибридните суперкондензатори са перспективни системи за съхранение на енергия. Въпреки засиленият изследователски интерес и интензивната работа в тази област, постигането едновременно на висока енергийна плътност и плътност на мощността чрез използване на екологосъобразни материали е актуална задача, която изисква допълнителни разработки. Установено, че свързващото вещество действа върху структурата на порите и оттам върху работните параметри на суперкондензаторите системи.

Полипентафлуоростиренът и неговите съполимери предизвикват интерес поради наличието на лабилен флуорен атом, разположен на p-позиция в ароматното ядро, който позволява лесно модифициране на полимерната верига. Интерес представлява използването за първи път на polyvinylidene fluoride–co-hexafluropropylene (PVDF-co-HFP) като свързващо вещество в електродната активна маса на суперкондензаторни клетки.

Целта бе получаването на високомолекулен съполимер и охарактеризирането му с помощта на гелово-проникваща хроматография. Определени са стойности за средни бройна (Mn) и масова (Mw) молекулни маси от 78 kDa и 225 kDa, респ. и полидисперсност (Mw/Mn) 2.86

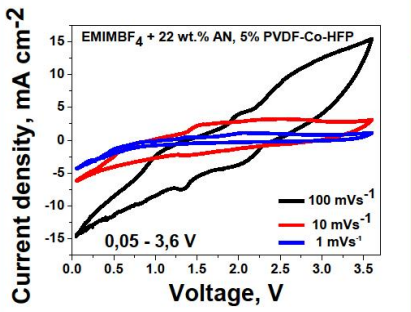
Синтез на poly(PVDF-co-HFP)



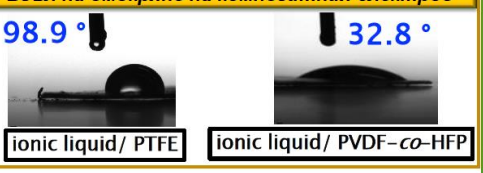
Като въглероден електроден материал е подбран активен въглен, търговски продукт на фирма "Kuraray Europe" GmbH, получени от биомаса - YP-50F. Той е морфологично и структурно охарактеризиран и е показано, че притежава висока специфична микропореста повърхност (S_{BET} = 1756 m^2g^{-1}) и основен характер. За композитен електроден материал е използван αβ-$Ni(OH)_2$, който показва високи и стабилни капацитивни характеристики.

Асемблирани са хибридни суперкондензаторни клетки с електролит 1-ethyl-3-methylimidazolium tetrafluoroborate ($EMIMBF_4$) и добавка на 22 тегл.% ацетонитрил (AN). Проведени са електрохимични тестове и *ex-situ* физикохимични анализи.

Циклични волтамперометрични (CV) криви при различни скорости на разгъване на потенциала

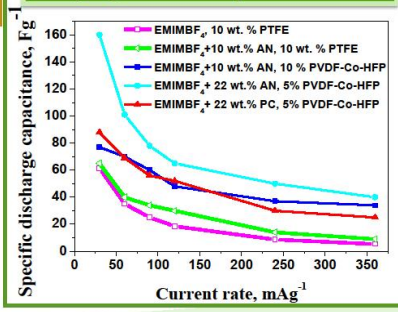


Ъгъл на омокряне на композитния електрод



Сравнението между традиционно използваното в тези системи свързващо вещество- политетрафлуоретилен (PTFE) и синтезирания съполимер показва, че структурата на PVDF-co-HFP играе съществена роля за подобряване на омокряемостта на електродите и съответно на електрохимичните характеристики на изследваните суперкондензатори.

Зарядно/разрядни тестове, зависимост на разрядния капацитет от токовото натоварване на хибридни суперкондензаторни клетки



Изводи:

Хибридният суперкондензатор със свързващо вещество PVDF-*co*-HFP демонстрира повишени електрохимични характеристики:

- **По-висок разряден капацитет в сравнение с този на суперкондензатора с PTFE (с около 30-40%);**
- **Използването на PVDF-*co*-HFP като свързващо вещество намалява ъгъла на омокряне около два пъти в сравнение с PTFE, което е вероятна причина за получения положителен ефект.**
- **Наличието на оптимален брой къси полиетерни странични вериги в полимера допринасят за по-високата омокряемост на електродите**
- **Необходими са допълнителни проучвания, за да се изясни по-детайлно действието на полимерното свързващо.**

Благодарности: Тази работа е финансово подкрепена от Министерство на образованието и науката чрез национална научна програма Е+: Нисковъглеродна енергия за транспорта и бита, договор ДО1-214/2018

ДВАНАДЕСЕТА НАУЧНА СЕСИЯ „МЛАДИТЕ УЧЕНИ В СВЕТА НА ПОЛИМЕРИТЕ"

Постер 3

Polymer composite fibrous materials with imparted biological activity

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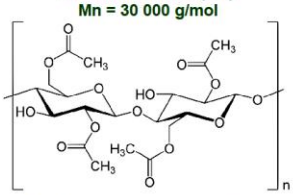
Grapevine trunk diseases, especially esca, are of major concern since they gradually alter vineyards worldwide and cause heavy economic losses. *Phaeomoniella chlamydospora* and *Phaeoacremonium aleophilum* are the two main fungal causal agents of esca. Cellulose acetate (CA) is one of the most important esters of cellulose. The advantages of CA are it's low cost, ease of solubility in solvents suitable for electrospinning, facile production and wide variety of applications. PEG is a biocompatible and nontoxic polymer . It is highly hydrophilic, with excellent solubility in water and in organic solvents. 8-Hydroxyquinoline and its derivatives manifest antibacterial and antifungal activities and are of low toxicity to humans. The aim of the present study was to explore the possibilities for designing innovative polymer composites that possess biological activity against the two fungal strains *Phaeomoniella chlamydospora* and *Phaeoacremonium aleophilum*.

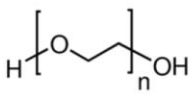
Materials

Cellulose acetate (CA)
Mn = 30 000 g/mol



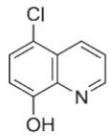
Biodegradable, biocompatible, nontoxic

Polyethylene glycol (PEG)
Mr = 1,900–2,200 g/mol



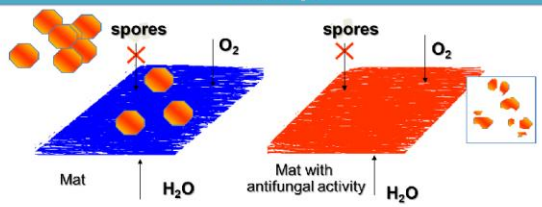
Biocompatible, nontoxic

5-chloro-8-hydroxyquinoline (5-Cl8Q)



antibacterial and antifungal* activities

Concept

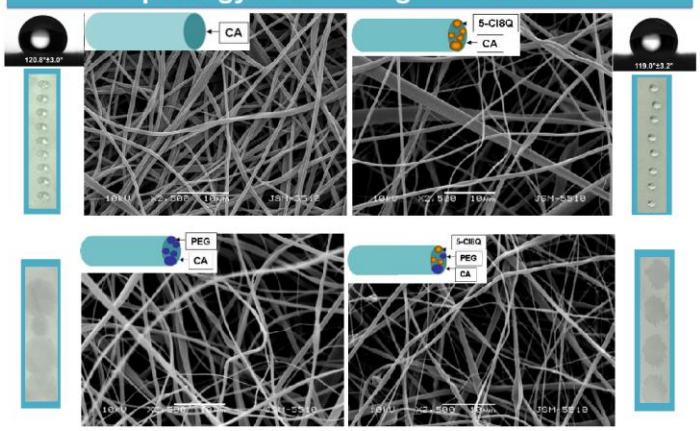


Passive protection
(impedes the penetration of pathogenic fungi)

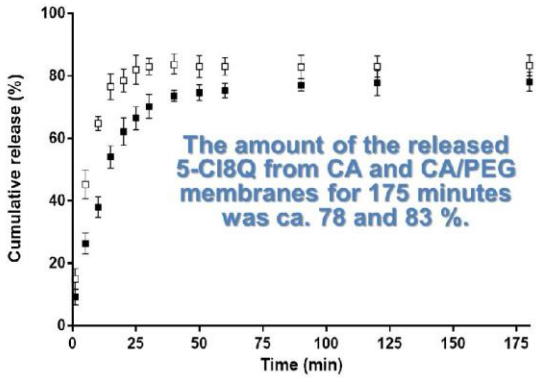
Active protection
(impedes the penetration and growth of pathogenic fungi)

There is no growth of any pathogenic fungi

Morphology and wetting of membranes



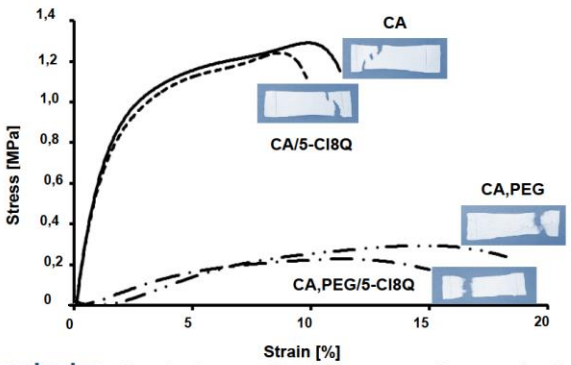
In vitro release of 5-Cl8Q from the membranes



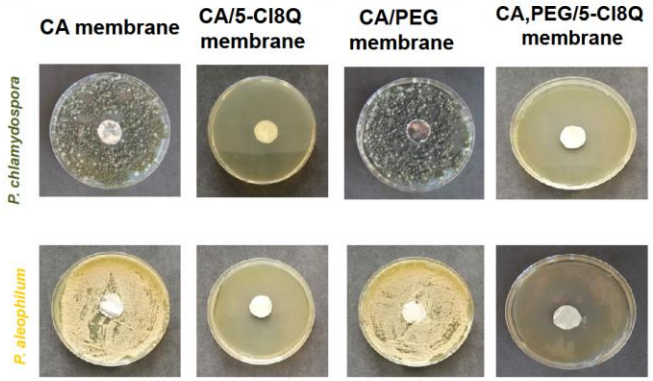
The amount of the released 5-Cl8Q from CA and CA/PEG membranes for 175 minutes was ca. 78 and 83 %.

CA/5-Cl8Q (■) and CA,PEG/5-Cl8Q (□)

Stress–strain curves of membranes



Antifungal activity



Conclusion. **Novel micro- and nanofibrous membranes of cellulose acetate and cellulose acetate/PEG containing 8-Hydroxyquinoline (5-Cl8Q) were successfully prepared by electrospinning. The addition of PEG led to the hydrophilization of the membranes and facilitated their wetting. It was demonstrated that the 5-Cl8Q release profile can be modulated by the appropriate selection of the composition of the electrospun membrane. The incorporation of 5-Cl8Q in the membranes imparted a considerable antifungal effect against *Phaeomoniella chlamydospora* and *Phaeoacremonium aleophilum* fungi. These features indicate that the obtained hybrid fibrous materials could find application in agriculture for plant protection against growth of pathogenic fungi.**

References: * [1] Spasova, M; N. Manolova; Rashkov, I. Composition of plant protection product. Utility model request №4353 in Patent office of Republic of Bulgaria, **2019**.
[2] Spasova, M.; Manolova, N.; Rashkov, I.; Naydenov, M. Electrospun 5-chloro-8-hydroxyquinoline-loaded cellulose acetate/polyethylene glycol antifungal mats against Esca. *Polymers* ,**2019**, 11, 1617, 1-13.
[3] Nachev, N.; Spasova, M.; Manolova, N.; Rashkov, I.; Naydenov, M. Polymer membranes from biodegradable polymer and chemical fungicide prepared by electrospinning. *IOP conference series*, **2021**, *submitted.*

Acknowledgement: Financial support from the Bulgarian National Science Fund (Grant KP-06-OPR03/2) is gratefully acknowledged.

Постер 4

Получаване, охарактеризиране и противогъбична активност на нови електроовлакнени материали от поли(3-хидроксибутират) и поливинилпиролидон, с включено производно на 8-хидроксихинолина

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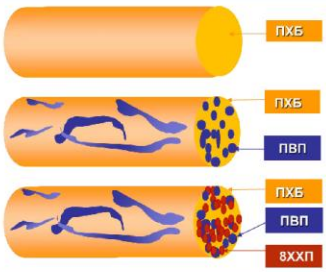
[1]Лаборатория „Биологично активни полимери", Институт по полимери, Българска академия на науките, Акад. Г. Бончев, бл. 103А, 1113 София, България ,[2]Катедра „Микробиология и екологични биотехнологии", Аграрен Университет, 4000 Пловдив, България

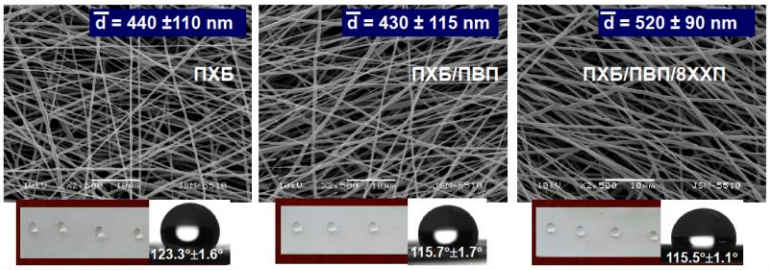
Целта на настоящето изследване е да се получат нови влакнести материали от поли(3-хидроксибутират) (ПХБ) и поливинилпиролидон (ПВП) с включено производно на 8-хидроксихинолина (8ХХП) чрез електроовлакняване. Цели се да бъде оценена и противогъбичната активност на получените влакнести материали спрямо два щама аскомицетни гъби *Phaeomoniella chlamydospora* и *Phaeoacremonium aleophilum* – основни причинители на заболяването еска по лозовите насаждения.

Схематично представяне и СЕМ микрографии на влакнестите материали

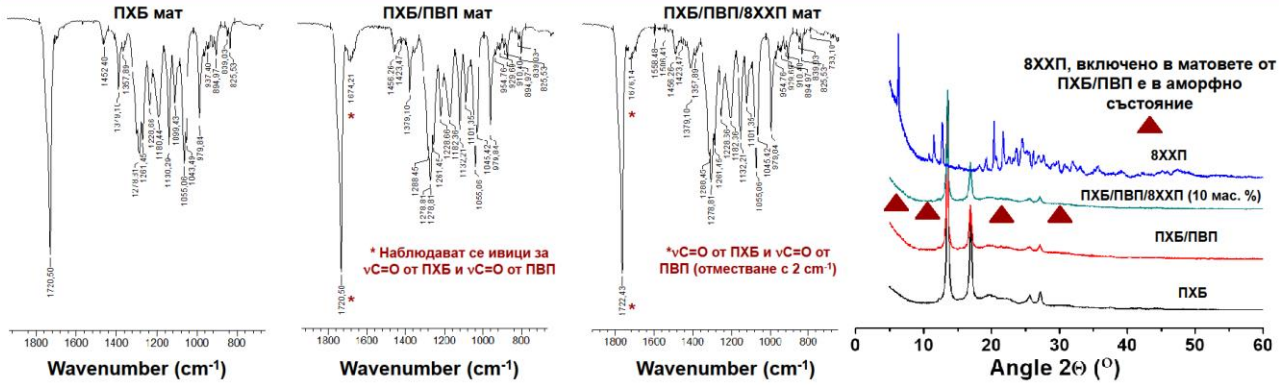


R^5 = Cl; R^7 = I

антимикробна и противогъбична активност



ИЧ спектри и рентгеноструктурен анализ



Противогъбична активност на влакнестите материали

Заключение: За първи път бяха успешно получени нови влакнести материали от ПХБ и ПВП и 8ХХП чрез едноетапно електроовлакняване. Установено беше, че 8ХХП, включено в материалите от ПХБ/ПВП е в аморфно състояние. Микробиологичните тестове показаха, че получените влакнести материали, съдържащи 8ХХП проявяват по-силно изразено фунгицидно действие спрямо гъбите *P. chlamydospora* отколкото спрямо гъбите *P. aleophilum*. Тези свойства правят получените влакнести материали перспективни кандидати за прилагане в селското стопанство за защита на лозовите насаждения от двата основни причинители на заболяването еска.

Благодарност: Авторите изказват благодарност на ФНИ (Договор КП-06-ОПР 03/2 от 14.12.2018 г) за финансовата подкрепа.

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Постер 5

EFFECT OF CONCENTRATION ON THE PHYSICO-CHEMICAL PROPERTIES AND DRUG RELEASE PROFILE OF CATIONIC POLYMER MICELLES

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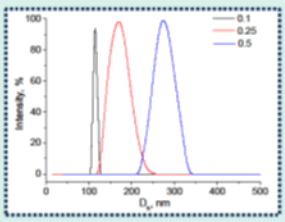
3 Theoretical and Physical Chemistry Institute, National Hellenic Research Foundation, 48 Vass. Constantinou Ave., 116 35 Athens, Greece

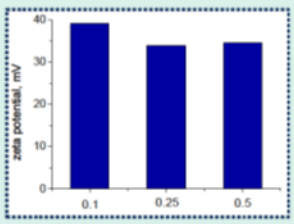
Aim

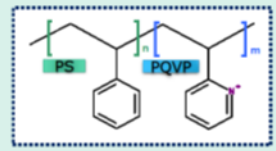
Cationic polymer micelles have been extensively studied because of their ability to transfer agents, such as drugs and nucleic acids.
This study aims at investigating the effect of micellar concentration on the physico-chemical as well as on the drug loading properties and release of cationic polymer micelles.

Polymer micelles

Polymer micelles were prepared at three different initial concentrations (0.1, 0.25 and 0.5 mg/ml) from polystyrene-b-poly(quaternized 2-vinylpyridine) (PS-PSPQVP) diblock copolymer (Mw=115 000 g/mol, Đ = 1.02, PQVP content 56 wt%). The resulting micelles consisted of a hydrophobic PS core and a positively charged hydrophilic PQVP shell.







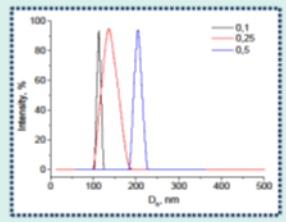
The hydrodynamic diameter (D_h) and polydispersity of the micelles were strongly dependent on their concentration. In contrast the zeta potential of the particles was only slightly influenced by the concentration.

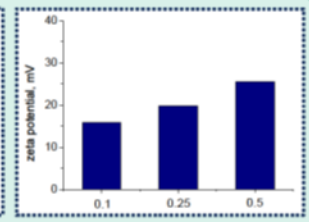
Drug loading of PS-PQVP micelles

The resulting polymer micelles were loaded with the antibiotic ciprofloxacin (CF) used as a model drug. The loading was achieved by sonicating micellar dispersions containing CF at a polymer to drug weight ratio 10:1 for 1 h at 60 °C. The shift of zeta potential to lower values suggested a possible interaction of PQVP with CF that is negatively charged at neutral pH.

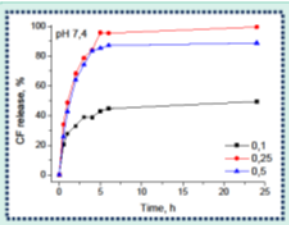
The encapsulation efficiency (EE) and drug loading content (DLC) were determined spectrophotometrically by the characteristic absorbance band of CF at 270 nm^{-1}.

Micellar concentration mg/ml	EE %	DLC %
0.1	95.9	13.4
0.25	97.6	10.2
0.5	97.7	10.4

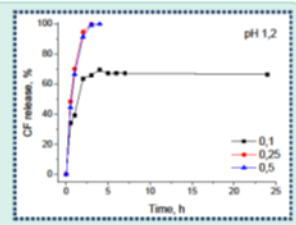




Drug release from PS-PQVP micelles



The drug release profiles were investigated in a 0.1 M HCl solution (pH=1.2) and phosphate buffer (pH=7.4) according to approved by USP/EP/BP methods. The amount of released CF was determined spectrophotometrically.
A strong concentration dependent release was observed independently from the medium used. The micelles observed at higher concentration (0.25 and 0.5 mg/ml) exhibited fast release for the first 4-5 h. In a contrast, the micelles of 0.1 mg/ml concentration showed a delayed release over the period of 24 h.



