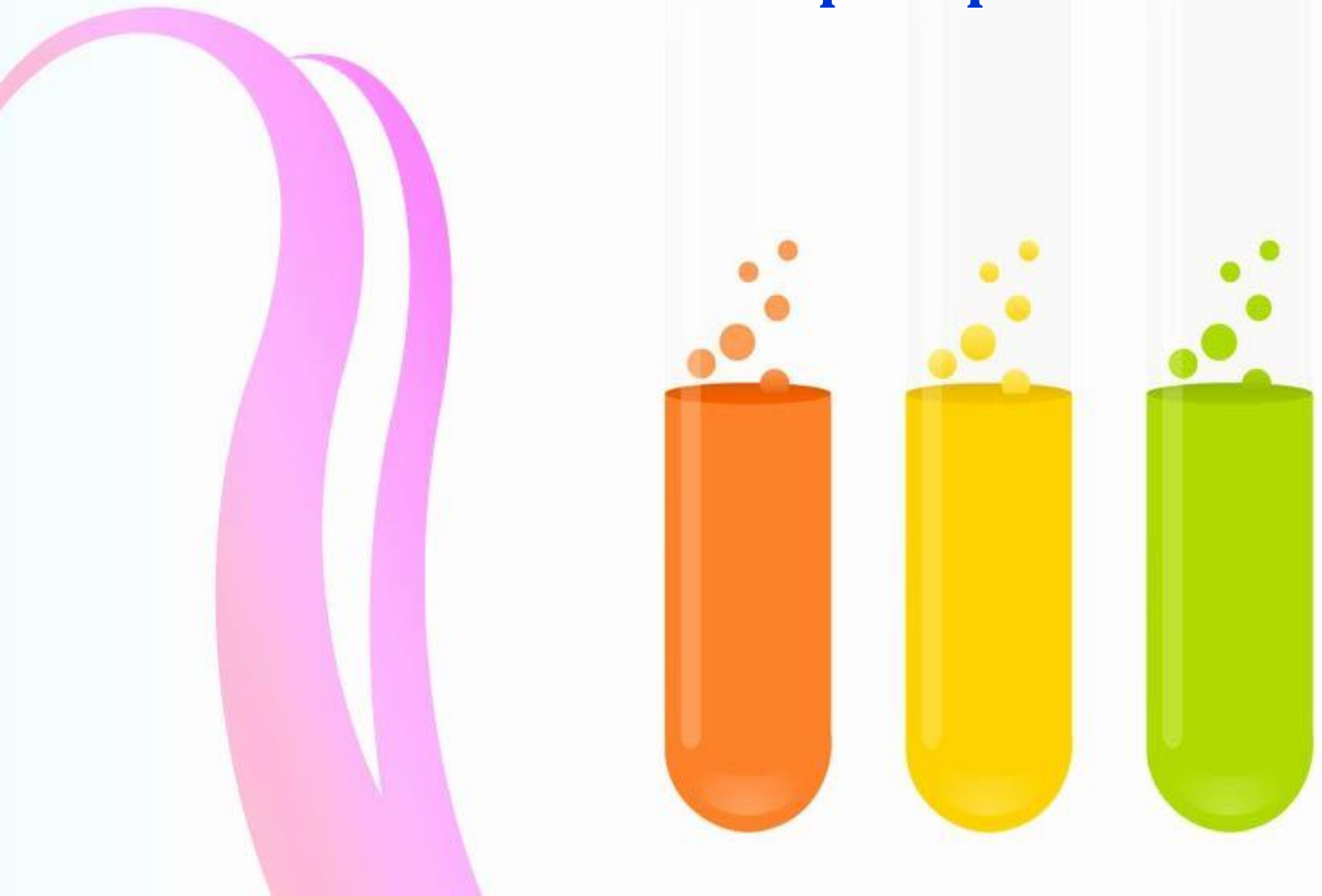
ИНСТИТУТ по ПОЛИМЕРИ
БЪЛГАРСКА АКАДЕМИЯ НА НАУКИТЕ

ТРИНАДЕСЕТА НАУЧНА СЕСИЯ „МЛАДИТЕ УЧЕНИ В СВЕТА НА ПОЛИМЕРИТЕ“

2 юни 2022 г. гр. София



Програма на научната сесия

10:30 ч. – 10:40 ч. ***Откриване***

Доклади

10:40 ч. – 11:00 ч. ***Кверцетин-съдържащи влакнести материали: получаване и биологична активност, Николета Стоянова, Мария Спасова, Невенка Манолова, Илия Рашков, Ани Георгиева, Ренета Тошкова***

11:00 ч. – 11:20 ч. ***Synthesis of polymer-nonphospholipid conjugates for surface modification of niosomes, Erik Dimitrov, Natalia Toncheva-Moncheva, Pavel Bakardzhiev, Rumena Stancheva, Denitsa Momekova, Aleksander Forys, Barbara Trzebicka, Stanislav Rangelov***

11:20 ч. – 11:40 ч. ***Получаване на нови композитни влакна тип „сърцевина-обвивка“ от полиетиленоксид и пчелен восък чрез електроовлакняване, Селин Кючюк, Диляна Панева, Даниела Карашанова, Надя Маркова, Ани Георгиева, Ренета Тошкова, Невена Манолова, Илия Рашков***

11:40 ч. – 12:00 ч. ***Полимерни композити с придадена противогъбична активност спрямо phaeomoniella chlamydospora и phaeoacremonium aleophilum, Наско Начев, Мария Спасова, Невенка Манолова, Илия Рашков, Младен Найденов***

12:00 ч. – 13:30 ч. ***Почивка***

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

15:30 ч. – 15:50 ч. ***Награждаване на отличени доклади и постери***

15:50 ч. – 16:00 ч. ***Закриване***

СПИСЪК НА УЧАСТНИЦИТЕ

Доклади

Доклад № 1

"Кверцетин-съдържащи влакнести материали: получаване и биологична активност"

Николета Стоянова[1], Мария Спасова[1], Невенка Манолова[1], Илия Рашков[1], Ани Георгиева[2], Ренета Тошкова[2]

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Доклад № 2

"Synthesis of polymer-nonphospholipid conjugates for surface modification of niosomes"

Erik Dimitrov[1], Natalia Toncheva-Moncheva[1], Pavel Bakardzhiev[1], Rumena Stancheva[1], Denitsa Momekova[2], Aleksander Forys[3], Barbara Trzebicka[3], Stanislav Rangelov[1]

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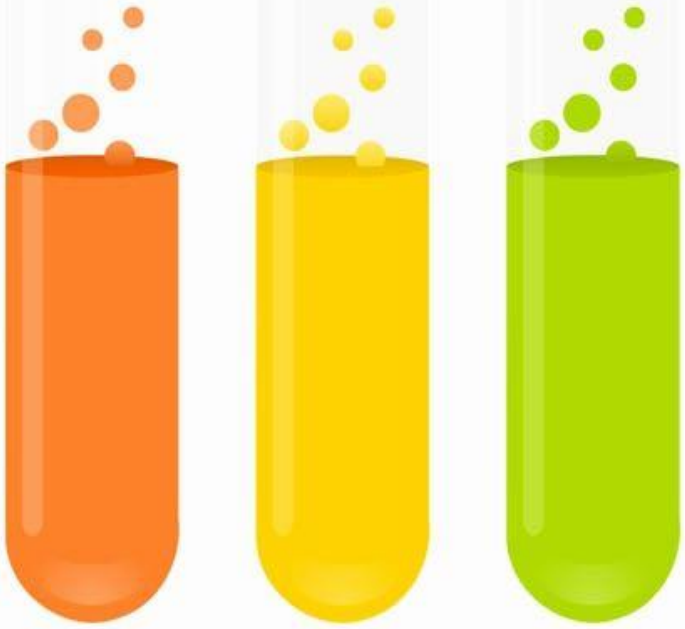