Conclusion

Cationic polymer micelles based on PS-PQVP diblock copolymer were prepared at three different concentrations. The hydrodynamic size of the resulting particles as well as their polydispersity were dependent on the micellar concentration as the value of both parameters increased with increasing concentration. The zeta potential of the micelles was only slightly influenced by their concentration. All dispersions exhibited zeta potential values in the 33.9 - 39.2 mV range. The micellar systems were successfully loaded with CF with EE of above 95.9 %. Both the D_h and zeta potential of CF loaded micelles shifted to lower values implying interactions of CF with the positive PQVP shell of the micelles due to the zwitterionic character of the drug exhibiting a negative charge at neutral pH and positive in acidic medium. The CF release from the PS-PQVP micelles was investigated at physiological conditions at dissolution media of pH 7.4 and 1.2. Strongly concentration dependent release profiles were observed. The micellar systems at higher concentrations (0.25 and 0.5 mg/ml) exhibited fast release for the first 4-5 h. In a contrast, the micelles of 0.1 mg/ml concentration showed a delayed release over the period of 24 h. It was noticeable also that the release was much faster at pH 1.2 that could be attributed to the protonation state of CF in acidic medium. We can conclude that the initial concentration of the resulting cationic polymer micelles was essential for their physico-chemical, drug loading and release properties providing control over a wide range of parameters.

Acknowledgement

This work was funded by the National Science Fund of Bulgaria, Project № КП-06-Н41/8.

Постер 6

MIXED POLYMERIC MICELLES OF DIFFERENT COMPOSITION AS VEHICLES FOR DELIVERY OF ANTIBIOTICS

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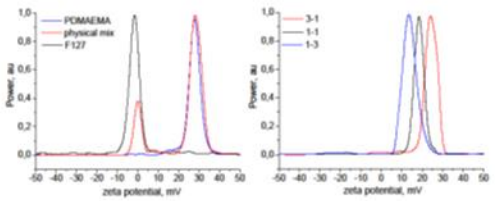
[1] Institute of Polymers, Bulgarian Academy of Sciences, Acad. G. Bonchev st bl.103A, Sofia 1113, Bulgaria
[2] Faculty of Biology, Sofia University "St. Kliment Ohridski", 8 Dragan Tsankov Blvd, 1164 Sofia, Bulgaria

INTRODUCTION

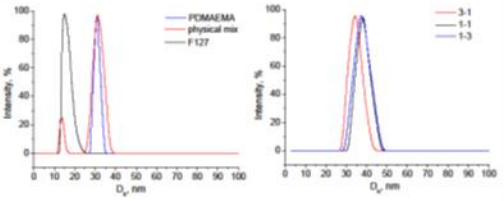
Ciprofloxacin (CF) is a wide spectrum antibiotic approved by FDA against various bacterial infections. The effective antimicrobial therapy, however, depends on the CF solubility and its efficient delivery to the target site of infection. Polymeric micelles (PMs) have been extensively studied as drug delivery carriers. In the recent years various micellar systems carrying a positive charge have been found to exhibited strong antibacterial activity.

In this work the loading of CF into polymeric micelles of different composition was investigated. Cationic polymer micelles (CPMs) based on poly(2-(dimethylamino)ethyl methacrylate)-b-poly(ε-caprolactone)-b-poly(2-(dimethylamino)ethyl methacrylate) triblock copolymer noted as PDMAEMA and non ionic polymer micelles (NPMs) formed from poly(ethylene oxide)-b-poly(propylene oxide)–b-poly(ethylene oxide) known as Pluronic F127 were used. Since the polycations are usually associated by pronounced cytoxicity, a mixed polymer micelles based on both copolymers were also prepared. All the systems were characterized by dynamic and electrophoretic light scattering. Their encapsulation efficiency (EE) and drug loading content (DLC) were determined spectrophotometrically. Finally a cytotoxicity evaluation of the resulting drug delivery systems was performed.

FORMATION OF POLYMER MICELLES



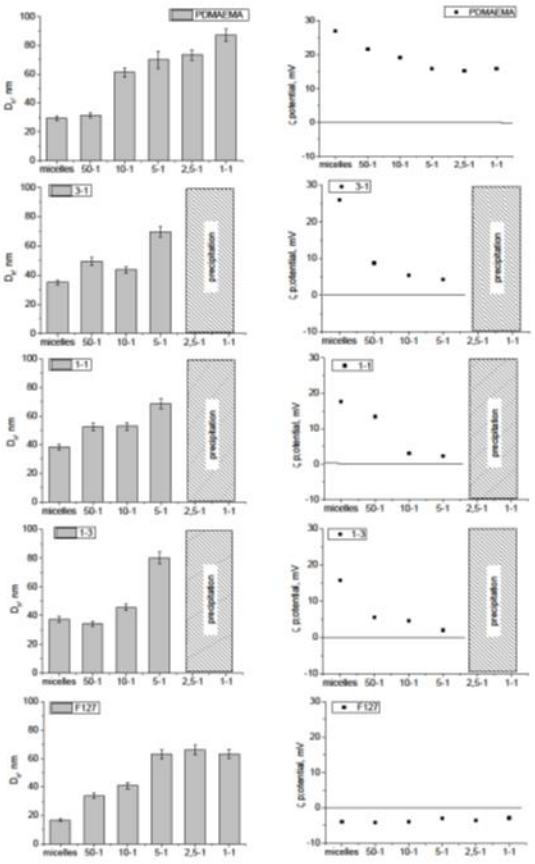
CPMs and NPMs were formed by dropwise addition of copolymer organic solution to aqueous media followed by dialysis against water. The mixed PMs were prepared by co-assembly of both copolymers following the same procedure. Three different molar ratios (3/1, 1/1 and 1/3) were used. The concentration of all micellar dispersions was 1 mg/ml.



LOADING OF CIPROFLOXACIN

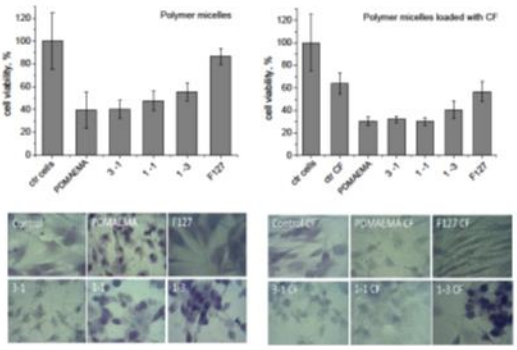
Loading of CF was performed by addition of drug powder to the micellar dispersions in order to obtain polymer to drug weight ratio in the rage of 1/1 to 50/1. The mixtures were first sonicated for 1 h at 60 °C for drug solubilisation and then filtered. The encapsulation efficiency (EE) and drug loading content (DLC) were determined spectrophotometrically.

Polymeric micelles	PDMAEMA		3/1		1/1		1/3		F127	
Micelles to CF ratio	EE %	DLC %	EE %	DLC %	EE %	DLC %	EE %	DLC %	EE %	DLC %
50-1	90.9	2.0	98.8	1.4	93.9	2.3	93.1	2.1	96,4	1.9
10-1	91.0	10.8	98.6	14.8	98.5	14.8	99.0	11.1	91.2	12.4
5-1	89.9	19.8	96.4	15-4	95-9	21.1	93.9	20.6	73.0	15-3
2.5-1	94.5	37.8	55.2	24.3	88.2	31.8	66.2	26.5	30.2	13.1
1-1	61.0	61.0	55-5	55-5	63.4	64.7	67.0	61.6	41.0	41.0



CYTOTOXICITY AND CELL MORPHOLOGY

The cytotoxicity of the resulting micellar systems was determined by standard crystal violet assay. Normal diploid human skin fibroblasts (HSF) were used for this study. Empty polymer micelles as well as loaded with CF systems were investigated. The possible deviations in cell morphology were also monitored under light microscope.



CONCLUSIONS

PMs were formed from cationic poly(2-(dimethylamino)ethyl methacrylate)-b-poly(ε-caprolactone)-b-poly(2-(dimethylamino)ethyl methacrylate) and non ionic poly(ethylene oxide)-b-poly(propylene oxide)-poly(ethylene oxide) triblock copolymers. Mixed polymer micelles based on both copolymers were also prepared. The micelles differ in composition as they were composed of mixed PCL/PPO core and mixed PDMAEMA/PEO shell. All systems were characterized by dynamic and electrophoretic light scattering. The micelles were of small size in the range of 16 to 38 nm depending on their composition. They were of positive ζ-potential excluding the micelles based on F127 exhibiting value close to 0.

All micellar systems were loaded with CF as various polymer to drug weight ratio were used. The EE and DLC were found to depend on this ratio as the optimum values were observed above 10-1 for all compositions. The size and ζ-potential of loaded micelles were also influenced by the various polymer to drug weight ratio. The D_h increase with CF amount while ζ-potential value start to decrease. In addition a zone of instability was reached at high CF concentration. This could be due to the partial electrostatic interaction between PDMAEMA and the drug which is with negative potential at neutral pH. In contrast the ζ-potential of F127 based micelles was independent from the CF amount.

The cytotoxicity of the systems was investigated as well. The empty micelles exhibited a strong composition depended cell viability. As expected their toxicity increase with PDMAEMA amount. In contrast the CF loaded micelles showed a well expressed cytotoxicity independently of their composition. The presence of micelles led to small changes in cell morphology associated mainly with disruption of cell contacts. No cell destruction or morphological signs of cell death were observed. This behavior could be associated with the ability of the micellar systems to deliver and released the loaded drug. Therefore they could be considered as promising candidates for treatment of bacterial infections.

Acknowledgement

This work was funded by the National Science Fund of Bulgaria, Project № КП-06-Н41/8.

Destruction of preformed bacterial biofilms by mixed polymeric micelles of different composition

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INTRODUCTION

Biofilms are communities in which bacteria are a serious risk factor for human health. The development of biofilms during infection is reported to be between 60 and 80%, because they are significantly more resistant to antibacterials than other microorganisms. The combination of multidrug resistance and their protective character puts forward the urgent need for the development of novel anti-biofilm agents.

The AIM of our study is to evaluates the effectiveness of polymer micelles differing by composition against pre-formed biofilms by Gram (+) and Gram (-) bacteria.

MATERIALS AND METHODS

Preparation of mixed polymer micelles and their loading with CF. Polymer micelles from poly(2-(dimethylamino)ethyl methacrylate)-b-poly(ε-caprolactone)-b-poly(2-(dimethylamino)ethyl methacrylate) (Mn =17100 g/mol, Đ = 1.20, noted as PDMAEMA) and poly(ethylene oxide)-b-poly(propylene oxide)-b-poly(ethylene oxide) (Mn=12600 g/mol, known as Pluronic F127) triblock copolymers as well as their mixtures at different molar ratio (3-1, 1-1 and 1-3, respectively) were used for this study. The micelles were additionally loaded with Ciprofloxacin (CF) at polymer to antibiotic weight ratio 10-1. The encapsulation efficiency was in the 91-99 % range. All systems were prepared at concentration 1 mg/ml. Their size and zeta potential were determined by dynamic and electrophoretic light scattering.

***In vitro* drug release.** Drug release profile from the systems was investigated in a phosphate buffer (pH=7.4) at physiological temperature. The amount of released CF was calculated spectrophotometrically by the characteristic absorbance band of CF at 270 nm^{-1}.

Biofilm biomass - Crystal violet (CV) assay. For comparative biofilm biomass estimation, the crystal violet assay (CV) was applied. For biofilm cultivation, M63 minimal salt medium was used. The bacterial strains used were *E. coli* 25922 (ATCC) and *S. aureus* 29213 (ATCC). An overnight bacterial TSB culture was diluted 1:100 in M63 medium, vortexed and distributed in the wells of 96-well U-shaped polystyrene plates, 150 ml per well, 5 wells per experimental variant. To avoid drying during biofilm cultivation, the wells at the periphery of the plate were filled with sterile distilled water. The plates were cultivated for 24 h at 37°C at static conditions. Then the non-adherent bacteria were removed, the wells were washed in 3 changes of PBS, and the wells were filled with 150 ml per well of cationic micelles, or cationic micelles loaded with CF. The agents were applied at final concentrations of 0.5 mg/ml^{-1}. The plates were incubated for 4h at 37°C. The plankton was removed, the wells were washed and stained for 15min with 0.1% aqueous solution of CV. Then the wells were rinsed extensively in several changes of PBS and the dye was solubilized with 70% ethanol. The absorbance of the solubilized dye was measured at 570nm. The results are presented as % of the control (addition of M63 only in the wells).

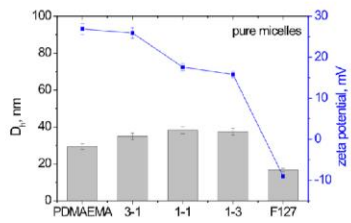
Metabolic activity of the biofilms. To estimate the metabolic activity of the biofilm bacteria, the redox indicator Alamar blue (Invitrogen) was used. Briefly, the biofilm was cultivated and treated with 0.5 mg ml_1 of micelles, AgNO3, or M_AgNPs for 4 h as above, with the same controls, 6 wells per variant. As a blank probe, wells containing M63 medium but no biofilm were included. Then, 5 ml of Alamar blue were added per well, and the plates were shaken for 5 min. Following incubation for 4 h at 37°C, the amount of reduced dye was measured at 620 nm, and also the amount of oxidized dye at 570 nm, using a plate reader. The percentage reduction of the dye due to the metabolic activity of the biofilm cells was calculated according to the formula:

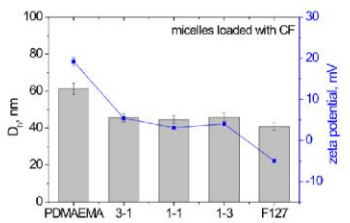
$$\frac{(\varepsilon ox)\lambda 2 x A\lambda 1-(\varepsilon ox)\lambda 1 x A\lambda 2}{(\varepsilon red)\lambda 1 x A'\lambda 2-(\varepsilon red)\lambda 2 x A'\lambda 1} x100$$

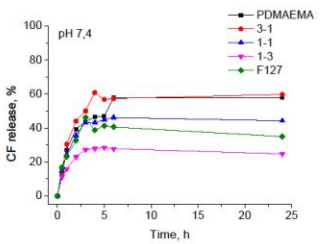
where the values of εox and εred were the molar extinction coefficients for the respective wavelengths (λ1 = 570nm and λ2 =620 nm), which were provided in the instructions of the producer; 'A' stands for the absorbances at the respective wavelengths, and 'A' to the absorbances at the two wavelengths of the blank probe (M63 with no biofilm). The results were plotted as the percentage reduction of the Alamar blue dye.

RESULTS

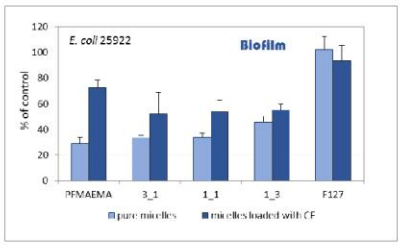
CHARACTERIZATION OF POLYMER MICELLES AND IN VITRO DRUG RELEASE

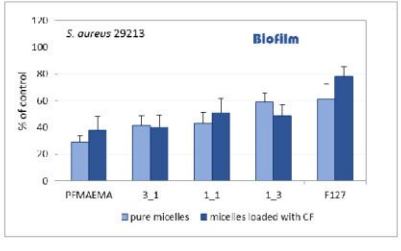




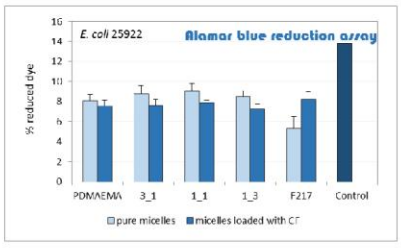


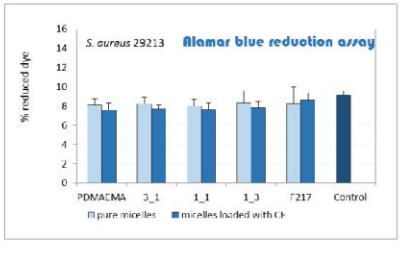
THE POLYMER MICELLES REDUCE SIFGNIFICANTLY THE BIOMASS OF PRE-FORMED BIOFILMS





REDUCTION OF BIOMASS IS ACCOMPANIED WITH REDUCTION OF METABOLIC ACTIVITY





Conclusion:

Polymer micelles based on cationic poly(2-(dimethylamino)ethyl methacrylate)-b-poly(ε-caprolactone)-b-poly(2-(dimethylamino)ethyl methacrylate) and nonionic poly(ethylene oxide)-b-poly(propylene oxide)-b-poly(ethylene oxide) triblock copolymers as well as their mixtures were prepared. The micelles are characterized by small size below 40 nm and narrow size distribution (PDI< 0.2). The zeta potential of the micelles was strongly influenced by their composition varying from 26.9 to -9.1 mV. All micellar compositions showed a high encapsulation efficiency of CF (> 90%). The ability of the systems to release the drug was investigated as well. Delayed profiles were observed in a phosphate buffer (pH=7.4) over the period of 24 h. All micelles were capable to detach pre-formed bacterial biofilms, but the application of the CF-loaded micelles resulted in more residual undetached biomass. This could be related with their reduced zeta potential compared to the non-loaaded micelles. However, when the metabolic activity of the biofilm is concerned, it was even more strongly suppressed by the loaded micelles which indicates successful drug delivery. Therefore, we can conclude that the investigated systems have great potential as antibacterial agents.

Acknowledgements: This work was supported by the National Science Fund at the Ministry of Education and Science, Bulgaria (Research Grant KP-06-H41/8; 30.11.2020).

12TH SCIENTIFIC SESSION "YOUNG SCIENTISTS IN THE POLYMER WORLD" JUNE 03, 2021, SOFIA, BULGARIA

Poly(N,N-dimethylacrylamide)/β-cyclodextrin nanogel for drug delivery

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INTRODUCTION

Aripiprazole is an atypical antipsychotic. It is primarily used in the treatment of schizophrenia and bipolar disorders. However, it's poorly soluble in water. Many researches are dedicated to finding ways for improving its solubility. Creating a drug delivering system is one of the methods. In this contribution we obtained inverse nano-emulsion nanogel comprising β-cyclodextrin (β-CD) moieties. The nanogel was synthesized by crosslinking of N,N-dimethylacrylamide (DMAA) and β-CD triacrylate (β-CD-Ac_3), using ammonium persulfate (APS) and N,N,N′,N′-tetramethylethylenediamine (TEMED) as initiators. The nanogel carrier was loaded with Aripiprazole via procedure favoring inclusion of drug molecules into the hydrophobic cavity of β-CD. Our goal is to improve Aripiprazole's solubility by forming inclusion complexes with β-CD and thus creating a favorable release profile of the drug delivering system.

SYNTHESIS OF β-CD

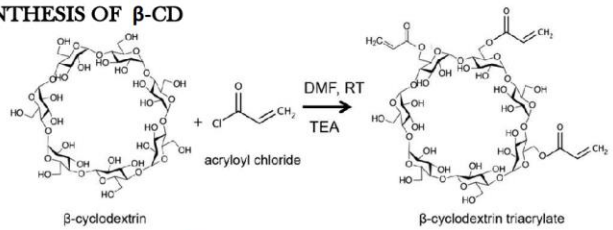

Figure 1. Synthetic scheme of β-CD-Ac_3 preparation.

In the first step, β-CD-Ac_3 crosslinking agent was obtained by reacting acryloyl chloride and β-CD in the presence of triethylamine. An excess of acryloyl chloride was used to ensure attachment of several acrylate groups onto one β-CD molecule.

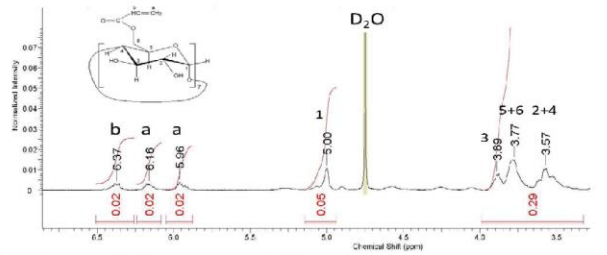

Figure 2. Proton NMR spectrum of β-CD-Ac_3 in D_2O

Both type of signals characteristic for the vinyl protons and oligosaccharide protons were identified on the spectrum. The degree of substitution (DS) was determined taking into account the relative peak integrals assigned to the β-CD protons at 5.0 ppm and the vinyl protons at 5.8–6.5 ppm. Hence, DS~3 was calculated, which means that a crosslinking agent with three reactive groups was synthesized.