Доклад 3

"Получаване на нови композитни влакна тип „сърцевина-обвивка" от полиетиленоксид и пчелен восък чрез електроовлакняване"

Селин Кючюк,[1] Диляна Панева,[1] Даниела Карашанова,[2] Надя Маркова,[3] Ани Георгиева,[4] Ренета Тошкова,[4] Невена Манолова,[1] Илия Рашков[1]

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Доклад 4

"Полимерни композити с придадена противогъбична активност спрямо phaeomoniella chlamydospora и phaeoacremonium aleophilum"

Наско Начев[1], Мария Спасова[1], Невенка Манолова[1], Илия Рашков[1], Младен Найденов[2]

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Постери

Постер № 1

“Наногелове от природни продукти за доставяне на противотуморни вещества”

К. Каменова[1], С. Симеонов[2], Л. Радева[3], К. Йончева[3], П.Петров[1]

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Постер № 2

“Ciprofloxacin-loaded mixed polymeric micelles: Effects of micellar concentration on bacterial biofilm detachment “

Ts. Damyanova[1], R. Stancheva[2], I. Zhivkova[3], P.D. Dimitrova[1], Ts. Paunova-Krasteva[1], E. Haladjova[2]

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[3]Faculty of Biology, Sofia University “St. Kliment Ohridski”

Постер № 3

“Novel biocompatible anti-biofilm agents based on mixed polymeric micelles”

R. Stancheva,[1] E. Haladjova,[1] Ts. Paunova-Krasteva,[2] P. Dimitrova,[2] T. Damyanova,[2] T. Topouzova-Hristova,[3] S. Stoitsova,[2] P. Petrov[1]

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Постер № 4

"Fibrous composites based on PLA/PVP/Hydrozincite - antibacterial and photocatalytic efficiency"

Silvia Dimova[1], Katerina Zaharieva[2], Venelin Hubenov[3], Iva Varbacheva[3], Georgy Grancharov[1], Filip Ublekov[1], Hristo Penchev[1], Maria Shipochka[4], Ognian Dimitrov[5], Irina Stambolova[4]

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Постер № 5

"Получаване на pH-чувствителни хидрогелове на основата на природни продукти"

Стилияна Стоянова[1], К. Каменова[1], С. Симеонов[2], П.Петров[1]

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Постер № 6

"Multicomponent hydrophilic polymer networks as potential dexamethasone delivery platforms"

Mariela Alexandrova[1], Dilyana Georgieva[2], Sijka Ivanova[1], Bistra Kostova[2], Darinka Christova[1]

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[2]Department of Pharmaceutical Technology and Biopharmacy, Faculty of Pharmacy, Medical University of Sofia

Постер № 7

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

Siyka Stoilova [1,2], Yavor Danov [1], Bistra Kostova[2], Petar Petrov [1]

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Постер № 8

"Получаване на фосфорсъдържащи полимерни добавки на основа рециклиран ПЕТ"

Симона Захова, Ивелина Цачева, Кольо Троев, Виолета Митова

Институт по полимери - Българска академия на науките, ул. Академик Георги Бончев бл. 103, София

Постер № 9

"Enhanced adsorption capacity of modified MCM-48 and SBA-15 silicas"

Oyundari Tumurbaatar[1], Hristina Lazarova[1], Margarita Popova[1], Violeta Mitova[2] and Neli Koseva[2]

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Постер № 10

"Hybrid porous silica – biopolymer carriers for target delivery of Curcumin"

Ivalina Trendafilova[1], Denitsa Momekova[2] , Hristina Lazarova[1], Neli Koseva[3], Margarita Popova[1]

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Постер № 11

"Synthesis of grafting agents for modification of egg shell membrane"

Antonia Bakalova, Desislava Dineva, Yana Petrova, Zornica Todorova

Institute of Polymers, Bulgarian Academy of Sciences, Acad. G. Bonchev St., bl. 103A, 1113 Sofia, Bulgaria

Постер № 12

"Silica nanoparticles derived from agrarian wastes"

Ioanna Veleva[1], Oyundari Tumurbaatar[2], Hristina Lazarova[2], Margarita Popova[2], Violeta Mitova[1] and Neli Koseva[1]

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Постер № 13

"Solid lipid nanoparticles as vehicles for quinine delivery- synthesis and characterization"

Stephaniya Gaydarova[2], Denitsa Nikolova[1], Christo Tzachev[2], Konstans Ruseva[1], Elena Vasileva[1]

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Постер № 14

"Novel hybrid materials obtained via polymer-controlled calcium phosphate formation"

Konstans Ruseva [1], Marin Simeonov [1], Elena Dyulgerova[2], Pavletta Shestakova[3], Elena Vassileva[1]

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Постер № 15

"Контролирана промяна на формата на двуслоен полимерен хидрогел посредством външни стимули"

Николай Петров , Констанс Русева, Елена Василева

Факултет по химия и фармация към СУ "св. Климент Охридски"

Постер № 16

"Нови електроовлакнени материали от полимлечна киселина и производно на хитозана и 8-хидроксихинолина: Получаване, охарактеризиране и противотуморна активност"

И. Анастасова[1], М. Игнатова[1], И. Рашков[1], Н. Манолова[1], А. Георгиева[2], Р. Тошкова[2]

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Постер № 17

"Non-phospholipid conjugate of poly(2-isopropyl-2-oxazoline) for design of surfactant vesicles"

Enis Hasan[1,2], Erik Dimitrov[1], Natalia Toncheva-Moncheva[1], Stanislav Rangelov[1]

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ДОКЛАДИ

Доклад 1

КВЕРЦЕТИН-СЪДЪРЖАЩИ ВЛАКНЕСТИ МАТЕРИАЛИ: ПОЛУЧАВАНЕ И БИОЛОГИЧНА АКТИВНОСТ

Николета Стоянова[1], Мария Спасова[1], Невенка Манолова[1], Илия Рашков[1], Ани Георгиева[2], Ренета Тошкова[2]

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Кверцетинът (QUE) е флавоноид, който се съдържа в големи количества в различни видове плодове и зеленчуци. Това биологично активно съединение притежава забележителни антиоксидантни, противовъзпалителни, антибактериални и противотуморни свойства. Бионаличността на това съединение може да се увеличи чрез неговата аморфизация. Един обещаващ подход за преодоляване на това ограничение е включването му в подходящи микро- и нановлакнести полимерни носители, получени чрез електроовлакняване.

Получени бяха нови нановлакнести материали, съдържащи целулозен ацетат (CA) и полиетилен гликол (PEG), натоварени с природното биологично активно съединение – кверцетин, както и беше оценена биологичната им активност[1]. Получените нови материали бяха охарактеризирани чрез сканираща електронна микроскопия, ИЧ-спектроскопия, рентгеноструктурен анализ, определяне на контактния ъгъл на омокряне спрямо вода, диференциална сканираща калориметрия и UV-VIS спектроскопия. Влакнестият CA/PEG/QUE материал прояви висока антиоксидантна и цитотоксична активност спрямо две ракови клетъчни линии. Получените резултати разкриват кверцетин-съдържащите материали като обещаващи кандидати за биомедицински и фармацевтични приложения.

Ключови думи: *целулозен ацетат, кверцетин, електроовлакняване, антиоксидантни и противотуморни свойства;*

Благодарности: *Авторите изказват своята благодарност на МОН за финансовата подкрепа по Националната научна програма „Иновативни нискотоксични биологично активни средства за прецизна медицина (БиоАктивМед)“, одобрена с РМС №658 от 14.09.2018 г., договор ДО1-217/30.11.2018 и споразумения ДО1-323/18.12.2019, ДО1-358/17.12.2020 и ДО1-278/03.12.2021.*

[1] Nikoleta Stoyanova, Mariya Spasova, Nevena Manolova, Iliya Rashkov, Ani Georgieva, Reneta Toshkova; *Antioxidants*. 2020, 9 (232), 1-16.

Доклад 2

SYNTHESIS OF POLYMER NONPHOSPHOLIPID CONJUGATES FOR SURFACE MODIFICATION OF NIOSOMES

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Recently one of the fastest growing areas in the modern pharmaceutical science and technology is targeted drug delivery. The practical realization of this concept is possible thanks to recent advances in nanotechnology. In the field of nanoscale drug carriers, niosomes attract increasing scientific interest as a novel drug delivery system and offer several advantages as vesicles for drug encapsulation, codelivery of lipophilic/water insoluble and hydrophilic compounds, biocompatibility, low-immunogenicity, stability (physical, chemical and osmotic) and controlled release and targeting properties. In general, niosomes are composed of nonionic surfactants and cholesterol. The amphiphilic properties of surfactant molecules enable them to form bilayer structures by self-assembly in aqueous media. By adding appropriately designed polymers, niosomes membranes can be modified. This strategy offers many possibilities for fabricating highly effective carriers which, in addition, can release the incorporated drugs in a controlled manner. In this regard, non-phospholipid conjugates of poly(2-isopropyl-2-oxazoline) or polyglycidol were synthesized and characterized in detail using “click” chemistry reactions. Novel noisome formulations using various surfactants and the polymer amphiphiles were prepared and characterized in terms of size, size distribution, and morphology.

Keywords: click chemistry, niosomes, polycaprolactone, polyglycidol

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Доклад 3

ПОЛУЧАВАНЕ НА НОВИ КОМПОЗИТНИ ВЛАКНА ТИП „СЪРЦЕВИНА-ОБВИВКА“ ОТ ПОЛИЕТИЛЕНОКСИД И ПЧЕЛЕН ВОСЪК ЧРЕЗ ЕЛЕКТРООВЛАКНЯВАНЕ

Селин Кючюк,[1] Диляна Панева,[1] Даниела Карашанова,[2] Надя Маркова,[3] Ани Георгиева,[4] Ренета Тошкова,[4] Невена Манолова,[1] Илия Рашков[1]

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Разработен е оригинален подход за получаване на композитни влакна със структура „сърцевина-обвивка“, от полиетиленоксид/пчелен восък чрез електрооовлакняване, като сърцевината е изградена от полиетиленоксид (PEO), а обвивката - от пчелен восък (BW) [1]. Този тип влакна бяха получени без използване на устройство за коаксиално електрооовлакняване. Получаването им беше отдадено на самоорганизиране на BW на повърхността на влакната в процеса на електрооовлакняване. Структурата на влакната беше доказана чрез рентгенова фотоелектронна спектроскопия, сканираща и трансмисионна електронна микроскопия. Включването на 5-нитро-8-хидроксихинолин като моделно лекарствено вещество във влакната позволи получаването на влакнести материали с антимикробна и противоракова активност и с добра съвместимост с нормални човешки клетки. Тези предимства на новите материали ги правят перспективни като носители на лекарствени вещества с потенциал за биомедицинско приложение.

[1] Kyuchyuk S., Paneva D., Karashanova D., Markova N., Georgieva A., Toshkova R., Manolova N., Rashkov I. *Macromolecular Bioscience* First published: 22 April **2022**; https://doi.org/10.1002/mabi.202200015.

Ключови думи:
пчелен восък; полиетиленоксид; самоорагнизация;сърцевина-обвивка; електрооовлакняване; антимикробна активност; противоракова активност

Благодарности:
Авторите изказват благодарността си на Фонд „Научни изследвания“ (Договор КР-06-N39/13/2019) за финансовата подкрепа. В тези изследвания е използвано оборудване на Разпределената научна инфраструктура ИНФРАМАТ, част от Националната пътна карта на България за научна инфраструктура, подкрепена финансово от Министерство на образованието и науката.

Доклад 4

ПОЛИМЕРНИ КОМПОЗИТИ С ПРИДАДЕНА ПРОТИВОГЪБИЧНА АКТИВНОСТ СПРЯМО *PHAEOMONIELLA CHLAMYDOSPORA* И *PHAEOACREMONIUM ALEOPHILUM*

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Болестите по лозовите насаждения намаляват продължителността на живот на лозята и увеличават разходите за производство на грозде и вино. Те се причиняват главно от гъбични патогени като *Phaeomoniella chlamydospora*, *Phaeoacremonium aleophilum* и др. Една от най-разпространените болести по лозята е еска. Симптомите на заболяването се проявяват в тежки или хронични форми, които могат да засегнат цялото растение или отделни части от него. Към момента няма лечебни подходи за борба с това заболяване, а се прилагат само превантивни методи.

Получени бяха влакнести композитни материали от биоразградим полиестер и фунгициди – производни на 8-хидроксихинолина с придадена противогъбична активност срещу *P. chlamydospora* и *P. aleophilum* [1]. Получените биоматериали бяха охарактеризирани чрез сканираща електронна микроскопия, инфрачервена спектроскопия, рентгеноструктурен анализ, определяне на контактния ъгъл на омокряне спрямо вода, UV-VIS спектроскопия и физико-механични изпитания. Включването на 8-хидроксихинолиновите производни във влакнестите материали води до инхибиране на растежа на гъбите. Получените материали са перспективни кандидати за защита на лозята от проникване и растеж на гъбни патогени.

Ключови думи: *композитен биоматериал, противогъбична активност, защита на лозя, еска;*

Благодарности: *Авторите изказват своята благодарност на Фонд „Научни изследвания“ (договор КП-06-ОПР 03/2) за финансовата подкрепа.*

[1] Nasko Nachev, Mariya Spasova, Petya Tsekova, Nevena Manolova, Iliya Rashkov and Mladen Naydenov, Electrospun Polymer-Fungicide Nanocomposites for Grapevine Protection, *Polymers* 2021, 13, 3673, 1-14.

Постери

Постер 1

НАНОГЕЛОВЕ ОТ ПРИРОДНИ ПРОДУКТИ ЗА ДОСТАВЯНЕ НА ПРОТИВОТУМОРНИ ВЕЩЕСТВА

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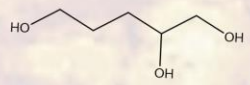
Въведение

Наногеловете са наночастици, образувани от физически или химически омрежени триизмерни полимерни мрежи с размери обикновено между 10 и 200 nm. Поради тяхната много ниска токсичност, биосъвместимост, биоразградимост, стабилна структура, голяма специфична повърхност и висок капацитет на натоварване, те придобиват все по-голямо значение като системи за доставяне на лекарствени вещества. Наногеловете могат да бъдат проектирани така, че да реагират на определени стимули (напр. промени в йонната сила, pH и температура), което е от съществено значение за съвременната наномедицина.

Цел: Целта на настоящата работа е да се синтезира и охарактеризира pH-чувствителен биоразградим наногел от пентан-1,2,5-триол и лимонена киселина като потенциална наноразмерна платформа за доставяне на лекарствени вещества.

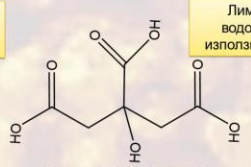
Синтез на наногел

Пентан-1,2,5-триол (PT) е алкохол, който се получава като страничен продукт при преработката на лигноцелулоза.



Пентан-1,2,5-триол

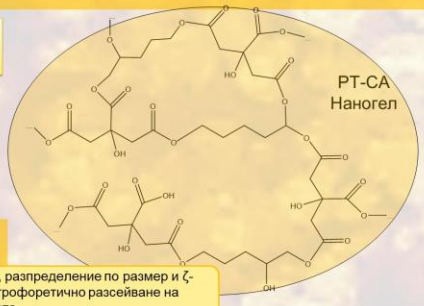
Лимонената киселина (CA) е нетоксично, водоразтворимо вещество, което често се използва за омрежване на целулозни деривати.