SYNTHESIS OF THE NANOGEL

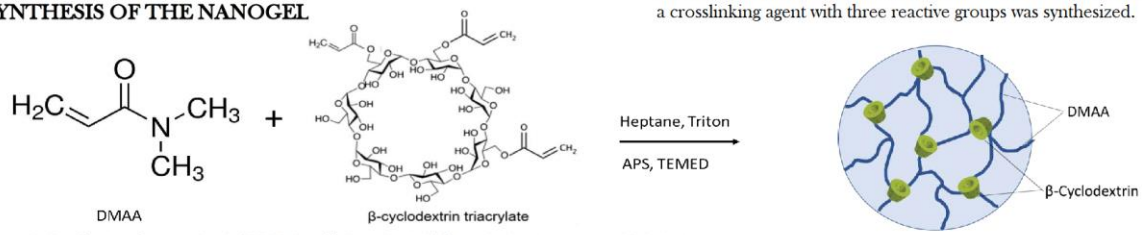

Figure 3. Synthetic scheme of poly(N,N-dimethylacrylamide)/β-cyclodextrin nanogel fabrication.

The nanogel was synthesized as follows: Triton (surfactant) was dissolved in heptane (oil phase), APS, TEMED, β-CD-Ac_3 and DMAA were dissolved in water (aqueous phase). The mixture (emulsion) was left under stirring for about 20 h, so that nanogel was formed. The heptane was removed via evaporation and the triton via extraction. After that a dialysis was performed. The sample was frozen, followed by lyophilization to remove the water. Yield: 81,7 %.

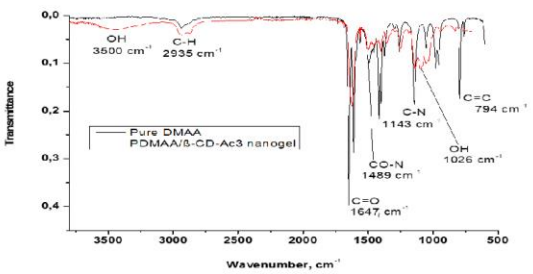

Figure 4. FTIR-spectra of DMAA monomer and the nanogel.

The FTIR-spectroscopy demonstrates that the monomer (DMAA) and the crosslinking agent (β-CD-Ac_3) are incorporated into the gel network.

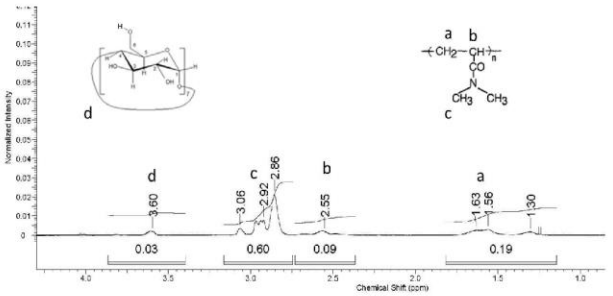

Figure 5. Proton NMR spectrum of the nano gel.

The NMR spectrum gives us qualitative and quantitative analysis. It shows that the ratio of PDMAA and β-CD is approximately close to the initial ratio (5:1).

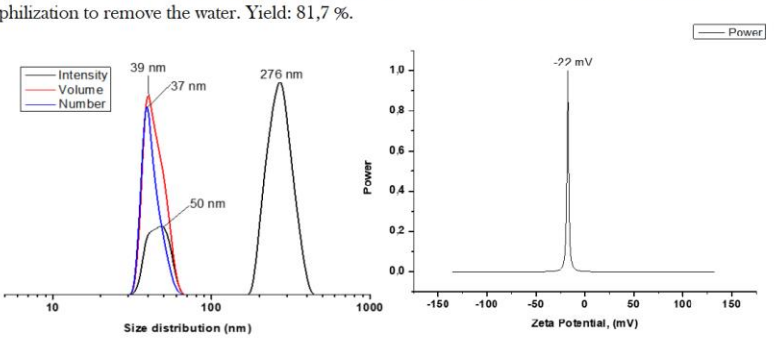

Figure 6. Dynamic Light Scattering (DLS) and Electrophoretic Light Scattering (ELS) graphs.

DLS measurement proved that the particles obtained are nano-sized, while the ELS measurements revealed a negative surface charge (sample concentration – 5 mg/ml).

DRUG LOADING

Firstly, Aripiprazole was dissolved in acetone and, then, added to an aqueous solution of nanogel. The loading was triggered by evaporating the organic solvent. The ability of the carrier to release the drug is yet to be examined.

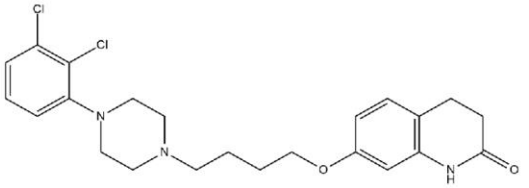

Figure 7. Structural formula of Aripiprazole.

CONCLUSION

Novel nanogel was developed by crosslinking DMAA and β-CD-Ac_3, using APS and TEMED as initiators. The incorporation of β-CD-Ac_3 in the PDMAA net was proven by FTIR and NMR spectroscopies. The nano size of the particles was confirmed by performing measurements on a Zetasizer (DLS and ELS). Aripiprazole was loaded onto the carrier. The drug loading efficiency of the carrier and the release of the drug are yet to be explored.

ИНСТИТУТ по ПОЛИМЕРИ
БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ

ДВАНАДЕСЕТА НАУЧНА СЕСИЯ *"МЛАДИТЕ УЧЕНИ В СВЕТА НА ПОЛИМЕРИТЕ"*

БЪЛГАРСКА АКАДЕМИЯ на НАУКИТЕ 1869

Preparation, antibacterial and photocatalytic properties of Polylactide/Hydrozincite and Polylactide/Hydrozincite/Polyvinylpyrrolidone nanofilms

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[1]Institute of Polymers, Bulgarian Academy of Sciences
[2]Institute of Catalysis, Bulgarian Academy of Sciences
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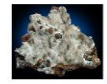
In recent years, the interest in the development of inorganic/polymer hybrid materials on nanometer scale has grown due to a wide range of potential opportunities for application in various fields. New composite material is expected to possess synergistic effect and improved properties between the polymer and inorganic part namely biodegradability, photocatalytic and antibacterial properties.

In the present study was used a simple method for obtaining composites in the spirit of Green Chemistry. A minimum number of non-toxic reagents and mild conditions were used. Two hybrid polylactide/hydrozincite nanocomposite and poly(lactide)/hydrozincite/polyvinylpyrrolidone films were prepared. The nanosized hydrozincite exhibits photocatalytic and antibacterial activities, and is therefore a very attractive component for incorporation in new hybrid materials.

AIM

- Preparation of poly(lactide)/hydrozincite and poly(lactide)/hydrozincite/polyvinylpyrrolidone films.
- Characterization of synthesized nanocomposite films using FT-IR spectroscopy and XRD analysis.
- To study the photocatalytic ability of the new materials in the reaction of degradation of Malachite Green dye under UV light and antibacterial activity towards the pathogen *Escherichia coli*.



Hydrozincite $Zn_5(CO_3)_2(OH)_6$ – also known as zinc bloom.

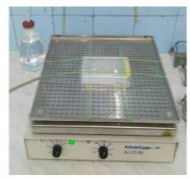
EXPERIMENTAL

Preparation of nanostructured films via sol gel method

Nanocomposite PLA/Hydrozincite film were prepared by the following steps: (i) Preparation of a suspension of hydrozincite ($Zn_5(OH)_6(CO_3)_2$), 1wt% (synthesized by hydrothermal method at 180°C using Mint extract) and dichlormethane; (ii) Add solution poly(lactide) PLA in dichlormethane. After mixing hydrozincite and PLA, the resulting solution was sonicated for 15 minutes until the suspension is homogeneous; (iii) Thin films were prepared. Nanofilm PLA/Hydrozincite with copolymer polyvinylpyrrolidone, 1wt% was prepared as described above, but dissolving PVP in ethanol added to the nanocomposite suspension.

PLA/Hydrozincite/PVP

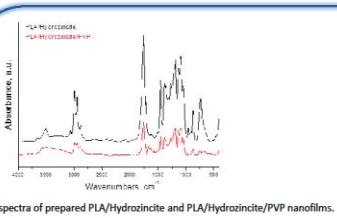
PLA/Hydrozincite



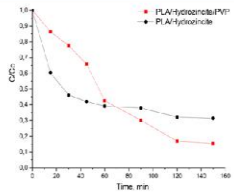
Samples were prepared using 24 well test plate (Techno Plastic Products AG, Switzerland). It was shake continuously using Advantage-Lab, AL05-06 at 150 rpm. The shaker was kept in thermostatic room at 20 ± 1°C.

Sample 1 – PLA
Sample 2 – PLA/Hydrozincite 1%
Sample 3 – PLA/Hydrozincite 1%/ PVP 1%
Control – *E. coli* K12 suspension (1,5-3,0 * 10^6 CFU)

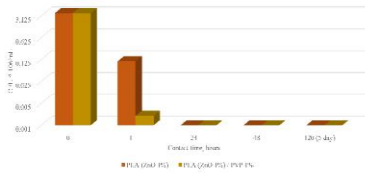
RESULTS



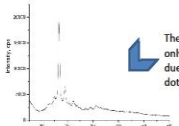
FT-IR spectra of prepared PLA/Hydrozincite and PLA/Hydrozincite/PVP nanofilms.



The concentration ratio C/C_0 of Malachite Green dye as a function of the time of UV illumination using prepared PLA/Hydrozincite and PLA/Hydrozincite/PVP nanofilms.

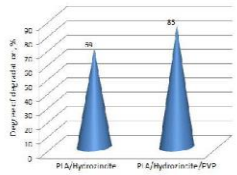


Antibacterial effect of different polymers depending of time and polymer type.



The presence of PLA was registered only. The absence of the hydrozincite is due to that it is in the form of quantum dots.

XRD pattern of prepared PLA/Hydrozincite/PVP nanofilm.



Degree of degradation of Malachite Green dye in aqueous solution after 150 minutes under UV light using synthesized PLA/Hydrozincite and PLA/Hydrozincite/PVP nanofilms.

CONCLUSION

- The photocatalytic degradation of Malachite Green (MG) dye as model pollutant in aqueous solution (5 ppm) under UV light was investigated using synthesized PLA/Hydrozincite and PLA/Hydrozincite/PVP nanofilms as photocatalysts.
- The results established that the prepared PLA/Hydrozincite/PVP nanofilm possesses the higher photocatalytic ability towards degradation of MG dye in comparison with the PLA/Hydrozincite.
- PLA/Hydrozincite 1%/PVP 1% film has excellent bactericidal activity against *E.Coli*. It show strong antibacterial effect even after 1 hour of contact the other composite reach the same result after 24 hours.
- In conclusion, the work indicates that the two biocomposites film are suitable for food packaging application because it shows excellent antimicrobial activity to *E. Coli* already after 24 h.

POLY(VINYL ACETALS) FROM AROMATIC ALDEHYDES FOR NANOCOMPOSITE AQUEOUS GRAPHENE DISPERSIONS AND THIN FILMS

Mariela Alexandrova[1], Sijka Ivanova[1], Nikolay Minev[2], Vera Marinova[2], Darinka Christova[1]

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BACKGROUND

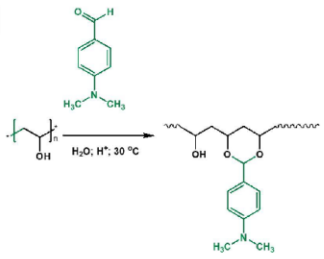
Graphene is a nano-carbon material with a 2D network structure that attract increasing attention owing to properties such as large specific surface area, high mechanical strength, and superior electrical and thermal conductivity. Currently, graphene is being applied in various products such as thermal sensors, battery electrode materials, and super capacitors.
On the other hand, polyvinyl alcohol (PVA) is an interesting commercial polymer with production over 1.2 billion kg annually including its derivative poly(vinyl acetals)s such as poly(vinyl formal) and poly(vinyl butyral). In the past two decades, researchers have increasingly exploited naturally occurring aromatic molecules as building blocks for sustainable polymers. The inclusion of such bioaromatics often confers improved thermal and mechanical properties. One approach is to incorporate the bioaromatic within the main-chain of the polymer, but an alternative approach is to introduce the bioaromatic onto the polymer as pendent groups, e.g. via acetalization.

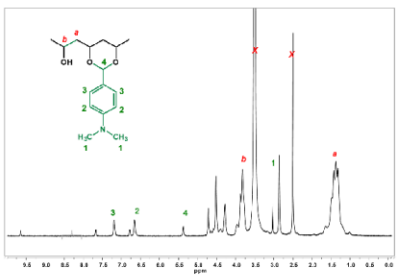
Objective: to synthesize poly(vinyl acetals) from PVA and aromatic aldehydes and to study the possibility of obtaining nanocomposite thin films by using poly(vinyl acetal)/graphene aqueous dispersions

RESULTS

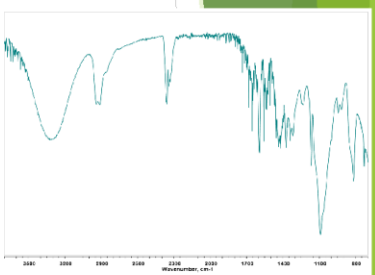
POLY(VINYL ACETALS) SYNTHESIS AND CHARACTERIZATION

PVA-DMABA



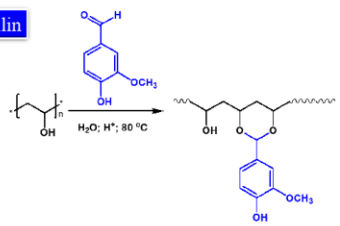


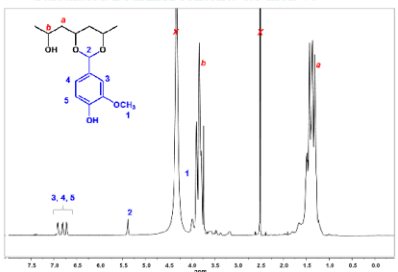
NMR spectrum of DMABA-modified PVA
Calculated DMABA content: 4.6 mol. %



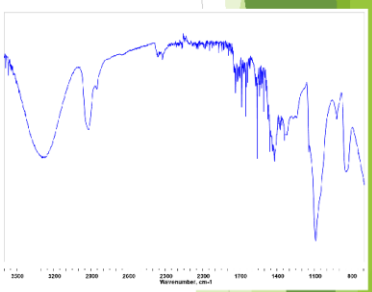
FTIR spectrum of DMABA-modified PVA

PVA-Vanillin





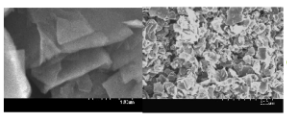
NMR spectrum of vanillin-modified PVA
Calculated vanillin content: 2.3 mol. %



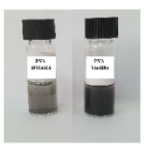
FTIR spectrum of vanillin-modified PVA

POLYMER/GRAPHENE AQUEOUS DISPERSIONS AND THIN FILMS

Graphene nanopowder supplied from Graphene Supermarket in the form of flakes with 8 nm average size (20-30 monolayers) was used.



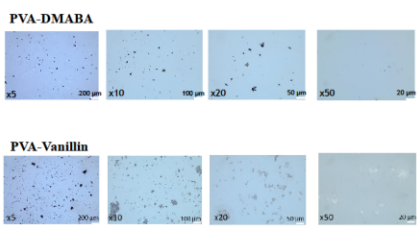
SEM images of dry graphene nanopowder



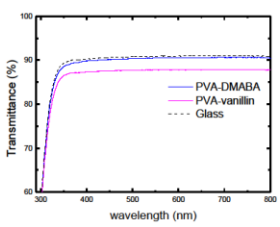
Aqueous polymer/graphene dispersions were obtained at copolymer concentration 10 g/L and graphene content 0.6 g/l. Dispersions were used to obtain thin films on glass substrates by applying spin-coating method at following conditions:

- **0.250 mL of the solution**
- **first step - 10 s at 1000 rpms**
- **second step - 40 s at 4000 rpms**

Optical images of PVA-DMABA and PVA-Vanillin thin films deposited on glass substrates



Transmittance spectra of PVA-DMABA and PVA-Vanillin thin films at UV-VIS range



CONCLUSIONS AND FUTURE OUTLOOK

Poly(vinyl acetal) copolymers are obtained at environmentally friendly reaction conditions by using natural aromatic aldehydes. Synthesized copolymers are water soluble and show increased affinity to graphene providing medium for preparation of PVA-graphene stable dispersions and quality thin films with potential sensor applications.

Acknowledgments

M. Aleksandrova acknowledges Bulgarian Ministry of Education and Science for support under the National Research Programme "Young scientists and postdoctoral students" approved by DCM # 577 / 17.08.2018.

Нови лекарствени носители за модифицирано лекарствено доставяне на тимолол малеат на базата на поли(сулфобетаин метакрилат) и хитозан

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[3] *Лаборатория по технология на лекарствените форми и биофармация, Факултет по химия и фармация, СУ „Св. Климент Охридски“, София 1164, България, бул. Джеймс Баучер №1*

I. Въведение:

Глаукомата е очно заболяване, засягащо и двете очи, при което повишеното вътреочно налягане води до прогресивно намаляване на зрението и до пълна слепота. Конвенционалното лечение включва терапия с неселективния бета блокер тимолол малеат (ТМ), внасящ се в окото под формата на капки за очи. Те не осигуряват ефективно терапевтично действие, поради краткото време на контакт между лекарството и очната повърхност, дължащо се на отмиването му от сълзата.

Добавянето на полимерен носител, който едновременно да взаимодейства с очната лигавица и лекарственото вещество, би увеличило времето за контакт между ТМ и окото, което да доведе до по-голяма лекарствена бионаличност, а оттам и по-ефективно действие на лекарствената форма.

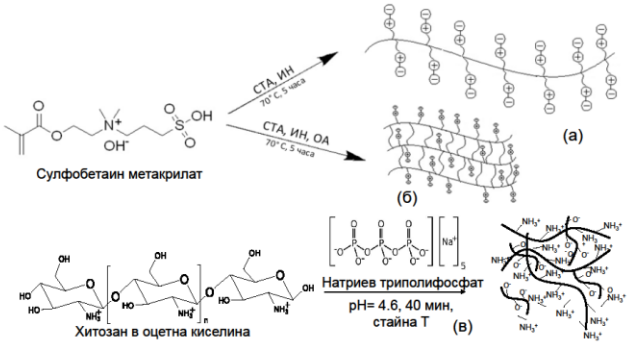
II. Цел:

Целта на настоящата работа е разработването на нови лекарствени носители за тимолол малеат на базата на поли(сулфобетаин метакрилат) (PSB) и хитозан. Тези носители се очаква да: (i) взаимодействат по-силно с очната лигавица, поради положителния заряд на хитозана, като по този начин удължат престоя на лекарствената форма в окото; (ii) да освобождават ТМ контролирано в окото благодарение на антиполиелектролитния ефект на PSB, а едновременно с това (iii) те са доказано биосъвместими и нетоксични.

III. Експериментална част:

III.1. Синтез на лекарствените носители

Синтезирани са три типа наногелни частици: (i) от PSB, омрежен с поли(етиленгликол диакрилат) (PSB NP); (ii) от хитозан, омрежен с натриев триполифосфат (ТПФ), както и (iii) от линеен PSB (PSB Lin) (Фигура 1).



Фигура 1. Схема на синтез на (а) линеен поли(сулфобетаин метакрилат) (PSB Lin); (б) наночастици поли(сулфобетаин метакрилат) (PSB NP); наночастици хитозан (Chi NP).

Таблица 1 обобщава химичните формули на използваните реагенти.

Таблица 1. Химични формули и роля на използваните реагенти

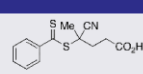
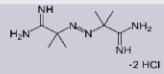
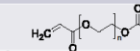
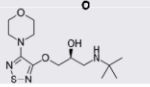
Име на реагента	Роля на реагента	Химична формула
4-Циано-4-(фенил-карбонотиоилтио) пвнтанова киселина	Агент за пренос на веригата	
2,2´-Азобис(2-метилпропионимидин) дихидрохлорид	Инициатор	
Поли(етиленгликол диакрилат)	Омрежващ агент	
Тимолол малеат	Лекарствено вещество, използвано за лечение на глаукома	

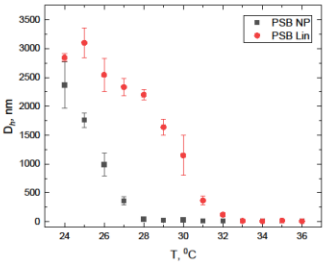
Таблица 2. Състав на Chi NP.

Проба	Хитозан об.части	ТПП об.части
C1	3	1
C2	4	1
C3	5	1

Таблица 2 представя три различни състава на наночастиците от хитозан.

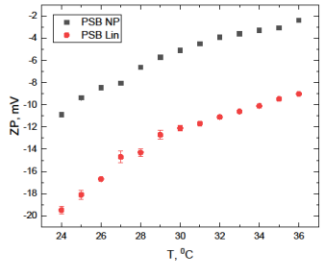
IV. Резултати:

IV.1. Размер и ζ- потенциал на лекарствените носители



Полимерните носители на базата на PSB показват долна критична температура на разтваряне (ДКТР), като PSB NP имат по-ниска ДКТР в сравнение с PSB Lin. Вероятно, омрежената им структура, пречи на тяхната агломерация със съседни частици, доказателство за което е и размера на двата вида частици при по-високите температури - ~6 nm за PSB Lin и ~11 nm за PSB NP.

Фигура 3. Температурна зависимост на хидродинамичния диаметър на полимерните носители на базата на PSB



PSB NP имат по-малък ζ- потенциал, в сравнение с PSB Lin, който може да се обясни с омрежената им и по-запречена структура. Така резултатите от тези два независими експеримента потвърждават ефективността на омрежване.

Фигура 4. Температурна зависимост на ζ- потенциала на полимерните носители на базата на PSB

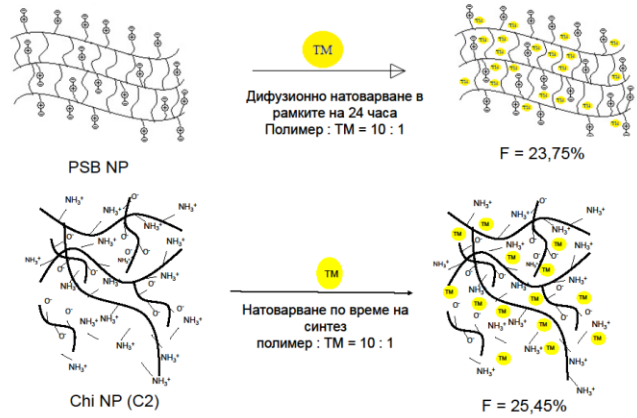
Проба хитозанови частици	Хидродина-мичен диаметър [nm]	ζ- потенциал [mV]
C1	299.7 ±5.4	22.5 ± 13
C2	244.9 ± 1.5	22.4 ± 12.9
C3	230.4 ± 3.2	-

Таблица 3. Хидродинамичен радиус и ζ- потенциал на пробите хитозан

Размерът и ζ- потенциалът на хитозановите наночастици не зависи от количеството омрежващ агент.

IV.2. Ефективност на лекарствено натоварване (F)

Използвани бяха два начина за лекарствено натоварване – по време на синтеза на Chi NP и дифузионно натоварване за PSB NP. Ефективността и при двата типа частици е сравнима.



Заключение:

Синтезирани и охарактеризирани са лекарствени носители на основата на PSB и Chi. Определена е и тяхната степен на натоварване с лекарствено вещество тимолол малеат. Предстои изследване на техния профил на лекарствено освобождаване.

Благодарност: Тази работа се осъществява с финансовата подкрепа на Фонд научни изследвания на СУ"Св. Кл. Охридски",
Проект в подкрепа на докторанти No 80-10-72 / 25.03.2021 г.

Получаване на синтетичен полимерен слой с потенциално антибактериално действие

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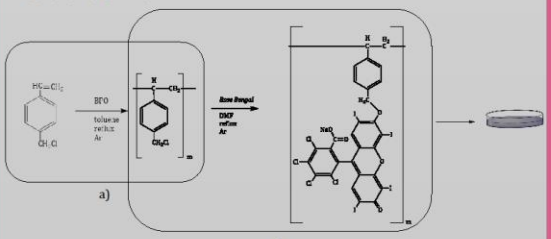
Въведение

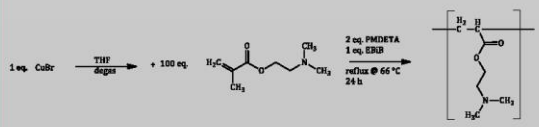
През последните години разработването на филтърни материали за индустрията и за персонална защита е с все по-нарастващо значение. Основна цел на много изследвания е получаването на иновативни самопочистващи се материали, които да филтрират биологични и небиологични частички. Настоящата работа представя получаване на активен полимерен слой с функция за елиминиране на бактерии и вируси, който да бъде използван като част от нов филтърен материал (Фиг. 1). Този слой представлява филм на базата на поли(хлорометилстирен) (PCMS) и поли(диметиламиноетилметакрилат) (PDMAEM), носещ фотосенсибилизатор (Бенгалска роза (RB)).

Процедура

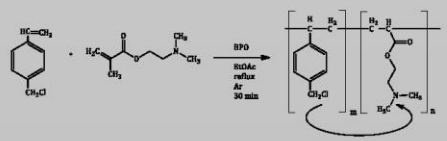
А) а) Получаване на poly(CMS); б) Присъединяване на RB върху poly(CMS);



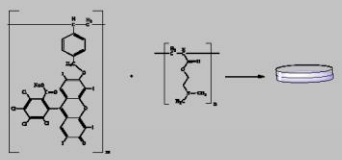
Б) Получаване на poly(DMAEMA) чрез ATRP-полимеризация;



В) Радикаловата полимеризация между p-CMS и DMAEMA до получаване на poly(CMS-co-DMAEMA);



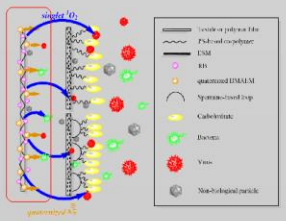
Г) Получаване на филм от poly(RB-MS) и poly(DMAEMA).



Методи

Получените полимерни слоеве са доказани и охарактеризирани чрез ИЧ-спектроскопия, ГПХ-анализ, ЯМР-спектроскопия (Bruker 250 MHz и 600 MHz) и ТГА.

Резултати

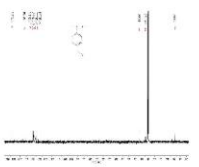


Фиг. 1. Двуслоен филтърен материал.

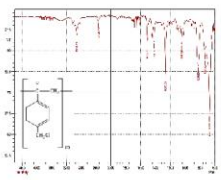
	Продукт	Резултат
А а)	poly(CMS)	полимер
А б)	poly(MS-RB)	филм
Б)	poly(DMAEMA)	полимер
В)	poly(CMS-co-DMAEMA)	гел
Г)	poly(DMAEMA) и poly(MS-RB)	филм

Таблица 1. Синтетични полимерни слоеве.

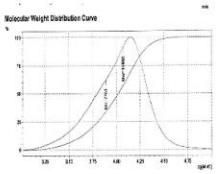
PCMS



Фиг. 2. ^{13}C NMR на poly(CMS).



Фиг. 5. ИЧ-спектър на poly(CMS).

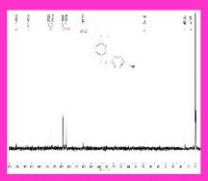


Фиг. 8. ГПХ-анализ на poly(CMS).

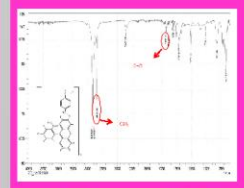
Mn	7760
Mw	11900
Mz	16800
Mn/Mw	1.53

Таблица 2. Молекулно-масови характеристики на PCMS..

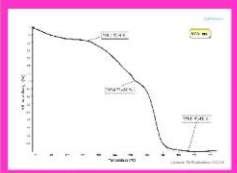
PMS-RB



Фиг. 3. ^{13}C NMR на poly(MS-RB).



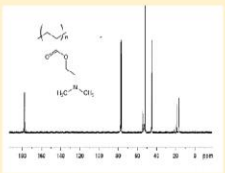
Фиг. 6. ИЧ-спектър на poly(MS-RB).



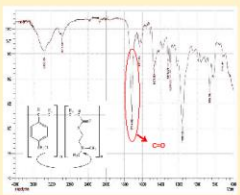
Фиг. 9. ТГА-анализ на poly(MS-RB).

Фиг. 11. Полимерен филм от poly(CMS-RB).

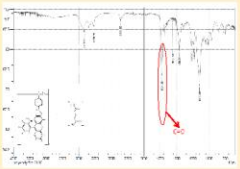
PCMS и PDMAEM



Фиг. 4. ^{13}C NMR на poly(DMAEMA).



Фиг. 7. ИЧ-спектър на poly(CMS-co-DMAEMA).



Фиг. 10. ИЧ-спектър на полимерен филм от poly(DMAEMA) и poly(CMS-RB).

Фиг. 12. Полимерен филм от poly(DMAEMA) и poly(CMS-RB).

Заключение

В настоящата работа бе получен нов синтетичен полимерен слой, съдържащ Бенгалска роза с понтенциално антибактериално действие. Слоят следва да бъде допълнително оптимизиран и кватернизиран. Предстоят антибактериални и антивирусни тестове за определяне на ефективността на материала, както и тестове за определяне на физико-механични свойства.

Благодарности

NATIONAL PROGRAMME „POST-DOCTORAL STUDENTS" Funded by the Bulgarian Ministry of Education and Science (MES): Research equipment of Distributed Research Infrastructure INFRAMAT, part of Bulgarian National Roadmap for Research Infrastructures, supported by Bulgarian Ministry of Education and Science was used in this investigation.

Shell-crosslinked mixed micelles for intracellular drug release

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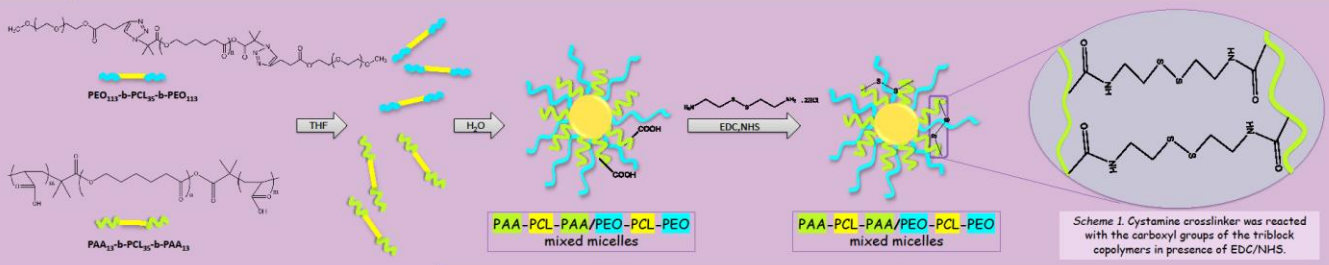
Introduction

Good structural stability and controlled release profile are of primary importance for any advanced drug delivery system. In particular, polymer micelles-based carriers can possess superior *in vivo* stability as well as the release of cargo can be precisely controlled. Redox-responsive systems containing cystamine moiety have been widely studied as the bioreducible disulfide (DS) bonds can be cleaved in the presence of a redox reagent. DS linkages are relatively stable under normal physiological conditions such as in the blood stream, but they can be easily cleaved in the presence of reducing agents such as glutathione (GSH) and dithiothreitol (DTT).

Aim:

The aim on this work was to obtain stabilized polymeric micelles via crosslinking with cystamine for glutathione-mediated intracellular drug release. Nanocarriers were prepared by co-assembly of two well-defined amphiphilic triblock copolymers, poly(ethylene oxide)-block-poly(ε-caprolactone)-poly(ethylene oxide) (PEO-b-PCL-b-PEO) and poly(acrylic acid)-block-poly(ε-caprolactone)-block-poly(acrylic acid) (PAA-b-PCL-b-PAA). Caffeic acid phenethyl ester (CAPE) was selected as the model drug to evaluate drug loading and release capacity of non crosslinked and crosslinked mixed micelles.

Preparation of crosslinked mixed micelles



Scheme 1. Cystamine crosslinker was reacted with the carboxyl groups of the triblock copolymers in presence of EDC/NHS.

Determining particles size, size distribution and ζ-potentional by Dynamic Light Scattering

Copolymers	D_h (nm)	ζ potential (mV)	CMC (g L^{-1})
PEO_{113}-b-PCL_{35}-b-PEO_{113}	26 nm	-0,6 mV	0.090
PEO_{113}-b-PCL_{35}-b-PEO_{113} / PAA_{13}-b-PCL_{35}-b-PAA_{13} (mol. ratio 3:1)	32 nm	-22 mV	0.078
PAA_{13}-b-PCL_{35}-b-PAA_{13}	86 nm	-33 mV	0.063

Table 1. Physical chemistry characteristics of polymeric micelles

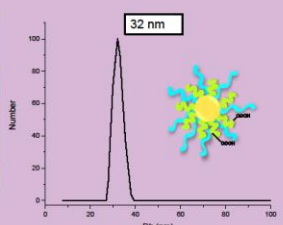


Figure 1. Size distribution of non-crosslinked mixed micelles (3:1 mol ratio)

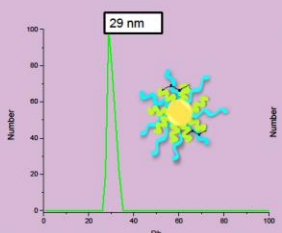


Figure 2. Size distribution of crosslinked mixed micelles

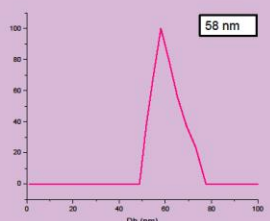
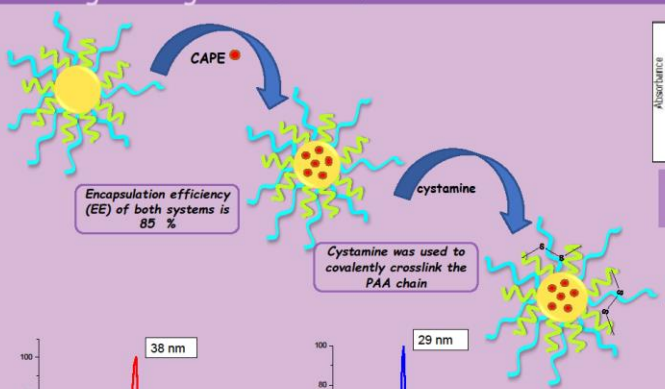
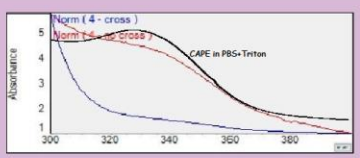


Figure 3. Size distribution of crosslinked mixed micelles dialyzed against THF

Drug loading into mixed micelles





Graphic 2. *Comparison of UV spectra of releasing CAPE in PBS/Triton X-114 at the 4th hour from crosslinked and non crosslinked micelles and UV spectra of 0,05 mg/ml CAPE in PBS/Triton X-114 .*

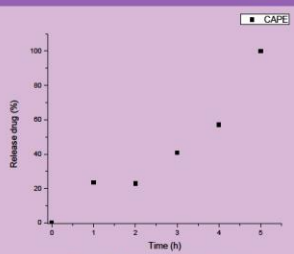


Figure 6. *Drug release profile of non-crosslinked micelles*

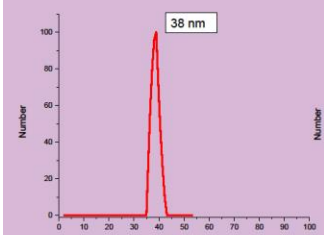


Figure 4. *Size distribution of CAPE loaded non crosslinked mixed micelles*

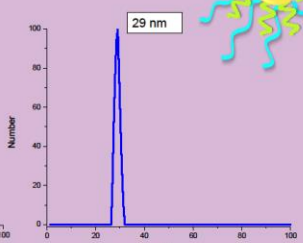
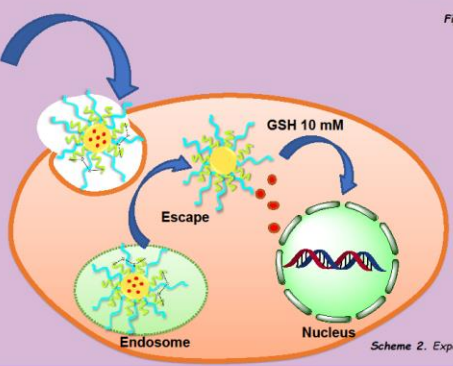


Figure 5. *Size distribution of CAPE loaded crosslinked mixed micelles*



Scheme 2. *Expected mechanism of action into the cell*

HYPOTHESIS: ***The breaking up of the DS bonds in the presence of 10 mM GSH could trigger drug release from the inner core.***

Conclusions

Functional micellar nanocarriers were successfully developed by co-assembly of PEO_{113}-b-PCL_{35}-b-PEO_{113} and PAA_{13}-b-PCL_{35}-b-PAA_{13} in water. The proper design of copolymer composition, macromolecular characteristics and functionality afforded the formation of nano-sized carriers comprising a PCL core, a middle PAA/PEO layer and a protecting PEO outer layer. CAPE was entrapped into the PCL core via hydrophobic interactions. Crosslinked micelles were obtained by crosslinking the micellar shell with cystamine. CLMs showed good stability and excellent ability against extensive dilution by aqueous solution. The in vitro release profiles indicated that this mixed polymeric micelles had burst drug release. In the simulated normal physiological environment (pH 7.4), the drug release of the crosslinked polymeric micelles was negligible.

Acknowledgements: This study was supported by the National Science Program "Young scientists and postdoctoral candidates", module "Young scientists" (project RD-15-25/17.03.21)

New strategy for preparation of Spherical Nucleic Acids with hybrid lipid/polymer cores

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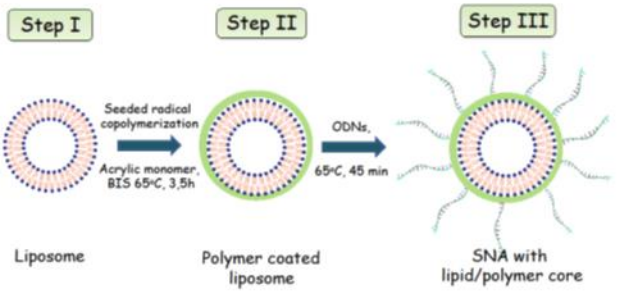
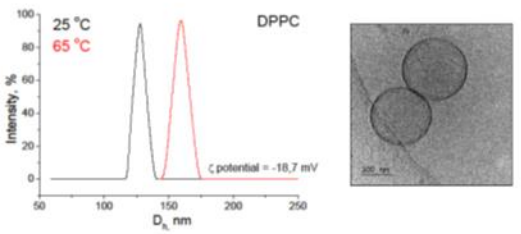
Introduction

Spherical nucleic acids (SNAs) are nanostructures composed of inorganic or organic cores to the surface of which highly oriented oligonucleotide strands are covalently attached thus forming a dense layer. The three-dimensional architecture of these structures gives rise to specific properties of SNAs that are different from those of their linear nucleic acid counterparts and are of great interest.

Herein, we employ a novel synthetic approach for preparation of SNAs with hybrid lipid/polymer cores. The approach involves three steps: (i) generation of a liposomal core, (ii) coating the core with a cross-linked polymeric shell, and (iii) grafting of the shell with oligonucleotide strands.