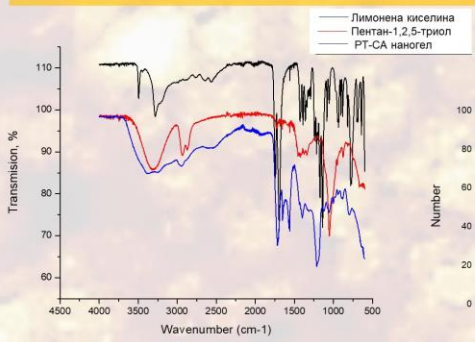
Лимонена киселина

EDC, DMAP

THF, 25°C, 72 ч

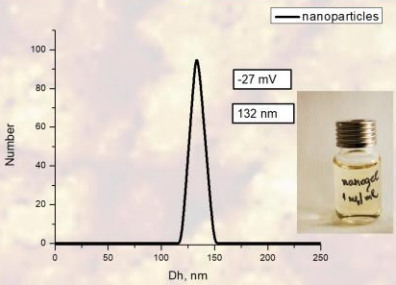


Охарактеризиране на PT-CA наногел

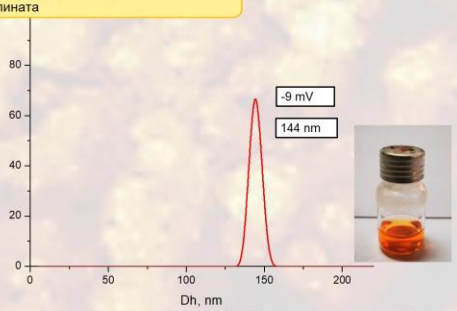


ИЧ на лимонена киселина (черен цвят), пентан-1,2,5-триол (червен цвят) и PT-CA наногел (син цвят)

Определяне на размер на частиците, разпределение по размер и ζ-потенциал чрез динамично и електрофоретично разсейване на светлината



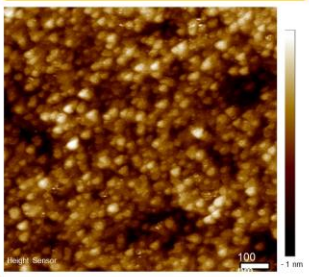
Разпределение по размер на PT-CA наногел

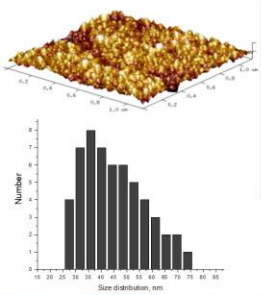


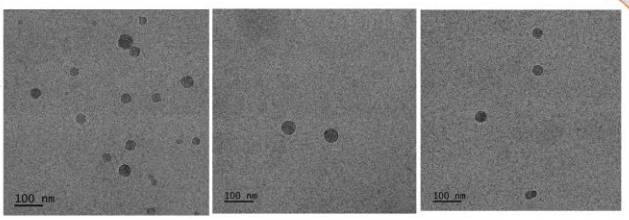
Разпределение по размер на PT-CA наногел натоварен с Dox

Атомно силова (АСМ) микроскопия и криогенна трансмисионна електронна микроскопия (крио-ТЕМ)

Морфология на частиците



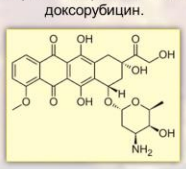


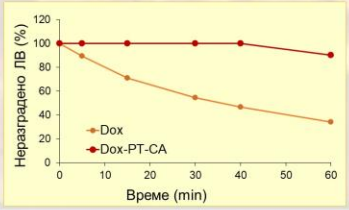


АФМ и крио-ТЕМ микрографиите показват само сферични частици с размери 15-70 nm.

Натоварване на наногела с лекарствено вещество

Като моделно лекарствено вещество в настоящото проучване бе подбран противотуморният антрациклинов антибиотик доксорубицин.





Стабилност на енкапсулиран в PT-CA наногел доксорубицин

Стабилността на свободен (Dox) и включен в наногел доксорубицин (Dox-PT-CA) бе проследена след UV-индуцирано светлинно облъчване. Резултатите показаха значително разграждане на доксорубицин в референтен разтвор и запазване на веществото при включването му в наногел.

Заключение

Успешно беше получен нов pH-чувствителен наногел чрез естерификация на пентан-1,2,5-триол с лимонена киселина. DLS измерванията показват, че получените наночастици имат хидродинамичен диаметър 132 nm и отрицателен зета-потенциал -27 mV. АФМ и крио-ТЕМ анализът потвърдиха, че геловете имат сферична форма и наноразмери. Наногелните частици бяха успешно натоварени с доксорубицин (Dox), което води до стабилизиране на веществото при светлинна експозиция.

Благодарности: *Тази работа беше финансово подкрепена от Фонд научни изследвания (Договор КП-06-ОПР 01/2).*

Постер 2

Ciprofloxacin-loaded mixed polymeric micelles: Effects of micellar concentration on bacterial biofilm detachment

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[1]The Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences
[2]Institute of Polymers, Bulgarian Academy of Sciences
[3]Faculty of Biology, Sofia University "St Kliment Ohridski"

INTRODUCTION

Biofilms are consortia of adherent microorganisms embedded in extracellular polymeric substances (EPS). EPS protects biofilm bacteria from environmental hazards including the access of antibacterial substances. The structural and functional characteristics of biofilms determine the high drug tolerance of biofilm infections. The evidence for the role of biofilms in chronic, persistent and recurrent infections puts forward the necessitate the development novel drug-delivery systems capable to overcome the EPS barrier. Such systems have to be both effective and biocompatible.

Polymeric micelles based on poly(2-(dimethylamino)ethyl methacry-late)-b-poly(ε-caprolactone)-b-poly(2-(dimethylamino)ethyl methacrylate) and poly(ethylene oxide)–b-poly(propylene oxide)–b-poly(ethylene oxide) triblock copolymers were used. Five micellar compositions differing by molar ratio have been prepared and were used empty or loaded with ciprofloxacin. Our previous data have shown that, applied as 1 mg/ml, the micelles show some not neglectable cytotoxicity.

In order to reduce this, the **Aim** of the present poster is to examine the exfoliating activity of the micelles at lower concentrations - 0,5 mg/ml, 0,25mg/ml and 0,125mg/ml.

MATERIALS AND METHODS

- **Preparation of polymer micelles**

  Polymeric micelles were formed by dropwise addition of initial or mixed copolymer organic solution to aqueous media followed by dialysis against water. Three different molar ratios (3/1, 1/1 and 1/3) were used. The concentration of micellar dispersions varies in range 0,125 to 1 mg/ml.

- **Loading of Ciprofloxacin**

  Ciprofloxacin was loaded into polymeric micelles as 10/1 polymer to drug weight ratio was used. The encapsulation efficiency (EE) and drug loading content (DLC) were determined and were above 98% and 10% respectively.

- **Bacterial strain and cultivation**

  Model microbial strains *E. coli* 25922 (ATCC) and *S. aureus* 29213 (ATCC) were used for the experiments. The pure culture was stored frozen at -80 °C in TSB medium containing 8% DMSO. For the biofilm experiments, strains were sub-cultured in Tryptic Soy Broth (TSB) overnight, to early stationary phase, at 37 °C and transferred to slant Tryptic Soy Agar (TSA). Prior to each experiment, 18-h TSB cultures were grown at 37 °C, as a source of inoculum.

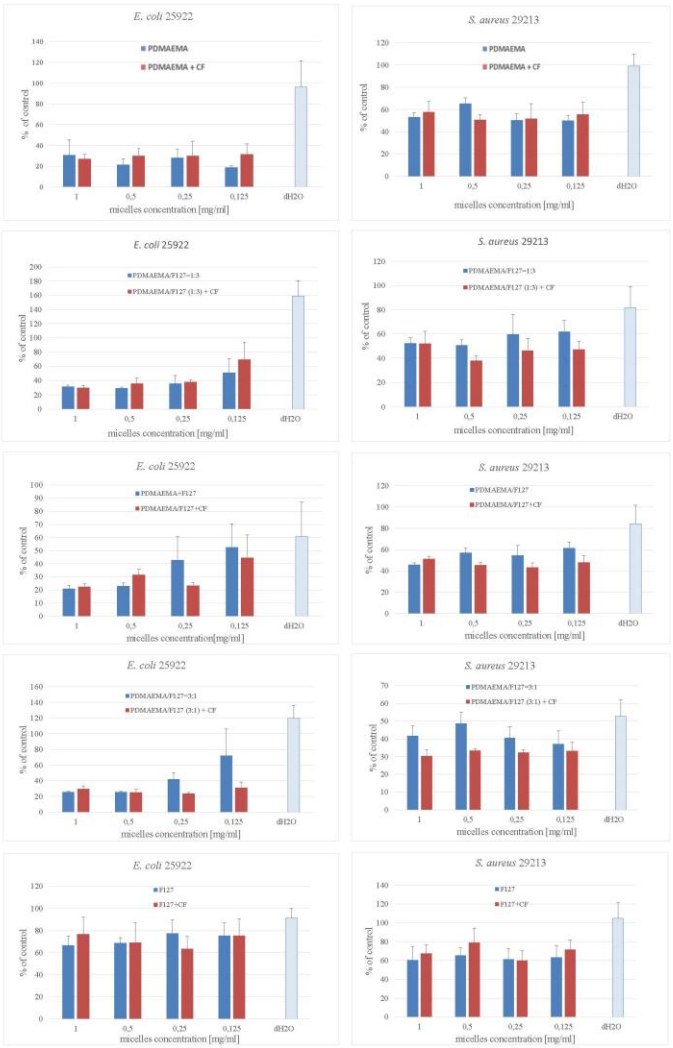
- **Biofilm formation.**

  M63 minimal salt medium was used for the experiments. 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. The plates were cultivated for 24h at 37°C at static conditions. The non-adherent bacteria were removed with PBS and the wells were washed in 3 changes of PBS. 150µl of micelles solutions at concentrations of 1 mg/ml, 0.5 mg/ml, 0.25 mg/ml and 0.125 mg/ml were added to the wells. A control for the activity of the solvent without micelles was included, with sterile deionized H_2O. To estimate the amount of mature biofilm prior to the treatments, a "0 h" control was performed as well. The plates were incubated for 4h at 37°C. After the incubation micelles solutions were removed, the wells were washed with PBS 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. The absorbance of the solubilized dye was measured at 570nm. The results were calculated as % of the "0 h" control.

Strain	Micelles	Biofilm destruction efficiency (%)			
		1 mg/ml	0.5 mg/ml	0.25 mg/ml	0.125 mg/ml
***E.coli* 25922**		No loaded micelles			
	PDMAEMA	69,1 ± 14,7	78,5 ± 5,9	72,1 ± 8,9	81,3 ± 1,8
	P:F 1:3	68,4 ± 1,8	70,4 ± 1,7	64,4±11,2	48,9 ± 20,1
	P:F 1:1	79 ± 2,7	76,9 ± 2,2	57,1±17,7	47,5 ± 18
	P:F 3:1	74,5 ± 1	74,6 ± 1	58,2 ± 8,4	27,7 ± 33
	F127	33,5 ±8,4	31,4 ± 4,9	22,5±12,3	24,6 ± 11,6
		Micelles loaded with ciprofloxacin			
	PDMAEMA+CF	73 ±4,4	70,2 ± 7,3	70 ± 14,1	68,4 ± 10
	(P:F 1:3) +CF	69,9 ± 2,5	64,4 ± 7,8	62,4 ± 3	30,7 ± 25
	(P:F 1:1)+CF	77,6 ± 2,4	68,6 ± 4,7	76,8 ± 2,4	55,6 ± 17,5
	(P:F 3:1)+CF	70,5 ± 3,8	75,1 ± 4,2	76,4 ± 1,6	68,8 ± 7,2
	F127+CF	23,4 ±15,3	31 ± 18,3	36,7±11,2	24,8 ± 15
***S. aureus* 29213**		No loaded micelles			
	PDMAEMA	47 ± 4,1	34,5 ± 5	49,6 ± 5,8	50 ± 4,9
	P:F 1:3	47,6 ± 4,8	49,5 ± 4,6	40,3±16,7	38,2 ± 9,5
	P:F 1:1	54,3 ± 2	43 ± 4,4	45,5 ± 9,3	38,5 ± 6
	P:F 3:1	58,3 ± 5,7	51,3 ± 6,4	59,5 ± 6,4	62,8 ± 7,3
	F127	39,4 ± 14,3	34,7 ± 8,3	38,7±11,7	36,5 ± 12,7
		Micelles loaded with ciprofloxacin			
	PDMAEMA+CF	42,3 ± 9,7	49,4 ± 5,2	48,2±13,6	44,6 ± 11,4
	(P:F 1:3) +CF	48,2 ± 10,5	62 ± 4	53,7±10,1	52,8 ± 6,6
	(P:F 1:1)+CF	48,8 ± 2,4	54,3 ± 2,9	56,8 ± 4,5	51,9 ± 6,4
	(P:F 3:1)+CF	69,8 ± 3,7	66,7 ± 1,2	67,8 ± 1,7	66,8 ±4,9
	F127+CF	32,7 ± 9,5	20,9 ± 15,1	39,8±10,5	28,5 ± 10,3

Exfoliating effect of micelles in different concentrations presented as a percentage of removed biofilm in different treatments

RESULTS



Quantity of biofilm presented as a percentage of control after treatment with micelle solutions

CONCLUSION

The results show that mixed micelles prepared at molar ratio 3/1 have stable exfoliating activity within the range of 70% no matter the dilutions.

Acknowledgement: 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).

13th Scientific Session "Young scientists in the polymer world", 2 June 2022, Sofia, Bulgaria

Постер 3

Novel biocompatible anti-biofilm agents based on mixed polymeric micelles

R. Stancheva,[1] E. Haladjova,[1] Ts. Paunova-Krasteva,[2] P. Dimitrova,[2] T. Damyanova,[2] T. Topouzova-Hristova,[3] S. Stoitsova,[2] P. Petrov[1]

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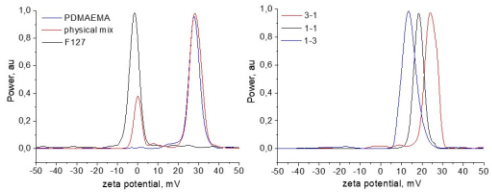
[2]The Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences
[3]Faculty of Biology, Sofia University "St. Kliment Ohridski"

INTRODUCTION

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

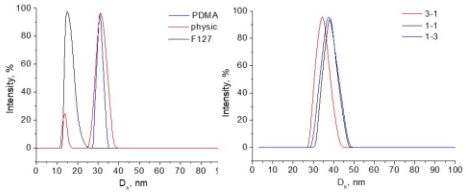
In this work loading of Ciprofloxacin (CF) into polymeric micelles of different composition was investigated. Polymeric micelles were formed from cationic poly(2-(dimethylamino)ethyl methacrylate)-b-poly(ε-caprolactone)-b-poly(2-(dimethylamino)ethyl methacrylate) (noted as PDMAEMA) and non-ionic poly(ethylene oxide)–b-poly(propylene oxide)–b-poly(ethylene oxide) (known as Pluronic F127) triblock copolymers as well as from their mixtures at different molar ratios. The encapsulation efficiency, drug loading content and drug release profile of polymer carriers were determined. A cytotoxicity evaluation of the resulting drug delivery systems was performed. The biomass reduction of pre-formed bacterial biofilms was estimated as well as their metabolic activity.