1.Preparation of liposomal cores

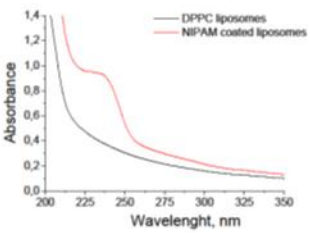


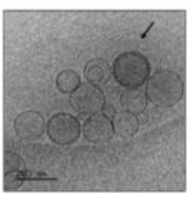
Liposomes were prepared by freeze-thawing and extrusion of aqueous dispersions of 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC). Cholesterol was used as a membrane stabilizing agent.

2.Coating of liposomal cores

The coating of liposomes was achieved by seeded radical copolymerization of *N*-isopropylacrylamide, NIPAM, and N,N-methylenbisacrylamide used as a cross-linking agent, initiated by 2,2'-azobis(2-methylpropionamidine) dihydrochloride. The polymer shell thickness was controlled by the initiator to monomer (I/M) molar ratio.

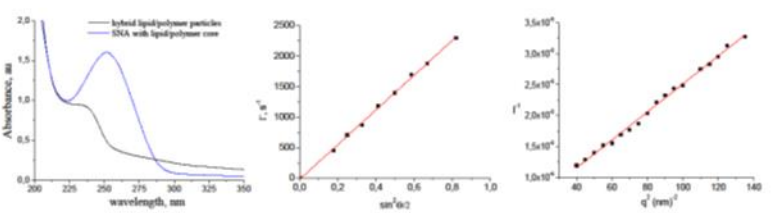
I/M ratio	$R_h^{25\,°C}$ Before coating nm	$R_h^{65\,°C}$ Before coating nm	$R_h^{65\,°C}$ After coating nm	Shell thickness nm	ζ potential ^{25} °C Before coating mV	ζ potential ^{25} °C After coating mV
0.1	78.5	82.8	92.0	9.2	-10.7	-4.1





3.Grafting with oligonucleotide strands

The surface functionalization of the resulting lipid/polymer cores was achieved by oligonucleotide strands with non-specific base sequence, functionalized with a methacrylamide group. The oligonucleotide strands were covalently attached to the PNIPAm shell by copolymerization reaction with an additional portion of NIPAm.



R_g nm	$D_0 \times 10^{12}$ $m^2.s^{-1}$	R_h nm	R_g/R_h	ζ potential mV	Number oligo molecules per liposome	Grafting density nm^{-2}
88.5	3.13	78.3	1.13	-14,2	5868	0.076

Conclusions

A new strategy for preparation of SNAs with hybrid lipid/polymer cores was proposed. The obtained liposomes were of small size, narrow size distribution and negative ζ potential. Polymer layer based on NIPAM was successfully formed on the liposomal surface. The presence of polymer coating was proved by UV absorption, dynamic and electrophoretic light scattering. The particles were visualized by cryo-TEM showing their spherical morphology and vesicular structure. The successful formation of the oligonucleotide-grafted particles was demonstrated spectrophotometrically. For detailed characterization of the resulting hybrid SNAs as well as for determination of the oligonucleotide grafting density static and dynamic light scattering were employed. The R_g was consistent with R_h, giving rise to R_g/R_h value compatible with morphology of spherical vesicles with thin shells. The strategy give rise to obtain SNAs with high number of oligonucleotide strands per particle and grafting density comparable of those of conventional SNAs.

Acknowledgement:

This work was funded by the National Science Fund of Bulgaria, Project № DN19-8.

Colloidal dispersions of methyl acrylate grafted poly(vinyl alcohol)s: synthesis and application for optical sensing of acetone

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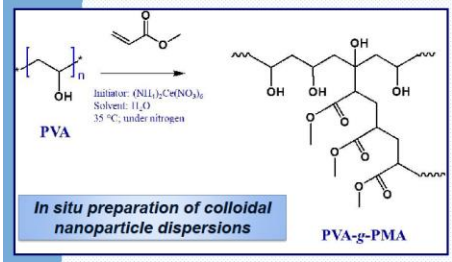
AIM

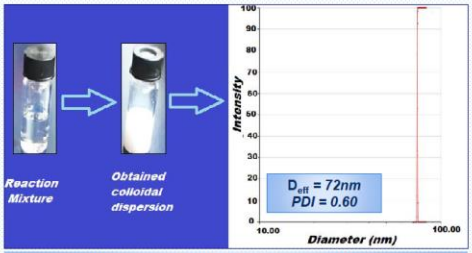
The aim of this work was to design and synthesize acetone-sensitive copolymers for optical sensing application. Grafting of poly(methyl acrylate) (PMA) side chains onto poly(vinyl alcohol) (PVA) precursor was performed in aqueous solution and in situ generated copolymer aqueous dispersions were used to obtain thin films on silicon substrates by applying spin-coating method. In order to evaluate sensing properties of studied PVA-*g*-PMA, optical characteristics of the films were investigated and change of the reflectance spectra in the presence of acetone vapors was followed.

RESULTS

Series of PVA-g-MA polymers were synthesized by grafting methyl acrylate (MA) onto PVA using cerium ammonium nitrate as an initiator. The polymerization reaction was carried out under a nitrogen atmosphere in aqueous medium at 35 °C thus applying environmentally friendly reaction conditions.
The obtained copolymer aqueous dispersions were purified from reagents residues by dialysis. Copolymer composition and structure were studied by using Proton Nuclear Magnetic Resonance (^{1}H NMR) and Fourier-transform Infrared spectroscopy (FTIR). Nanoparticle morphology and size were determined by using Transmission Electron Microscopy (TEM) and Dynamic Light Scattering (DLS).



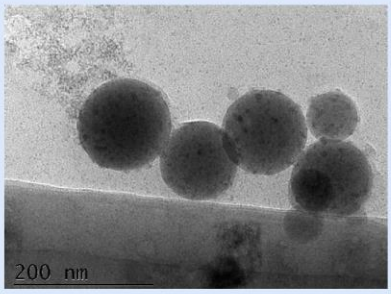
In situ preparation of colloidal nanoparticle dispersions



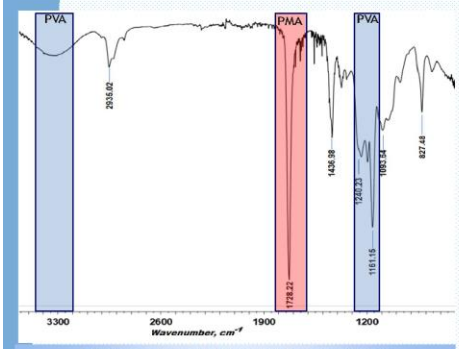
DLS report of PVA-g-PMA nanoparticles

Effective diameters (D_{eff}) and polydispersity index (PDI) of the obtained nanoparticles

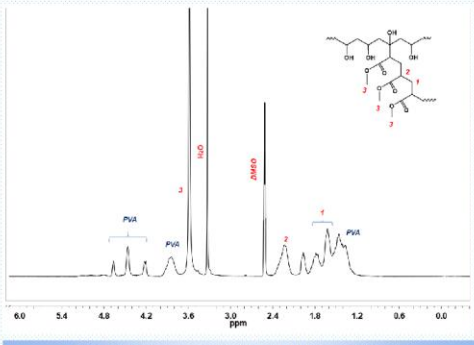
Sample	C g/L	D_{eff} (nm)	PDI
1	0.5	46.34	0.134
1	1	73.17	0.067
1	5	72.60	0.101
2	0.5	68.45	0.098
2	1	72.21	0.064
2	5	71	0.090
3	0.5	66	0.086
3	1	70	0.068
3	5	70.53	0.033
4	0.5	82.99	0.075
4	1	86	0.069
4	5	81.91	0.105



TEM image of PVA-g-PMA nanoparticles

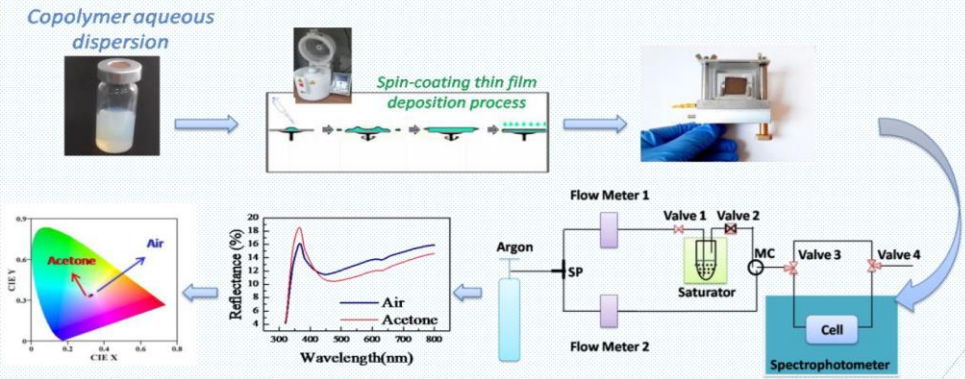


FTIR spectra of PVA-g-PMA copolymers



^{1}H NMR spectra of PVA-g-PMA copolymers

APPLICATION AS OPTICAL ACETONE SENSORS



Scheme of the sensor preparation and process of acetone vapors detection

As acetone is one of the widely used organic solvents, detecting its vapors indoor is of significant importance. In this context optical sensors have the important advantages such as room temperature detection without need of electrical power supply and easy detection based on color/reflectance change.

- ✓ Optical properties of the films including refractive index (*n*) and extinction coefficient (k), as well as thickness (d) were determined from measured reflectance spectra (R) by using two-stage nonlinear curve fitting method
- ✓ To evaluate sensing properties of the films they were placed in quartz cell and reflectance spectra (R) were measured in air, in argon and in acetone atmosphere. Then reflectance change (ΔR) was calculated.

- ❖ Acetone-sensitive copolymers are successfully designed by grafting poly(methyl acrylate) side chains onto poly(vinyl alcohol) precursor.
- ❖ Thin films of poly(vinyl alcohol)-*graft*-poly(methyl acrylate) of different composition are successfully deposited via spin-coating method.
- ❖ The successful sensing of acetone vapors by using thin films of poly(vinyl alcohol)-*graft*-poly(methyl acrylate) copolymers was demonstrated.
- ❖ A possibility of acetone color detection in via measurements in reflectance mode is demonstrated.

Acknowledgments

S. Bozhilova acknowledges Bulgarian Ministry of Education and Science for support under the National Research Programme "Young scientists and postdoctoral students" approved by DCM # 577 / 17.08.2018.

EFFECT OF GRAPHENE OXIDE INCORPORATION ON THE BIOCOMPATIBILITY OF NATURAL POLYELECTROLYTE MULTILAYERS

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[1] Institute of Biophysics and Biomedical Engineering, Bulgarian Academy of Sciences, Sofia, Bulgaria;
[2] Institute of Experimental Morphology, Pathology and Anthropology with Museum, Bulgarian Academy of Sciences, Sofia, Bulgaria

Introduction

Polyelectrolite multilayer (PEM) films for biofunctionalization of surfaces provoke great interest worldwide and have strong potential for biomedical applications associated with drug delivery and fabrication of coatings for medical instruments[1,2].

Nowadays, the interest in biopolymers of natural origin to build-up multilayer films for medical applications is constantly growing. Constructed layer by layer films of natural charged biopolymers such as hyaluronic acid (HA) and chitosan (Chi) are biodegradable and do not induce an immune response when introduced into the body[3].

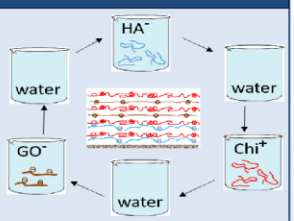
The insertion of non-polymer components into the polymer matrix is another strategy employed for modulation of the bulk and surface properties of PEM[4].

We have already found that incorporation of graphene oxide (GO)-layers into the highly hydrated HA/Chi films strongly affects their surface properties (roughness, stiffness, hydrophilicity, growth mechanism) and thrombo-resistance[5].

The present investigation is aimed to test the biocompatibility of hybrid polyelectrolyte multilayers constructed of Chi/HA and graphene oxide layers. GO is known as the thinnest and most robust carbon nanomaterial with unique electrical, thermal and mechanical features.

Materials and Methods

❖ Simplified scheme of PEM films build-up by *Layer-by-Layer (LbL) technique* of alternating adsorption of positively charged (Chi^+) and negatively charged (HA^-) polysaccharides.



PEMs were deposited onto 24-well plates as follows:

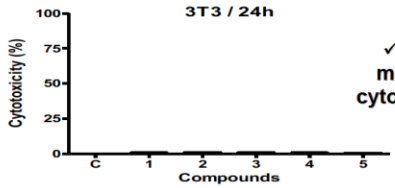
C – negative control, PEM's free plate; **1** - $[HA/Chi]_{10}$;
2 - $[HA/Chi]_9$**GO**;
3 - $[HA/Chi]_9$ **[GO**/Chi];
4 - $[HA/Chi]_2$ **[GO**/Chi$]_7$[HA/Chi];
5 - $[HA/Chi]_2$**[GO**/Chi$]_6$**GO**

❖ *Cell culture* – **Culture BALB/c 3T3** in Dulbecco Modified Eagle's medium (DMEM) with 10% Fetal Calf Serum, 100 units/ml penicillin and 100 µg/ml streptomycin in a humidified incubator at 37°C with 5% CO_2.

❖ *Cytotoxicity assay* – Neutral Red Uptake (NRU) cytotoxicity test and reading the results by ELIZA plate reader (TECAN, Sunrise TM, Grodig/Sazburg, Austria).

Results

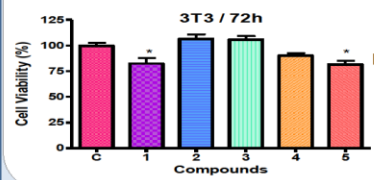
Cytotoxicity of HA/Chi/GO films



✓ **The investigated model PEMs are not cytotoxic to BALB/c 3T3 cells**

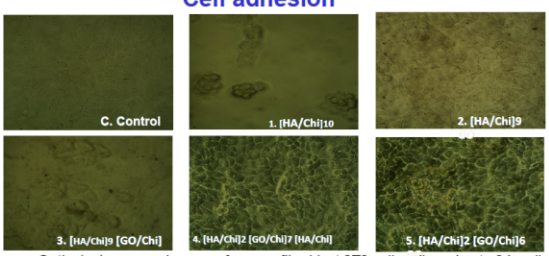
Note: cell cytotoxicity was expressed as percentage of dead cells

Antiproliferative effect of HA/Chi/GO films

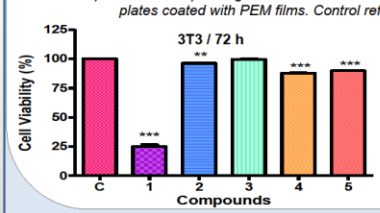


✓ **The hybrid nanocomposite films do not show a significant antiproliferative effect**

Cell adhesion



Optical microscope images of mouse fibroblast 3T3 cells adhered onto 24-well plates coated with PEM films. Control refers to well plate without coating.



✓ **PEM 1 shows a significant decrease in the cell adhesion.**
✓**PEMs 2-5 show cell adhesion comparable to the control**

Conclusions

Data demonstrate good biocompatibility of the studied hybrid multilayer films. The lack of any citotoxicity, weak antiproliferative effect and good adhesion potential provide strong evidence that the hybrid HA/Chi/GO films can be used to build up biocompatible surfaces for medical applications.

References

1. P. Bertrand, A. Jonas, A. Laschewsky, R. Legras Ultrathin polymer coatings by complexation of polyelectrolytes at interfaces: Suitable materials, structure and properties, Macromolecular Rapid Communications, 2000, 21, 319-348
2. C. Picart, F. Caruso, J.-C. Voegel, Layer-by-layer films for biomedical applications (1st ed.), Wiley-VCH Verlag GmbH & Co. KGaA (2015)
3. M. Rinaudo, Main properties and current applications of some polysaccharides as biomaterials. Polymer International, 2008, 57, 397–430
4. G. Shim, M-G. Kim, J. Park, Y-K. Oh, Graphene-based nanosheets for delivery of chemotherapeutics and biological drugs, Advanced Drug Delivery Reviews, 2016, 105, 205-227
5. T. Andreeva, S. Stoichev, S. Taneva, R. Krastev, Hybrid graphene oxide/polysaccharide nanocomposites with controllable surface properties and biocompatibility,Carbohydrate Polymers, 2018, 181, 78-85

***Acknowledgments**: This work was supported by grant КП-06-M21/4, Competition for financial support for basic research projects of young scientists and postdoctoral fellows – 2018, National Science Fund.*

MAGNETIC HYPERTHERMIA AND MAGNETOMECHANICAL TREATMENT ON BREAST CANCER CELLS

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Introduction

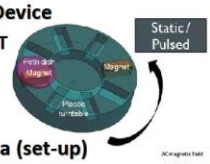
The exertion of magnetomechanical forces is a powerful tool for handling magnetic nanoparticles (MNPs) in biological environments by converting electromagnetic to mechanical energy, cousing stress on malignant cells. [1]. Magnetic hyperthermia is a potential cancer treatment aiming to increase the temperature of the body's cancerous tissues to 41-45°C, causing cell apoptosis [2].

Methods

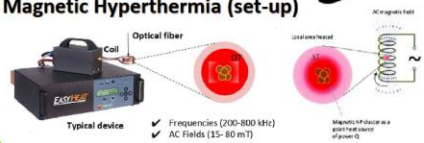
Magnetomechanical Device

Field amplitude: 200 mT

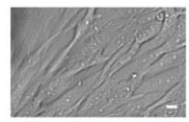
Frequency: 2 Hz



Magnetic Hyperthermia (set-up)

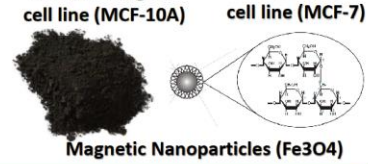


Materials



Non-tumorogenic cell line (MCF-10A)

Breast tumor cell line (MCF-7)



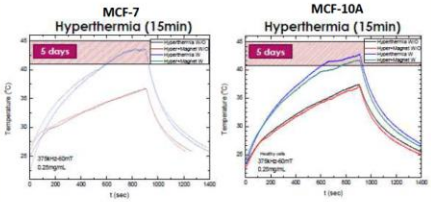
Magnetic Nanoparticles (Fe_3O_4)

Aim

The purpose of the current study was to investigate the cumulative effect of combination hyperthermia with magnetomechanical forces using magnetic nanoparticles (MNPs) against breast cancer cells.

Experiments

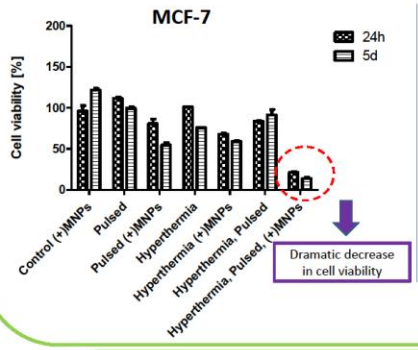
- Magnetite MNPs (Fe_3O_4) with a hydrodynamic diameter of 250 nm were used.
- To induce mechanical effects MNPs were applied inside a pulsed magnetic field (200 mT, f = 2 Hz, exposure duration 30 min) and/or in combination with hyperthermia (field amplitude 60 mT, f = 375 kHz, exposure duration 15 min)

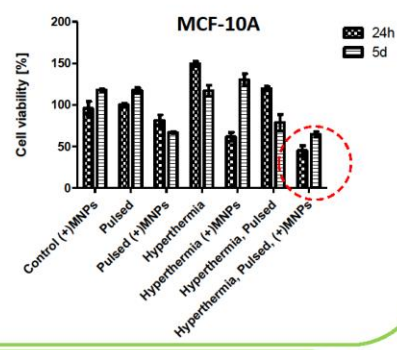


- MTT and phase-contrast microscopy data were collected at 24 and 120 hours to monitor the cell viability.