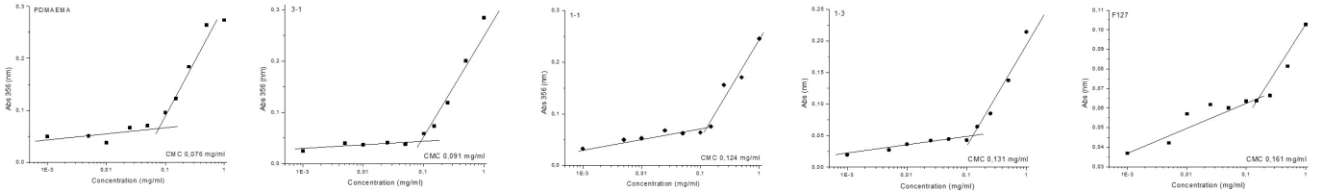
FORMATION OF POLYMER MICELLES



PMs 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.

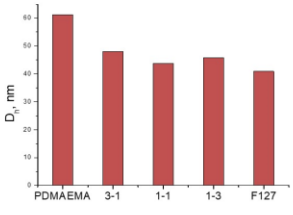
The resulting micelles were composed of mixed PCL/PPO core and mixed PDMAEMA/PEO shell. They were of small size in the range of 16 to 38 nm and ζ-potential dependent on their composition. The CMC were also found to depend on micellar composition.

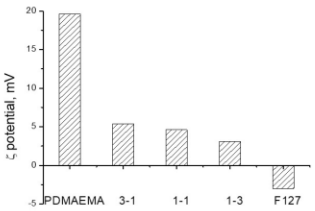




LOADING OF CIPROFLOXACIN

Loading of CF was performed by addition of drug powder to the micellar dispersions in order to obtain 10/1 polymer to drug weight ratio. The dispersions were first sonicated for 1 h at 60 °C for drug solubilisation and then filtered. The size of loaded micelles was hardly influenced while the ζ-potential value was strongly dependent on the micellar composition.



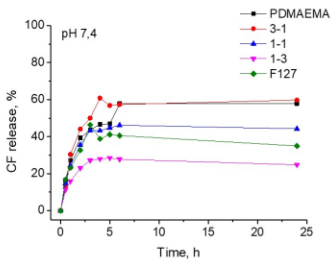


Polymeric micelles	Encapsulation efficiency %		Drug loading content %	
	UV	HPLC	UV	HPLC
PDMAEMA	98,7	98,1	10,4	10,4
3-1	98,9	98,8	10.9	9,8
1-1	99,2	99,2	10,8	10,9
1-3	99,1	99,4	10,3	10,3
F127	98,9	98,6	11,4	11,6

The encapsulation efficiency and drug loading content were determined by HPLC and UV spectrophotometry. Both methods showed high drug loading above 98% for all compositions studied.

RELEASE PROFILE OF CIPROFLOXACIN

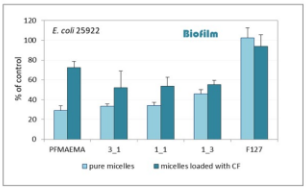
Ciprofloxacin release from the micellar systems was investigated in a phosphate buffer (pH=7.4) at physiological temperature. The amount of released drug was calculated spectrophotometrically by the characteristic absorbance band of CF at 270 nm^{-1}. Delayed profiles were observed for all compositions over the period of 24 h.

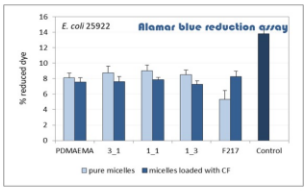


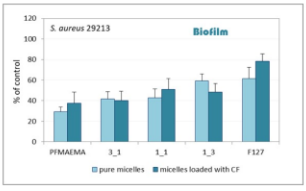
BIOFILM BIOMASS AND METABOLIC ACTIVITY

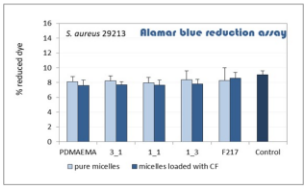
Biofilm biomass reduction was estimated by a crystal violet assay. For evaluation of the metabolic activity of the biofilm bacteria, the redox indicator Alamar blue was used. Two widespread bacterial strains *E. coli* 25922 (ATCC) and *S. aureus* 29213 (ATCC) were selected for these experiments.

All micellar systems were capable to detach pre-formed bacterial biofilms as significantly reduced their biomass 4h after treatment. The metabolic activity of the biofilm was even more strongly suppressed by the CF loaded micelles indicating the successful drug delivery and release.





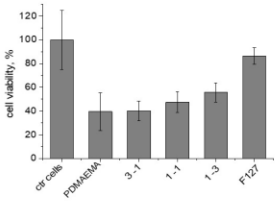


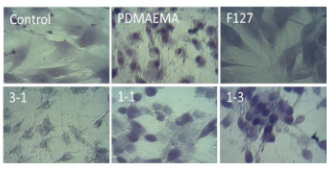


CYTOTOXICITY AND CELL MORPHOLOGY

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. The possible deviations in cell morphology were monitored under light microscope.

A composition depended cell viability was observed. As expected the cytotoxicity decrease with decreasing the PDMAEMA content. No cell destruction or morphological signs of cell death were observed.





CONCLUSIONS

We could conclude that the investigated systems based on mixed polymeric micelles have great potential as effective and biocompatible antibacterial agents for detachment of bacterial biofilms.

ACKNOWLEDGEMENTS

This work was funded by the National Science Fund of Bulgaria, Project № KP-06-H41/8. We would like to thank Chromassist Ltd for performing the HPLC analysis.

Постер 4

БЪЛГАРСКА АКАДЕМИЯ на НАУКИТЕ 1869

XIII НАУЧНА СЕСИЯ "МЛАДИТЕ УЧЕНИ В СВЕТА НА ПОЛИМЕРИТЕ"

Fibrous composites based on PLA/PVP/Hydrozincite - antibacterial and photocatalytic efficiency

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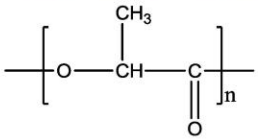
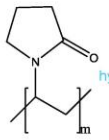
The present study shows the creation of new multifunctional hybrid materials from biodegradable polymers and inorganic materials (hydrozincite). The approach consists in combining methods such as sol gel and emulsion-electrospinning using a minimum number of non-toxic reagents and mild conditions. Two hybrid nanocomposites of polylactide/hydrozincite and poly (lactide)/polyvinylpyrrolidone/hydrozincite were prepared. The hydrozincite exhibits photocatalytic and antibacterial activity and it is therefore a very attractive component for incorporation into new hybrid mat.

Materials and Methods



Poly(L-lactide), PLA

biologically tolerable and biodegradable polymer



Polyvinylpyrrolidone, PVP

hydrophilic polymer with low toxicity and high biocompatibility

$Zn_5(OH)_6CO_3)_2$ hydrozincite

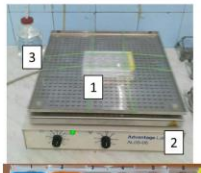
Synthetic mineral compatible with the environment, with antibacterial properties. Used for treatment of wastewater containing reactive dyes by photocatalysis.

The nanocomposite poly (lactide)/hydrozincite fibres is prepared by the following steps:

A. Preparation of a hydrozincite suspension ($Zn_5(OH)_6CO_3)_2$), 1wt% (synthesized by hydrothermal method at 180° C using Mentha Arvensis [D. Stoyanova et al., Appl. Sci. 12 (2022) 1096]) and dichloromethane;

B. A 15 wt% solution of commercial poly (lactide)/Nature Works 4032D/ in dichloromethane was added. After mixing the hydrozincite and PLA, the resulting solution was sonicated for 15 minutes until the suspension became homogeneous. Then a hybrid mats via electrospinning were obtained.

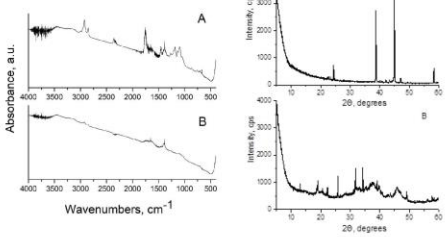
The fibers of poly (lactide)/hydrozincite with copolymer polyvinylpyrrolidone/PVP/ were prepared by emulsion-electrospinning from a mixiture of PLA/Hidrozincite in DCM and PVP dissolved in ethanol.



Samples were prepared using 24 well test plate (1)(Techno Plastic Products AG, Switzerland). It was shake continuously using Advantage-Lab, AL05-06 (2) at 150 rpm. The shaker was kept in thermostatic room at 20 ± 1°C (3-control thermometer immersed in water).

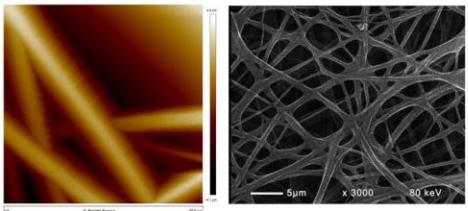
1.Blank – E. coli-K12 suspension
2.Control - E. coli-K12 suspension and aluminum foil
3.Sample - E. coli-K12 suspension and nanofibers applied on aluminum foil

CHARACTERIZATION



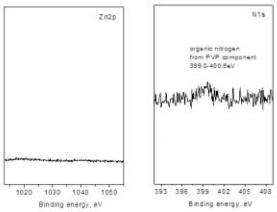
FT-IR spectra of A) PLA/ PVP/Hydrozincite fibers; B) PLA/PVP fibers.

PXRD patterns of A) PLA/ PVP/Hydrozincite fibers and B) PLA.

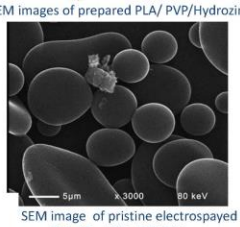


AFM 2-D and SEM images of prepared PLA/ PVP/Hydrozincite fibers.

XPS analysis



Deconvolution of Zn2p and N1s core level spectra of PLA/ PVP/Hydrozincite fibers.



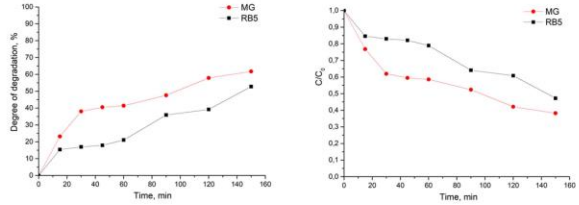
SEM image of pristine electrospayed PLA 15 wt% in DCM f ibers

The surface composition of prepared PLA/ PVP/Hydrozincite fibers established by XPS analyses is presented in Table.

Concentration of the elements on the surface in at. % by XPS.

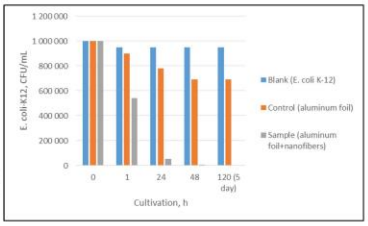
sample	C, at. %	O, at. %	Zn, at. %	Al, at. %	N, at. %
PLA/PVP/Hydrozincite fibers	8.3	85.5	-	5.0	1.2

Photocatalytic tests



The reactions of photocatalytic degradation of, Malachite Green (MG) and Reactive Black 5 (RB5) as model contaminants (5 ppm aqueous solution of dye), using prepared PLA/PVP/Hydrozincite fibers as photocatalyst under UV illumination were studied.

Antibacterial tests



The bacterial concentration of E. Coli (CFU/ml) in the bacterial solution and the same solution put in contact with aluminum foil and with nanofibers applied on aluminum foil as a function of the contact time (1, 24,48 h and 5 days) were estimated.

Conclutions

- The photocatalytic investigations established that prepared PLA/PVP/Hydrozincite fibers shows the highest photocatalytic activity towards degradation of MG in comparison with the other tested dye RB5. After 150 minutes of UV illumination, the tested dyes – MG and RB5 were degraded 62 %; 53 % in the presence of PLA/ PVP/Hydrozincite fibers.
- The results indicate that the antibacterial activity against E. Coli of pure foil is weak and after 5 days of incubation reached about 30 %. The nanofibers exposed clear antibacterial effect and after 24 hours of incubation the cell count were reduced about 94 %.

Постер 5

Получаване на pH-чувствителни хидрогелове на основата на природни продукти

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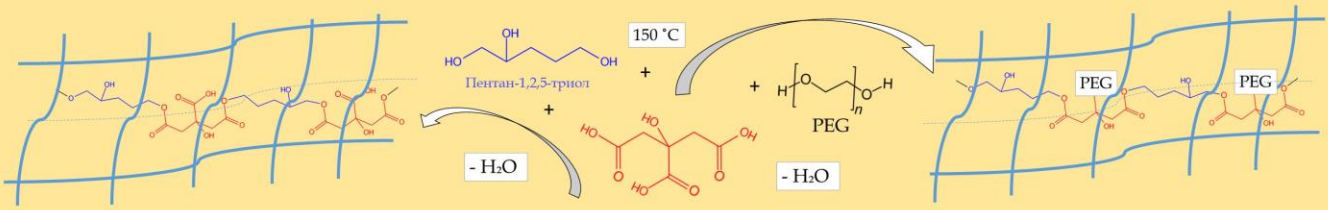
Въведение: Хидрогеловете са меки материали съставени от полимерна мрежа, набъбнала във вода или физиологична течност. Те притежават уникални свойства като биосъвместимост, биоразградимост и ниска токсичност. Хидрогеловете могат да бъдат получени от природни или синтетични полимери чрез химично или физично омрежване. Особен интерес представлява получаването на хидрогелове от възобновяеми ресурси и материали, които реагират на външни стимули, напр. pH, светлина, температура и др., известни също като интелигентни хидрогелове. Те намират все по-голямо приложение в медицината, като системи за доставяне на лекарства, тъканното инженерство и биотехнологиите.

Цел: Целта на настоящето проучване е получаването на pH-чувствителни хидрогелове чрез омрежване на пентан-1,2,5-триол и полиетилен гликол с лимонена киселина.

Синтез на хидрогелове



Хидрогеловете са получени чрез омрежване на пентан-1,2,5 - триол с лимонена киселина. Реакцията на поликондензация беше проведена за 24 часа при температура 150°C, под вакуум в отсъствие на разтворител.

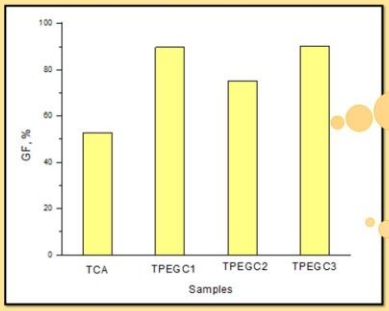
Лимонена киселина

Хидрогеловете са получени чрез омрежване на пентан-1,2,5 - триол и поли(етилен гликол) (Mm=600 g/mol) с лимонена киселина. Реакцията на поликондензация беше проведена за 24 часа при температура 150°C, под вакуум в отсъствие на разтворител.

Изследване на влиянието на съотношението на COOH / OH върху добива на гел фракция

Табл. 1. Добив на гел фракция (GF,%) и степен на набъбване (SD) на получените хидрогелове

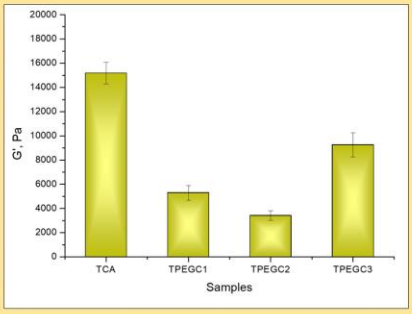
Име на пробата	Молно отношение на функционалните групи
TCA	1:1 Triol : CA
TPEGC1	1:1 OH : COOH
TPEGC2	1,4 : 1 OH : COOH
TPEGC3	1,4 : 1 COOH : OH



Фиг. 1. Добив на гел фракция (GF,%) на получените хидрогелове.