Results

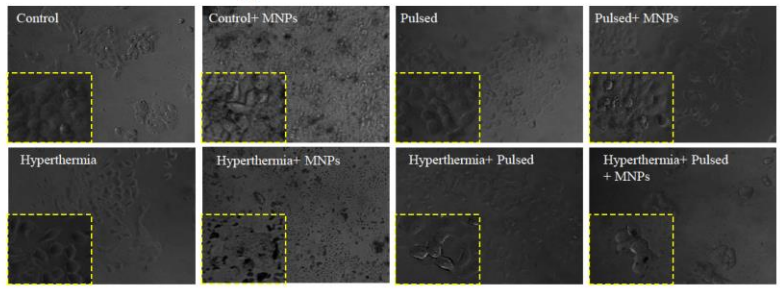
✓ Combined treatment (Hyperthermia and Magnetomechanical)



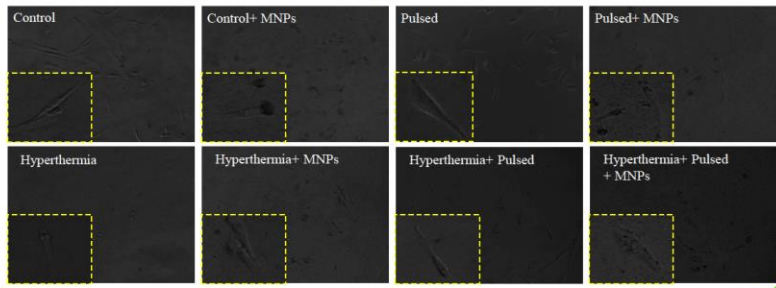


Results

✓ Phase-contrast microscopy of MCF-7 cells 120 h after treatment



✓ Phase-contrast microscopy of MCF-10A cells 5d after treatment



Conclusion

The combined treatment leads to:

- ✓ All samples with MNPs reached the hyperthermia limit
- ✓ Decreased viability in breast cancer cells
- ✓ After treatment cell viability of non-cancerous cells remained high
- ✓ Potential use in anti-tumor therapy with low side effects on normal cells

Nanoparticles are biocompatible and can be used for theranostic.

Acknowledgements: This work was supported by the National Research Program DCM#577/17.08.2018 "Young scientists and postdoctoral students".

References

[1] Spyridopoulou, K., Makridis, A., Maniotis, N., Kalogirou, O., et.al (2018) Effect of low frequency magnetic fields on the growth of MNP-treated HT29 colon cancer cells. Nanotechnology, 29(17), 175101.
[2] Périgo, E. A., Hemery, G., Sandre, O., et.al. (2015) Fundamentals and advances in magnetic hyperthermia. Applied Physics Reviews, 2(4), 1.

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Institute of Polymers

HIGHLY ADVANCED AEM WATER ELECTROLYZER WITH COMPOSITE POLYBENZIMIDAZOLE/ZIF-8 BASED POLYMER ELECTROLYTE MEMBRANE

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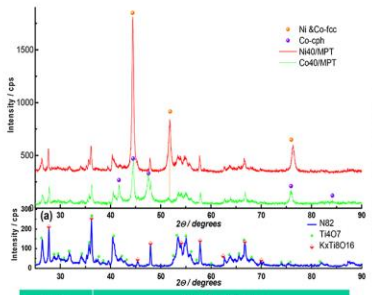
Introduction:

The AEM water electrolysis based on alkali-doped polymer electrolyte membrane is an efficient method to produce hydrogen with higher purity, which offers several advantages over the traditional technologies: higher current density, low ohmic resistance, possibility to operate at higher working pressure, as well as usage of platinum free electrocatalysts. The technology still has some problems such as non-sufficient stability of the polymer electrolyte at elevated temperature, low conductivity of the commercially available membranes, and intensive corrosion on the bipolar plates of the cell. This work presents a research on development of highly efficient and thermally stable membrane electrode assemblies (MEAs) with carbon free electrodes containing non-noble metal catalysts (Co and Ni supported on Magnelli phase titania), and three-layered composite meta-PBI based membranes with incorporated 20 wt.% commercial zeolitic imidazole framework, ZIF-8 microparticles (Basolite® Z1200, BASF) and its performance was compared with pristine m-PBI membrane, doped with KOH.

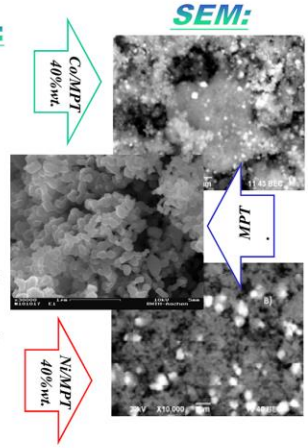
XDR measurements:



Samples	Crystallites size [nm]				
	hcp			fcc	
	D (100)	D(002)	D(101)	D(111)	D(200)
Ni/MPT	-	-	-	26±0.5	18±0.5
Co/MPT	16	33±8	22±4	-	-

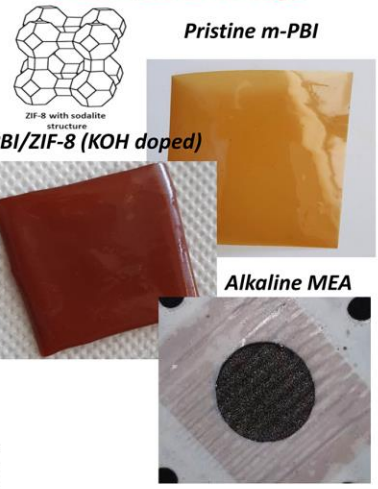
The XRD spectra show crystallographic orientation of the Ni particle mainly (D100, D002) and (D101). The calculated particle size variates in range 16nm to 33nm. The Co particle orientation are mainly (D111 and D200) with size 18nm to 26nm.

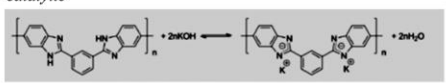
SEM:



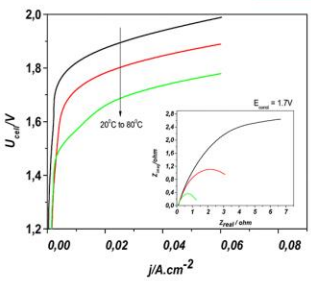
The both nano sized catalyst applicable for partial reactions are very well dispersed over the catalytic carrier surface.

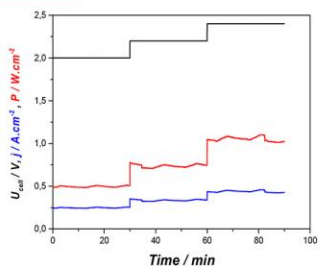
PEM screening:





EC results:





Conclusions:

- ✓ The developed membrane electrode assemblies demonstrates possibility to operate at 60^{0}C.
- ✓ The current density reach value at about 1A.cm^{-2} at elevated temperature.
- ✓ The composite multilayered polybenzimidazole/ZIF-8 membrane are suitable for AEM water electrolysis cells.

This research was performed on equipment of Research Infrastructure "Energy Storage and Hydrogen Energetics" (ESHER), included in the National Roadmap for Research Infrastructure 2017-2023", granted by the Ministry of Education and Science of Republic Bulgaria, grant agreement № DO1-160/28.08.2018

Institute of Electrochemistry and Energy Systems
Bulgarian Academy of Sciences

AEM WATER ELECTROLYZER IN STACK MODE WITH PBI-MEMBRANE

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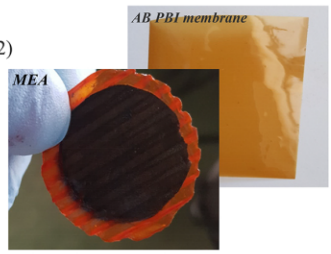
Introduction:

Water electrolysis based on alkali-doped polymer electrolyte membrane is an efficient method for production of very pure hydrogen. It offers several advantages over the traditional technologies like higher current density, lower ohmic resistance, and possibility for operation at higher working pressure. Both partial electrode reactions (hydrogen evolution reaction, HER, and oxygen evolution reaction, OER, are of particular interest as they appear to be the main sources of energy losses and membrane electrode degradation. The major problem of the technology is among of the active catalysts for both partial reactions. This work presents a development of laboratory water electrolyze with 4 MEAs with anion conductive membrane working without precious metal catalysts for both partial electrode reactions with optimized amount of non-noble catalysts for both partial reactions.

AEM and MEA



Experimental

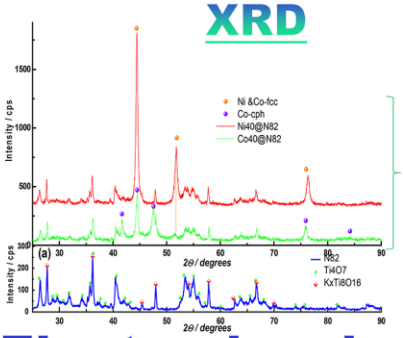
Catalyst synthesis: acetilacetonate precursors (M[$(C_5H_7O_2)_n$]m or M-acac, M=Ni, Co, MPT (N82)

Physical characterization: X-ray diffraction (XRD), Scanning Electron Microcopy (SEM)

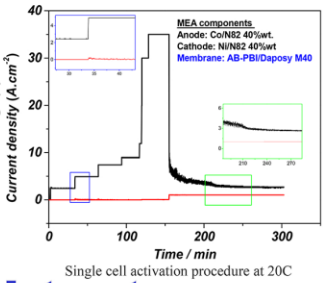
MEA (membrane electron assembly) preparation : Direct assembling in the electrochemical cell

Electrochemical characterization: polarization curves, dynamic stress test

XRD

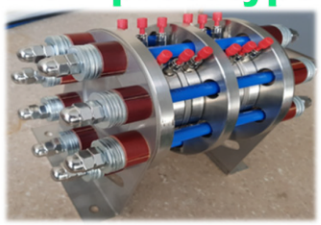


Activation

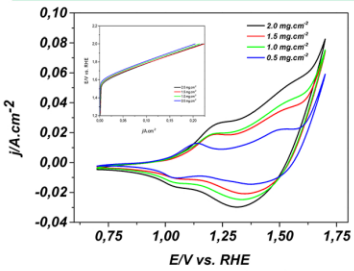


Single cell activation procedure at 20C

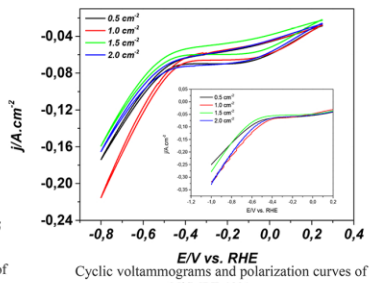
EC – prototype



Electrochemical tests

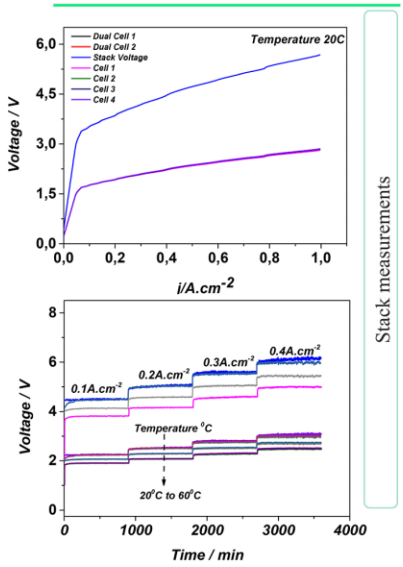


Cyclic voltammograms and polarization curves of Co/MPT 40% wt.



Cyclic voltammograms and polarization curves of Ni/MPT 40% wt.

PEM test cell



Conclusions:

- ✓ The optimal catalytic loading of anode catalyst is 0.5 mg.cm^{-2}
- ✓ The optimal catalytic loading of cathode catalyst is 1.0 mg.cm^{-2}
- ✓ The developed MEA demonstrates possibility to operate under 60C
- ✓ The developed stack demonstrates stable electrochemical parameters for all integrated MEAs

This research was supported by the National science fund under the grand agreement number КП-06-ОПР04/3. Part of the experiments are performed on equipment of Research Infrastructure "Energy Storage and Hydrogen Energetics" (ESHER), included in the National Roadmap for Research Infrastructure 2017-2023", granted by the Ministry of Education and Science of Republic Bulgaria, grant agreement № DO1-160/28.08.2018

Постер 20

ДНАзна и фосфолипазна активност върху липозомни сферични нуклеинови киселини

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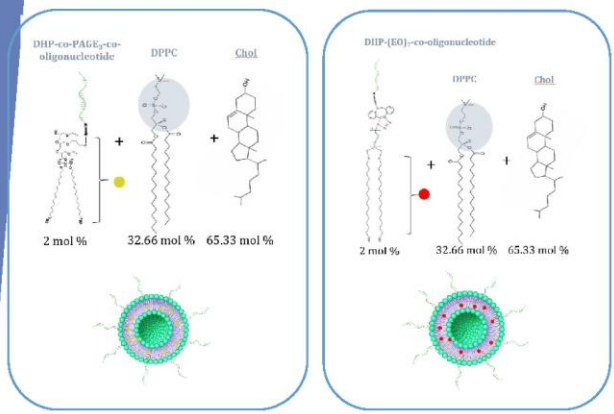
Въведение



Сферичните нуклеинови киселини (SNA) са наноструктури, състоящи се от нуклеинови киселини разположени около ядро от наночастици или липозоми. SNAs са **имат голям потенциал** като частици-преносители или регулатори на генната експресия поради тяхната **ниска токсичност, повишена стабилност**, сравнително лесното им преминаване през мембраната на клетките и способност да проникнат през бариерата на епидермиса. В последните години те намират приложение като адюванти във ваксини, ефективни регулатори на дълги некодиращи РНК молекули в клетките (lncRNA), при разработване на имунотерапия за ракови заболявания и др.

От особено значение при дизайна на SNAs е прилагането на различни методи за формиране на конюгатите между нуклеиновите киселини и липофилната структура, която участва в образуването на липозомите и определянето на взаимодействията им с различни биомолекули в клетката.

Тук ние представяме **нови липозомни структури** на база на конюгатите DPH-$(EO)_7$-co-oligonucleotide и DPH-co-PAGE3-co-oligonucleotide. Те се характеризират със следните основни свойса на получаване:

- Едностъпален реакционен процес.
- Меки реакционни условия.
- Без нужда от използването на инициатор.
- Използване на безвредни разтворители.
- Установката се състои от 6 LED-светодиоди излъчващи при фиксирана дължина на вълната от 365 nm, което прави употебата и подходяща и безвредна за различни полимерни и биологични материали, както и за функционални олигонуклеотиди.
- Бърза и високо ефективна тиол-ен „click” присъединителна реакция директно в разтвор.
- Количествено превръщане с висок добив.

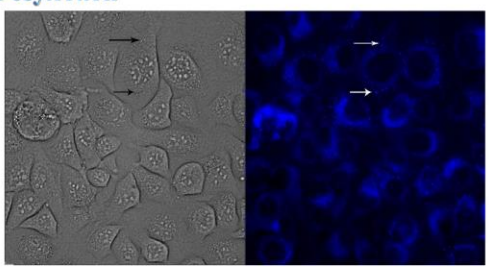
Цел

Целта на изследването е да бъде определено влиянието на ензимите ДНаза I и фосфолипаза A_2 върху липозомни сферични нуклеинови киселини съдържащи DPH-$(EO)_7$-co-oligonucleotide.

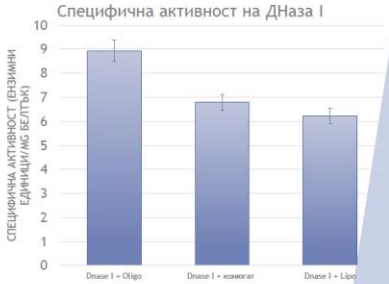
Методи

- За визуализиране на липозомите, съдържащи DPH-(EO)7-co-oligonucleotide, беше използвана A549 клетъчна линия. Клетките бяха инкубирани в среда DMEM с добавени 10% fetal calf serum и penicillin / streptomycin (0.1 mg/mL / 0.06 mg/mL) в термостат на 37°C и 5% CO_2. Клетките бяха инкубирани с 0,2 μg ДНК / $1x10^5$ клетки за 30 мин. За заснемането на третираните клетки беше използван микроскоп GE Delta Vision Ultra Microscopy System при увеличение 600x и филтър за 430 nm.
- Определянето на ендонуклеазната активност на ДНаза I върху конюгатите и липозомите се извърши чрез метода на Kuniz. Една ензимна единица беше дефинирана като количеството на ДНаза, което се добавя към 1 mg/mL олигонуклеотид, което предизвиква промяна на абсорбцията с 0,001 при 260 nm (A260). Ензимната реакция беше проведена в буфер със състав: 0.1 M NaOAc (pH 5.0) buffer, 4.2 mM $MgSO_4$ and 25 mM NaCl. Беше сравнена специфичната активност на ДНаза I върху липозоми съдържащи DPH-$(EO)_7$-co-oligonucleotide, 2) липозоми съдържащи само конюгата и 3) „чист“ олигонуклеотид.
- Фосфолипазната активност беше определена като изменение на абсорбцията при 280 nm след третиране на липозомите, конюгатите, и олигонуклеотида с фосфолипаза A_2 (pancreatic secreted PLA_2, EC 3.1.1.4, PLA2G1B, pPLA2) Ензимната реакция беше проведена в буфер със състав: 25 mM Tris HCl, pH 8.0, 5 mM $CaCl_2$,150 mM NaCl. Изменението на A260 беше отчитано в продължение на 15 мин през интервали от 1 мин.

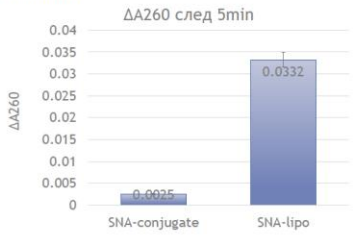
Резултати



Фиг.1 Визуализиране на липозомни сферични нуклеинови киселини, съдържащи DPH-$(EO)_7$-co-oligonucleotide, в клетки A549. Със стрелки са посочени липозомите.



Фиг. 2 Специфична активнност на ДНаза I върху липозомни сферични нуклеинови киселини, съдържащи DPH-$(EO)_7$-co-oligonucleotide.



Фиг. 3 Промяна на абсорбцията при 260 nm дължина на вълната на DPH-$(EO)_7$-co-oligonucleotide (SNA-cojugate) и липозоми, съдържащи DPH-(EO)7-co-oligonucleotide, 5 мин след третиране с фосфолипаза A_2.

Фиг. 4 Промяна на абсорбцията при 260 nm дължина на вълната, разтвор на липозоми, включващи DPH-$(EO)_7$-co-oligonucleotide при третиране с фосфолипаза A_2 за 15мин.

Извод: Заключение:
Липозомните сферични нуклеинови киселини съдържащи DPH-$(EO)_7$-co-oligonucleotide могат да навлизат в клетките и могат да се разграждат от клетъчните ДНази и фосфолипази.

Благодарности: Тези изследвания са извършени с финансовата подкрепа на договори №ДН19/8 от 10.12.2017 към ФНИ, МОН

Synthesis and characterization of liposomal spherical nucleic acids via incorporation of an original nucleolipid

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[2] Faculty of Biology, Sofia University "St. Kliment Ohridski" 8, Dragan Tsankov Blvd., 1164 Sofia, Bulgaria
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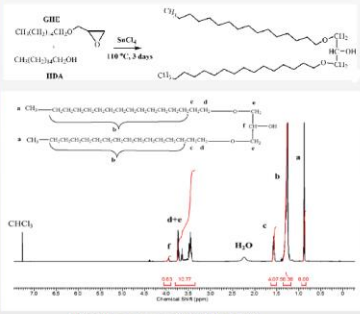
Spherical nucleic acids (SNAs) are nanostructures, composed of highly oriented and densely grafted oligonucleotides on the surface of a nanoparticle which can be inorganic, hollow or organic. The dense three-dimensional arrangement of the oligonucleotides imparts unique advantages over traditional nucleic acid delivery methods, including cellular uptake with no need of transfection agents, resistance to nuclease degradation and ability to overcome different biological barriers. SNAs with hollow architectures are one of the new forms of SNAs. These particles consist of liposomal cores composed of phospholipids, the surface of which is functionalized with DNA strands, modified with a hydrophobic residue, which intercalates into the phospholipid bilayer. In this study we develop a novel synthetic route for preparation of a conjugate to be intercalated in the phospholipid bilayer. The conjugate consists of a lipid-mimetic anchor to which an oligonucleotide strand is attached. The conjugation is performed by an initiator-free, click reaction in mild conditions not harmful for the nucleic acid.

Key words: Nucleic acid-polymer conjugates, "*click*" reactions, spherical nucleic acids, liposomes)

Synthesis of DHP (Mn=540 g.mol^{-1})

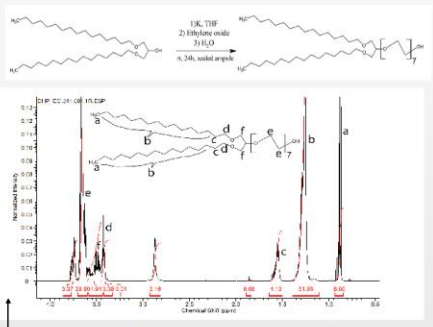
(DHP – dihexadecyl-propan-2-ol) was obtained from glycidylhexadecyl ether (GHE, Mn=298,5 gr.mol^{-1}), 1-Hexadecanol (HDA, Mn=242,44 g.mol^{-1}) and $SnCl_4$(260.52 g.mol^{-1}) (Scheme 1).



^{1}HNMR spectrum of DHP in $CDCl_3$

Synthesis of DHP-$(EO)_7$-OH (Mn=848 g.mol^{-1})

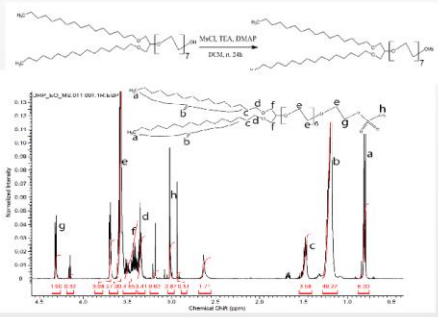
DHP-$(EO)_7$-OH was obtained by anionic polymerization of propylene oxide monomer. The number (n=7) of ethylene glycol functional units was calculated from ^{1}HNMR spectrum.



^{1}HNMR spectrum of DHP-$(EO)_7$–OH in $CDCl_3$

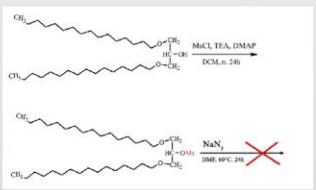
Mesylating DHP-$(EO)_7$-OH

The DHP-$(EO)_7$–OH was mesylated with mesyl chloride in DCMq using TEA and DMAP as a base.



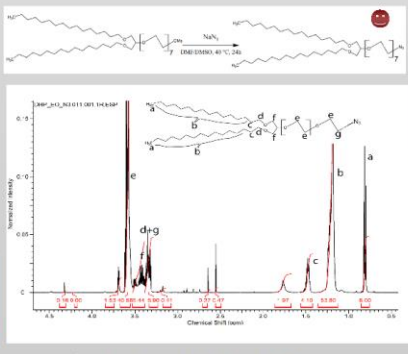
^{1}HNMR spectrum of DHP-$(EO)_7$–OMs in $CDCl_3$

First synthetic strategy



Azidation of DHP-$(EO)_7$-OMs

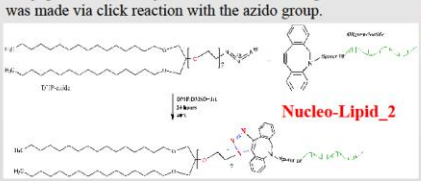
The mesylate functional group was substituted with azide at 40°C using DMF/DMSO as a solvent system.



^{1}HNMR spectrum of DHP-$(EO)_7$–N_3 in $CDCl_3$

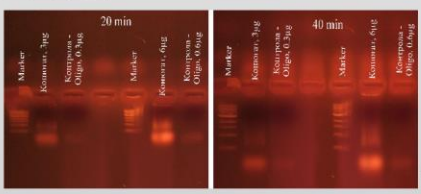
Conjugating with oligonucleotide

Conjugation with alkyne functioanalized oligonucleotide was made via click reaction with the azido group.

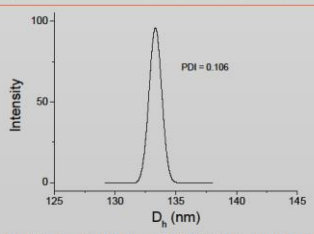


Sequence, composition, and molecular weight of the oligonucleotides used. DBCO – dibenzocyclooctyne, EG – ethylene glycol, spacer 18 – phosphodiester followed by 6 ethylene glycol units.)

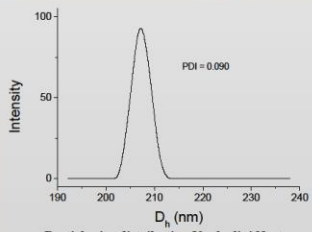
Code	Oligonucleotides composition Sequence (5'→3')	Mw (g.mol^{-1})	Ext. Coeff.
DBCO-Oligo	DBCO-$(EG)_4$-(spacer 18)$_1$ ta ata cga ctc act ata gg	6950	230 600



Agarose gel retardation analysis of functionalized oligonucleotides and DHP-co-PAGE$_3$-co-oligonucleotide

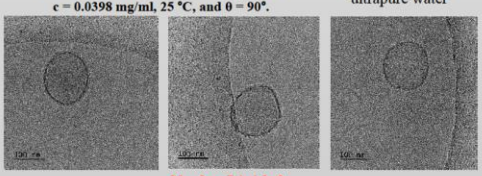


Particle size distribution of DPPC/Cholesterol?Nucleolipid2 liposomes at c = 2 mM total lipid, 25 °C, and θ = 90°.



Particle size distribution Nucleolipid2 at c = 0.0398 mg/ml, 25 °C, and θ = 90°.

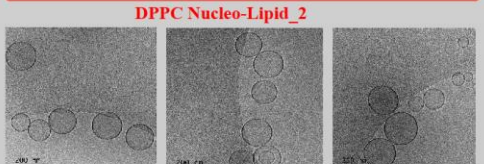
DHP-$(EO)_7$–OH - oligonucleotide after dialysis in 13ml ultrapure water



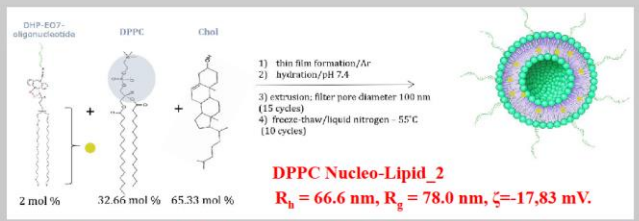
Nucleo-Lipid_2

Cryo-TEM

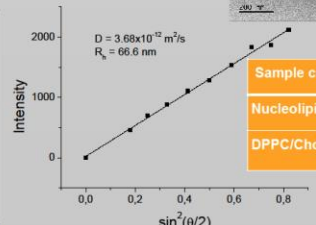
DPPC Nucleo-Lipid_2



Incorporating the conjugate in liposomes



DPPC Nucleo-Lipid_2
R_h = 66.6 nm, R_g = 78.0 nm, ζ=-17,83 mV.



Sample code	R_h (nm)	R_g (nm)	R_g/R_h	ζ (mV)
Nucleolipid2	115.1	112.0	0.97	-31.9
DPPC/Chol/Nucleolipid2	66.6	78.0	1.17	-17.8

Angular dependence of the relaxation rate (Γ) of DPPC/Cholesterol?Nucleolipid2 liposomes at c = 2 mM total lipid and 25 °C for determination of R_h.

Acknowledgements: This work was supported by the National Science Fund (Bulgaria) Project No DN19/8-2017.

Постер 22

Development of spherical nucleic acids from novel polystyrene/poly(chloromethylstyrene)/oligonucleotide conjugates via initiator-free click chemistry

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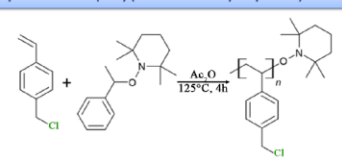
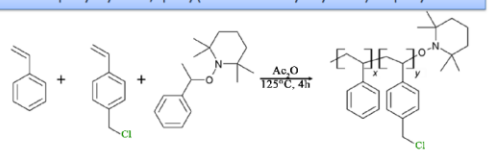
[1]Institute of Polymers, Bulgarian Academy of Sciences, Akad. G. Bonchev St. 103A, 1113 Sofia, Bulgaria, [2]Department of Biochemistry, Faculty of Biology, Sofia University "St. Kliment Ohridski" 8, Dragan Tsankov Blvd., 1164 Sofia, Bulgaria, [3]Theoretical and Physical Chemistry Institute, National Hellenic Research Foundation, Athens, Greece

Spherical nucleic acids (SNAs) are nanostructures, composed of highly oriented and densely grafted oligonucleotides on the surface of a nanoparticle which can be inorganic, hollow or organic (1,2). The dense three-dimensional arrangement of the oligonucleotides imparts unique advantages over traditional nucleic acid delivery methods, including cellular uptake with no need of transfection agents, resistance to nuclease degradation and ability to overcome different biological barriers. Here, we report synthesis of nucleic acid-polymer conjugates (SNAs) obtained by initiator free "click" coupling reactions of appropriately functionalized oligonucleotides with synthetic polymer chains of different chemical nature, composition, and properties, namely, poly(chloromethylstyrene)s. Nitcontrolledroxide mediated radical polymerization was used to synthesize the poly(chloromethyl styrene) (PCMS) homopolymer, the PCMS-b-PS block copolymer and the P(CMS-co-S) random copolymer. Further, they were functionalized with azido functional groups and conjugated with oligonucleotides. Resulting SNAs are amphiphilic and form stable aggregates in aqueous solution. The aggregates are thoroughly investigated by a variety of techniques – ^{1}H NMR, UV light measurement, static, dynamic, and electrophoretic light scattering and gel electrophoresis.

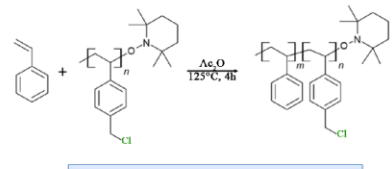
Synthesis of poly(chloromethylstyrene) homopolymer and polystyrene/ poly(chloromethylstyrene) copolymers



M_w=11 000 g.mol^{-1} M_w/M_n=1.45 Wt%$_{(PCMS)}$ = 100

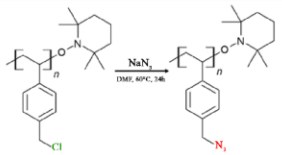


M_w=10 000 g.mol^{-1} M_w/M_n=1.28 Wt%$_{(PCMS)}$ = 30

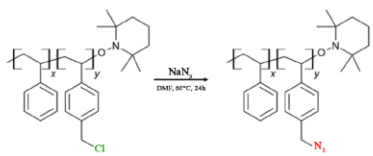


M_w=16 500 g.mol^{-1} M_w/M_n=1.14 Wt%$_{(PCMS)}$ = 11

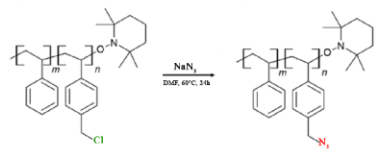
Functionalization of the polymers with azido-groups



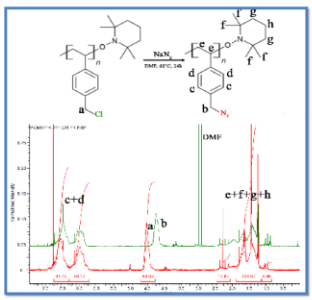
Degree of conversion 100%, Yield 86%



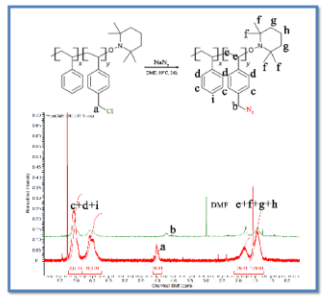
Degree of conversion 100%, Yield 99%



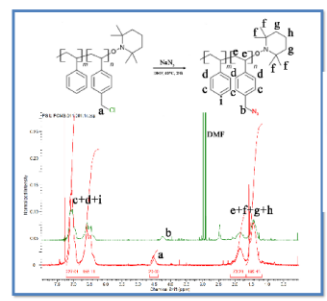
Degree of conversion 100%, Yield 99%



^{1}H NMR spectrum of PCMS before and after azidation $CDCl_3$ 600MHz.

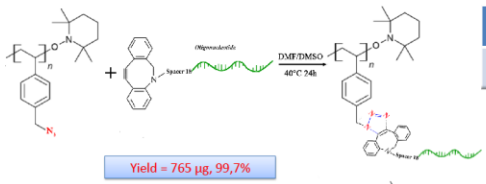


^{1}H NMR spectrum of P(ScoCMS) before and after azidation $CDCl_3$ 600MHz.

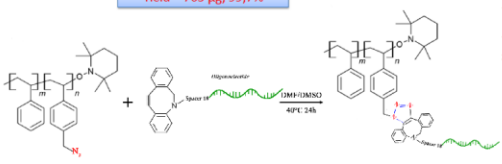


^{1}H NMR spectrum of PS-b-PCMS before and after azidation $CDCl_3$ 600MHz.

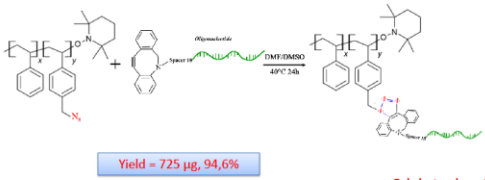
Conjugating the obtained polymers with oligonucleotides



Yield = 765 µg, 99,7%



Yield = 540 µg, 70,4%

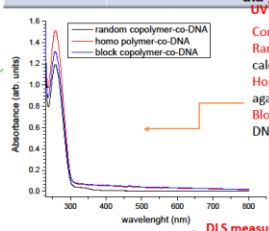


Yield = 725 µg, 94,6%

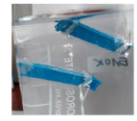
Sequence, composition, and molecular weight of the oligonucleotides used. DBCO – dibenzocyclooctyne, EG – ethylene glycol, spacer 18 – phosphodiester followed by 6 ethylene glycol units.)

Code	Oligonucleotides composition Sequence (5'→3')	Mw (g.mol^{-1})	Ext. Coeff.
DBCO-Oligo	DBCO-(EG)$_4$-(spacer 18)$_1$ ta ata cga ctc act ata gg	6950	230 600

UV measurements:

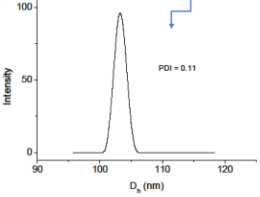


Concentration of the obtained conjugates obtained:
Random copolymer-co-DNA = 36.63 µg/ml (Yield=540 µg calculated against DNA strains)
Homopolymer-co-DNA = 45.5 µg/ml (Yield=720 µg calculated against DNA strains)
Block copolymer-co-DNA = 38.26 (Yield=765 µg calculated against DNA strains)

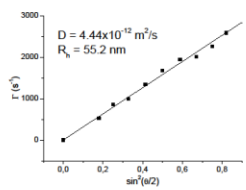


Conjugate Sample	R_h (nm)	R_g (nm)	R_g/R_h	ζ (mV)
Homopolymer-co-DNA	55.2	48.8	0.88	-17.9/-20.6
Random copolymer-co-DNA	60.2	52.6	0.87	-16.8/-11.4
Block copolymer-co-DNA	61.3	57.2	0.93	-15.6/-11.6

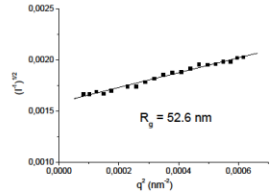
DLS measurements:



Particle size distribution PS-ON_Homo at c = 45.5 µg/ml, 25 °C, and θ = 100°.

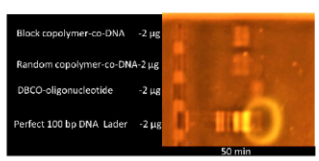


Angular dependence of the relaxation rate (Γ) for PS-ON-Homo at c = 45.5 µg/ml and 25 °C for determination of R_h.



Partial Berry plot of PS-ON_Random for determination of R_g.

Gel electrophoresis measurement



Acknowledgements: This work was supported by the National Science Fund (Bulgaria) Project No DN19/8-2017.

References:
1) N.Toncheva-Moncheva,M.Dangalov,N.G.Vassilev,Ch.P.Novakov.Thiol–enecouplingreactionachievementandmonitoringby"insitu"UVirradiationNMRspectroscopy.*RSCAdvances***2020**,*10*,25214.https://doi.org/10.1039/D0RA03902K
2) P.Bakardzhiev,N.Toncheva-Moncheva,K.Mladenova,S.Petrova,PVidev,V.Moskova-Doumanova,T.Topouzova-Hristova,I.Doumanov,S.Rangelov.Assemblyofamphiphilicnucleicacid-polymerconjugatesintocomplexesuperaggregates:Preparation,properties,andinvitroperformance.*EuropeanPolym.J.***2020**,*131*, 109692, https://doi.org/10.1016/j.eurpolymj.2020.109692
3) T. Tsoukatos, S. Pispas , N. Hadjichristidis, Macromolecules 2000 , 33 , 9504-9511, https://doi.org/10.1021/ma0011946

Novel amphiphilic polyglycidol/poly(ε-caprolactone) and polyglycidol/poly(α-cinnamyl-ε-caprolactone) copolymers as highly effective cannabidiol-loaded nanocarriers

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Recently drug delivery systems based on amphiphilic block copolymer nanoparticles have focused much attention for controlled delivery of biological active substances (low-molecular-weight drugs, enzymes, DNA, and RNA). Amphiphilic block copolymers frequently self-assemble in aqueous media into nanosized, spherical, core-shell micelles. Recently, for the synthesis of well-defined block copolymers the highly efficient "click" chemistry-reactions are preferred. In this work by applying the copper-catalyzed azide–alkyne cycloaddition, novel linear block copolymers comprising PEEGE(protected PG) and PCL was successfully obtained. Further, we report on the preparation, physicochemical and biological characterization of well defined nano-sized micellar carriers loaded with cannabidiol (CBD).

Linear Polyglycidol-polycaptolactone copolymers as novel platforms for controlled delivery of natural bioactive substances.

I. PG_{45}-b-(PO_4)-b-PCL_{35}-b-(PO_4)-b-PG_{35}

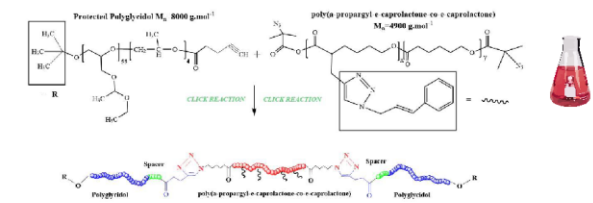
II. PG_{35}-b-(PO_4)-b-PCL_{35}-b-(PO_4)-b-PG_{35}

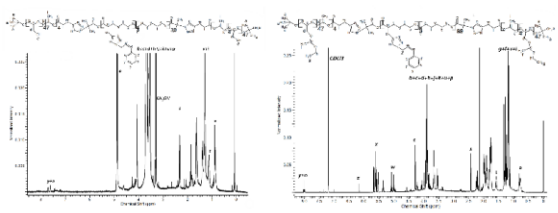
III. PG_{35}-b-(PO_4)-b-P(CyCL-co-CL)-b-(PO_4)-b-PG_{35}

Molar mass and dispersity of the copolymers

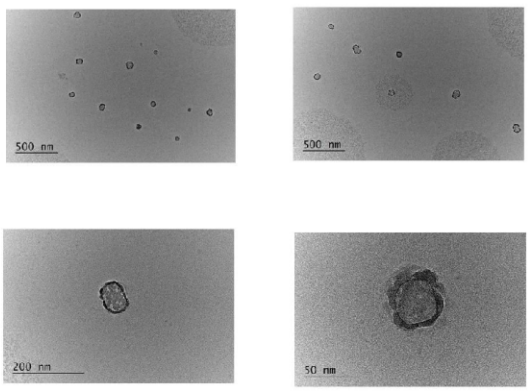
Copolymer	Mn (g.mol^{-1})	Mw/Mn
PG_{45}-b-(PO_4)-b-PCL_{35}-b-(PO_4)-b-PG_{35}	15,300	1.2
PG_{35}-b-(PO_4)-b-PCL_{35}-b-(PO_4)-b-PG_{35}	16,300	1.2
PG_{55}-b-(PO_4)-b-P(CyCL-co-CL)-b-(PO_4)-b-PG_{55}	13,500	1.1

Synthesis of polyglycidol/poly(α-cinnamyl-ε-caprolactone-co-ε-caprolactone) block copolymer by click reaction followed by deprotection of the glycidol –OH groups.



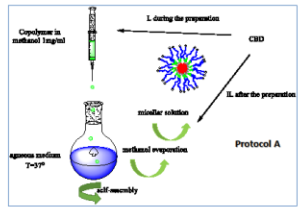


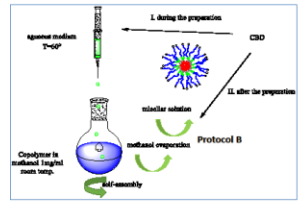
^{1}HNMR spectra of the copolymer before and after deprotection.



TEM micrographs of the well defined nano-sized micellar carriers loaded with cannabidiol (CBD).

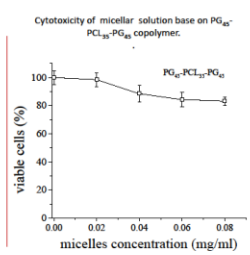
Micelle formation.

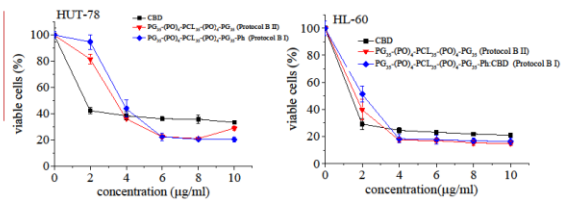




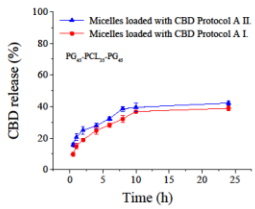
Physicochemical characterization of aqueous micellar solutions containing CBD.

Characteristics / Sample code	R_h (nm)	PDI	ζ-potential (mV)	EE (%)	Cell line: HL-60 IC$_{50}$ (μg/ml)	Cell line: HUT-78 IC$_{50}$ (μg/ml)
PG_{45}-PCL_{35}-PG_{45}	41 ± 4.2	0.45 ± 0.02	17.7 ± 1.2	-	-	-
PG_{45}-PCL_{35}-PG_{45}:CBD (Protocol A II, copolymer:CBD=10:1)	64 ± 3.8	0.35 ± 0.05	22.9 ± 2.4	82	2.29	6.21
PG_{45}-PCL_{35}-PG_{45}:CBD (Protocol A I, copolymer:CBD=10:1)	62 ± 2.7	0.22 ± 0.03	25.6 ± 2.1	91	2.33	5.21
PG_{35}-PPO_4-PCL_{35}-PPO_4-PG_{35}-Ph	130 ± 4.5	0.039 ± 0.01	35.7 ± 1.8	-	-	-
PG_{35}-PPO_4-PCL_{35}-PPO_4-PG_{35}:CBD (Protocol B II, copolymer:CBD=10:1)	155 ± 5.1	0.089 ± 0.02	32.9 ± 0.2	92	1.64	3.39
PG_{35}-PPO_4-PCL_{35}-PPO_4-PG_{35}:CBD (Protocol B I, copolymer:CBD=10:1)	140 ± 2.4	0.072 ± 0.01	37.1 ± 1.1		2.03	3.76
PG_{55}-b-(PO_4)-b-P(CyCL-co-CL)-b-(PO_4)-b-PG_{55}	35± 1.6	0.022 ± 0.01	18.2± 1.2	-	-	-
PG_{55}-b-(PO_4)-b-P(CyCL-co-CL)-b-(PO_4)-b-PG_{55} (Protocol A II, copolymer:CBD=10:1)	47± 1.4	0.012 ± 0.05	24.1 ± 2.5	91	0.004	0.008
PG_{55}-b-(PO_4)-b-P(CyCL-co-CL)-b-(PO_4)-b-PG_{55} (Protocol A I, copolymer:CBD=10:1)	45± 1.8	0.072 ± 0.06	29.4 ± 1.3	90	0.005	0.009
CBD	-	-	-	-	1.41	1.72
CBD	-	-	-	-	0.002	0.007

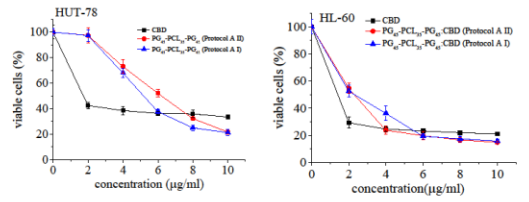


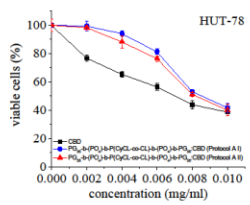


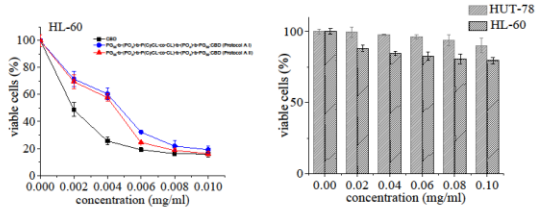
Cytotoxicity of micellar vs. free CBD against HUT-78 and HL-60 cell lines after 72h continues exposure at 37°C.



Cumulative drug release profile (%).







Cytotoxicity of micellar vs. free CBD against HUT-78 and HL-60 cell lines after 72h continues exposure at 37°C.

This research was supported in part by the Bulgarian Science Fund (Grant KP-06-OPR 03-10/2018) and by the Bulgarian Ministry of Education and Science (Grant D01-217/30.11.2018) under the National Research Programme "Innovative Low-Toxic Bioactive Systems for Precision Medicine (BioActiveMed)" approved by DCM # 658/14.09.2018).

Glycolysis of Polyethylene Terephthalate (PET) - Literature Search

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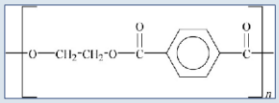
2. Institute of Polymers, Bulgarian Academy of Sciences

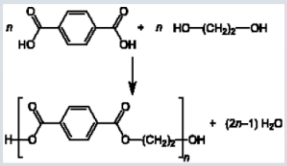
Polyethylene Terephthalate (PET)

- Thermoplastic polyester
- One of most widely produced plastics in the world.
- Main applications:
  - *Food Packaging (e.g. bottles, trays and films)*
  - *Non-food packaging (containers for cosmetics, healthcare, and detergents)*
  - *Fibres (e.g., for clothing and bags)*
  - *Non-woven fabrics*
  - *Carpets*

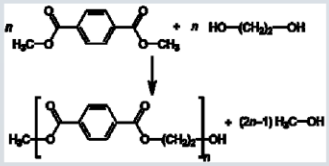


Synthesis of PET

- Esterification: ethylene glycol (EG) + terephthalate acid (TA) with elimination of water.



- Transesterification: Dimethyl terephthalate (DMT) with excess of EG and a basic catalyst. Methanol (CH3OH).



Methods of PET Recycling

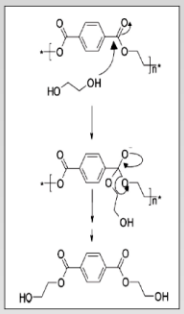
- **Mechanical Recycling:** : Melt reprocessing of PET waste (typically by extrusion or injection molding). Mechanical and rheological properties of the mechanical recycled PET are affected.
- **Chemical Recycling:** depolymerization of post-consumed PET to obtain the starting monomers and/or oligomers
- **Incineration for energetic gain:** thermovalorization of PET objects through incineration (heat value of PET 22.95 MJ/kg)

Chemical Recycling of PET

- Similarly to esters, PET undergoes hydrolysis, alcoholysis or glycolysis, acidolysis, aminolysis that lead to the cleaving of macromolecules.
- The mechanism of chemical recycling is always to open the ester bonds within the macromolecular chains.
- **Hydrolysis:** Reaction of PET with water allows the poly-ester chains to be broken down into TA and EG. The process can be carried out under neutral, acidic, or basic conditions.
- **Methanolysis:** treatment of PET with methanol at relatively high temperatures (180 - 280C) and pressures (20 - 40 atm), with formation of DMT and EG along with oligomers.
- **Aminolysis:** The aminolysis of PET produces diamides of TPA like bis (2-hydroxyethylene) terephthalamides (BHETA).

Glycolysis of PET

- Simplest and oldest method of PET depolymerization
- Molecular degradation of PET by glycols, in the presence of trans-esterification catalysts
- Main products obtained from glycolysis with EG: bis(2-hydroxyethyl) terephthalate (BHET) and other oligomers (PET glycolyzates).
- BHET can be used for PET production using any of the method based on either DMT or TPA.



Glycols used in Glycolysis reaction

- **Ethylene glycol (EG):**
- **Diethylene glycol (DEG)**
- **Glycerol**
- **Dipropylene glycol (DPG)**
- **Propylene glycol (PG)**
- **Neopentyl glycol (N**
- **1,3-propanediol**
- **Polyethylene glycols: PEGs (200, 400, 600, 1000 and 1500)**

Comparison the reactivity of glycols

In presence of titanium (IV) n-butoxide

The kinetics of PET glycolysis by DEG, DPG, glycerol (Gly) and mixtures of these glycols was studied with two experimental procedures: uncatalyzed at 220°C and catalyzed (0.5% weight titanium (IV) n-butoxide (TBT)) at 190°C. The obtained dada revealed reactivity order of glycols: **DEG > Gly > DPG** for uncatalyzed reaction at 220°C and **DEG > DPG > Gly** for catalyzed reaction at 190°C [1].

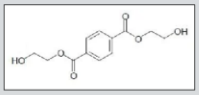
In presence of titanium (IV) phosphate

PET depolymerization by EG, DEG, and PG was studied in the presence titanium (IV)-phosphate. [2]

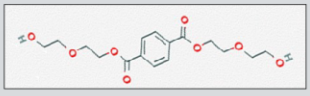
Table 1: Reaction conditions and main products of PET glycolysis

PET Grade	Diol	Temperature (°C)	Reaction Time (min)	SEC Analysis of the Glycolized Products			
				Monomer (%)	Dimer (%)	Trimer (%)	Tetramer (%)
Fiber Grade	EG	190 - 200	150	97.5*	1.6	0.7	0.2
Fiber Grade	DEG	220	12	91.2**	4.5	2.8	1.5
Fiber Grade	PG	180 - 188	480	93.6***	3.6	1.8	1
Bottle Grade	EG	190 - 200	105	66.7*	28.9	4.4	---
Bottle Grade	DEG	220	8	64.2**	3.3	2.1	30.4
Bottle Grade	PG	180 - 190	285	52.8***	27.8	11.6	5

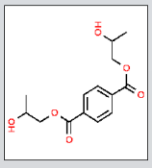
mol of PET/monomer unit = 0.13 mol of diol = 0.36.



bis(2-hydroxyethyl) terephthalate (BHET)*



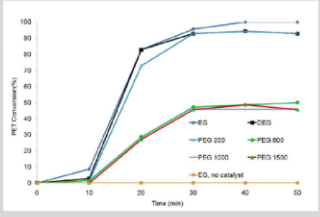
bis[2(2-hydroxyethoxy)-ethyl] terephthalate BHEET**



bis(2-hydroxypropyl) terephthalate BHPT***

Under microwave irradiation with zinc acetate as catalyst

Unreacted PET could not be detected in the reaction medium after 30 min of reaction with EG/DEG, but with higher glycols, the extent of PET conversion was much lower [3].



Effect of glycolysis time and molecular weight of glycol on the extent of PET conversion [3]. Reproduced with the permission of the "Wiley Materials" (John Wiley & Sons, Inc.)

Application of PET glycolysis products

- **Unsaturated polyester resin**
- **PU foams and PU dispersions**
- **Plasticizers**
- **Additives for construction materials**

References

1. Pardal, F., & Tersac, G. Comparative reactivity of glycols in PET glycolysis. Polymer Degradation and Stability 91 (2006) 2567e2578
2. Troev, K., Grancharov, G., Tsevi, R., & Gitsov, I. (2003). A novel catalyst for the glycolysis of poly(ethylene terephthalate). Journal of Applied Polymer Science, 90(8), 2301–2301. doi:10.1002/app.12711
3. Chaudhary, S., Surekha, P., Kumar, D., Rajagopal, C., & Roy, P. K. (2013). Microwave assisted glycolysis of poly(ethylene terepthalate) for preparation of polyester polyols. Journal of Applied Polymer Science, 129(5), 2779–2788. doi:10.1002/app.38970

Фоточувствителни дендримери като добра алтернатива на антимикробна фотодинамична терапия срещу Грам отрицателни бактерии с противотуморна активност

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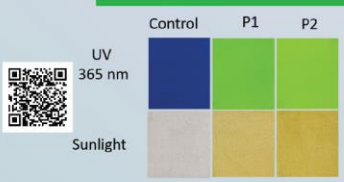
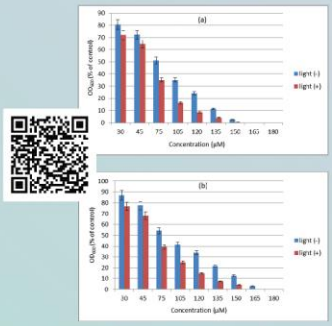
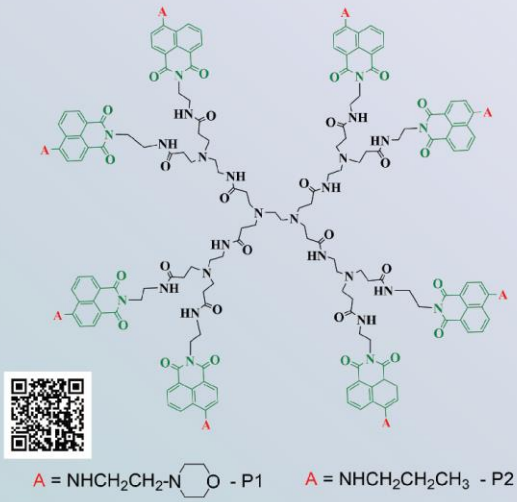
Резюме:
Този труд описва антимикробната и антитуморна активност на два фотоактивни PAMAM дендримера модифицирина с 1,8-нафталимиди(фигура 1 А и В). Изследваните структури абсорбират във видимия спектър и емитират жълто-зелена флуоресценция беше доказано, че тяхната антимикробна активност се увеличава повече от два пъти при облъчване с дневна светлина, което индикира възможността за интегрирането им като вещества за фотодинамична антибактериална терапия. Антибактериалната им активност се запазва след олагането им върху памучен плат. В случая деактивирането на бактериите се дължи на получаващия се синглетен кислород от фотоактивните дендримери. Неговото получаване е изследвано чрез фото-оксидация на KI до I^{3-} под UV светлина. Ефектът на дендримерите върху MDA-MB-231 туморни клетки също е изследван ин-витро Доказано бе, че заместителят на позиция С-4 от 1,8-нафталимидната структура има решаващо значение за биологичната активностна дендримера.



Фигура 1. Микрография на памучен плат необагрен (Control) и обагрен с дендримери P1 и P2 при облъчване с UV Светлина и слънчева светлина

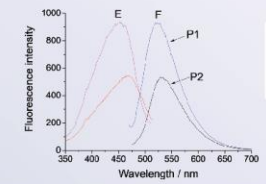


Фигура 3 Разтеж (изразен чрез OD600) на щам P. aeruginosa при различни концентрации на веществата при облъчване със светлина и на тъмно. (a) P1, (b) P2.



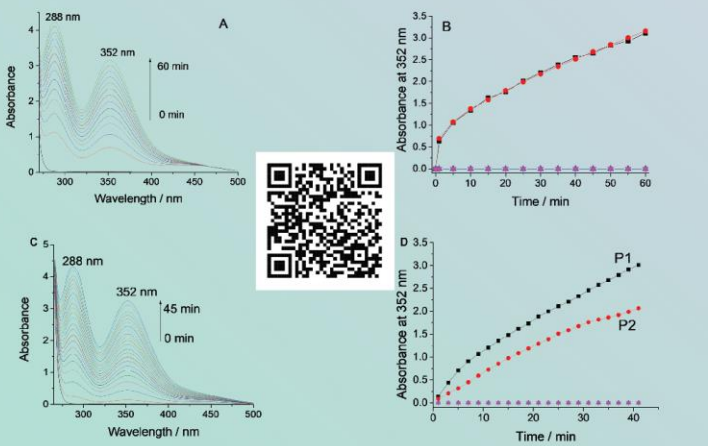
A = $NHCH_2CH_2$-N O - P1 A = $NHCH_2CH_2CH_3$ - P2

Схема 1. Структура на PAMAM дендримерите модифицирание с 1,8- нафталимидите P1 и P2

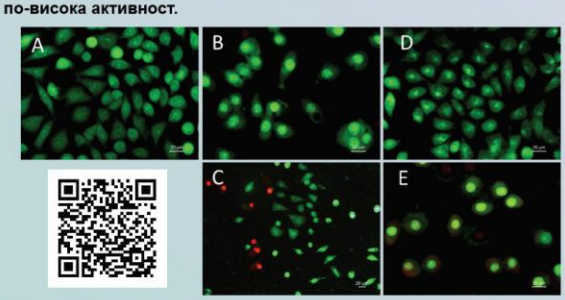


Фигура 2. спектър на възбуждане (E) и флуоресценция (F) на памучен плат обагрен с дендримери P1 аи P2

Изследвани са цветовите характеристики на два фотоактивни дендримера PAMAM, модифицирани с 1,8-нафталимиди и на памучни тъкани, обагрени с тях. Установено е, че боядисаните памучни тъкани имат блестящо жълт цвят, което се дължи на жълто-зелената флуоресценция, излъчвана от дендримерите. Антимикробната и противотуморната активност на фотоактивните дендримери PAMAM е изследвана in vitro. Антибактериалната активност на дендримерите е тествана срещу грам-отрицателни бактерии P. aeruginosa чрез теста за разреждане. Тестовете се извършват на тъмно и след облъчване с видима светлина. Получените резултати показват, че дендримерите имат двойно по-висока активност след облъчване с дневна светлина. Установено е също, че след отлагането на дендримерите върху памучната тъкан неговата хидрофилност намалява значително, което инхибира отлагането на бактерии на повърхността му. По-добрата антибактериална активност при светлинно облъчване се дължи на генерирането на синглетен кислород, който атакува клетъчната мембрана на бактериалните клетки. Образуването на синглетен кислород е изследвано чрез йодометричния метод, при който I- се трансформира в I_3^-, който абсорбира при 288nm и 352 nm. И двата дендримера проявяват много добра цитотоксичност спрямо човешки тройно отрицателни клетки на рак на гърдата (клетъчна линия MDA-MB-231). В този случай дендримерът P1 проявява по-висока активност.



Фигура 4. Абсорбционен спектър на 0.5M KI фотооксидиран до I_3^- в присъствието на дендример P1 като функция от времетона облъчване (A); Зависимост на абсорбцията при 352 nm, отговаряща на I_3^- получен в резултат на присъствието на P1 и P2 (B). Абсорбционен спектър на 0.5M KI фотооксидиран до I_3^- в присъствието на 1см2 памучен плат обагрен с P1 като функция от времето на облъчване (C); Зависимост на абсорбцията при 352 nm, отговаряща на I_3^- получен в резултат на присъствието на 1см2 памучен плат обагрен P1 и P2 (D).



Фигура 5 Човешки тройно отрицателни клетки на рак на гърдата (клетъчна линия MDA-MB-231) - среда: контрола (A); третирани с: 7.5 ⊠M от P1 за 48 ч.; (B); с 7.5 μM от P2 (C); 30 μM от P1 (D) и с 30 μM от P2 (E). Двойно оцветяване с акридин оранж и пропидиев йодид.

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