С повишаване на количеството на лимонената киселина се повишава добива на гел фракцията на получените гелове.

Добавянето на ПЕГ към изходните вещества повишава добива на гел фракцията.

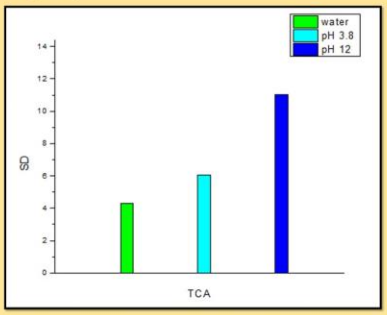


Фиг. 2. Влияние на състава върху модула на еластичност на получените хидрогелове.

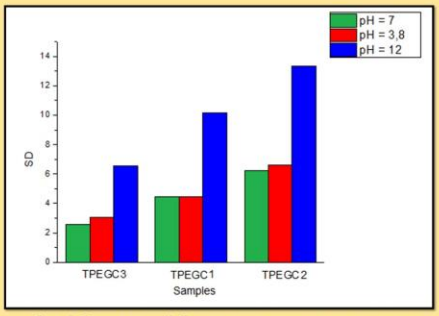
Изследване на pH чувствителността на получените гелове

Табл. 2. Резултати за степента на набъбване(SD) на геловете при различно pH на разтвора

Име на пробата	Молно отношение на функционалните групи	pH = 7	pH = 3,8	pH = 12
		SD	SD	SD
TCA	1:1 Triol : CA	4,31	6,03	11,02
TPEGC1	1:1 OH : COOH	4,47	4,44	10,17
TPEGC2	1,4 : 1 OH : COOH	6,22	6,62	13,36
TPEGC3	1,4 : 1 COOH : OH	2,58	3,04	6,57



Фиг. 3. Степен на набъбване на хидрогел, получен при омрежване на триол с лимонена киселина, без добавяне на PEG към изходните вещества, в буфер с различно pH.



Фиг. 4. Степен на набъбване на хидрогелове, получени при омрежване на триол с лимонена киселина с включен ПЕГ в състава, в буфер с различно pH.

Фиг. 5. Снимка на хидрогел набъбнал в разтвор на натриева основа с pH =12.

Фиг. 6. Снимка на хидрогел набъбнал в ацетатен буфер с pH =3,8.

Най-висока степен на набъбване се наблюдава при повишаване на pH на средата. Степента на набъбване се увеличава с около 2 пъти в сравнение с набъбването при ниско pH (7 и 3.8).

Заключение: Успешно бяха получени хидрогелове на основата на пентан-1,2,5-триол, полиетилен гликол и лимонена киселина чрез поликондензационна реакция. Реакцията е ефективна и добивът на гел фракцията е от 50% до 90%, в зависимост от съотношението на изходните вещества. Включването на ПЕГ в състава на хидрогеловете повиши добива на гел фракция, а най-висок добив беше наблюдаван при повишаване на количеството лимонена киселина.

Благодарности: *Тази работа беше финансово подкрепена от Фонд научни изследвания (Договор КП-06-ОПР 01/2).*

Постер 6

MULTICOMPONENT HYDROPHILIC POLYMER NETWORKS AS POTENTIAL DEXAMETHASONE DELIVERY PLATFORMS

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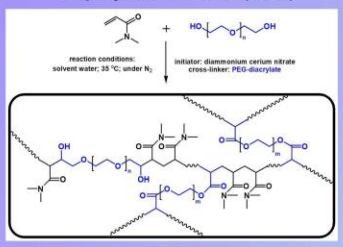
[1]*Institute of Polymers, Bulgarian Academy of Sciences*
[2]*Department of Pharmaceutical Technology and Biopharmacy, Faculty of Pharmacy, Medical University of Sofia*

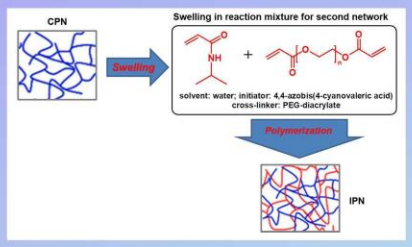
ABSTRACT: Multicomponent polymer networks were developed and investigated as new platforms for dexamethasone sodium phosphate (DSP) delivery. Copolymer network comprising poly(ethylene glycol) and poly(dimethyl acrylamide) segments was first synthesized and on its based interpenetrating polymer structure was obtained by introducing a second network of cross-linked poly(N-isopropylacrylamide). Networks were characterized by FTIR spectroscopy and swelling kinetics in different solvents. DSP loading and release investigations proved the feasibility of the developed multicomponent hydrophilic polymer networks as effective platforms for potential dermal application.

NETWORKS' SYNTHESIS

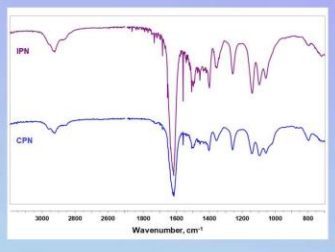
Copolymer network (CPN)



Interpenetrating polymer network (IPN)



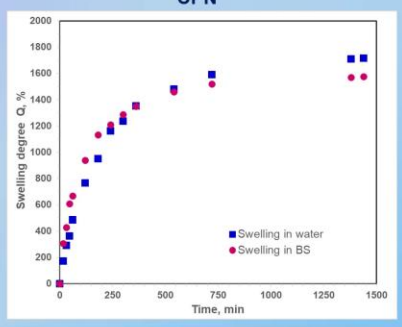
FTIR spectra of CPN and IPN



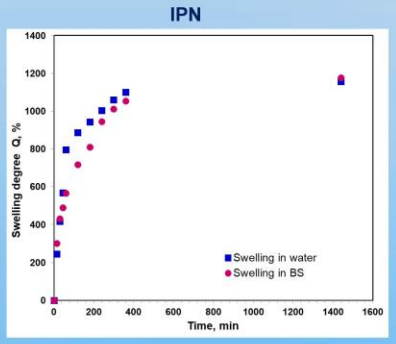
NETWORKS' PROPERTIES

Swelling kinetics or the developed multicomponent networks were investigated in water at 20 °C and in buffer solution of pH 7.4 at 37 °C.
Both CPN and IPN reached equilibrium swelling within 24 hours show high swelling degree which is indicative for their potential as drug carriers. In addition, IPN showed temperature-responsive swelling as the equilibrium swelling degree decreases considerably with increasing the temperature.

CPN

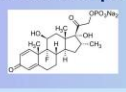


IPN



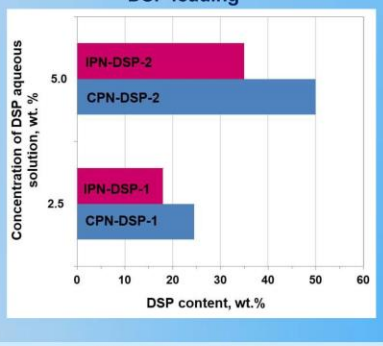
DRUG LOADING AND RELEASE

Dexamethasone sodium phosphate (DSP)

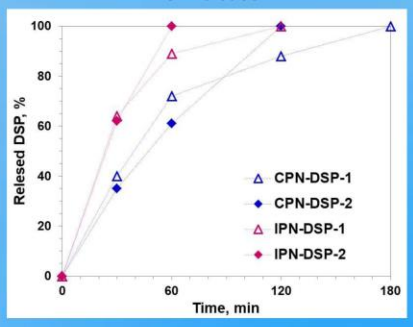


DSP is a corticosteroid used to treat a number of conditions including arthritis, blood / hormone / immune system disorders, allergic reactions, certain skin and eye conditions, breathing problems, certain bowel disorders, and certain cancers.
Networks were drug loaded by swelling in DSP aqueous solutions of varied concentration. DSP release was followed in buffer solution at 37°C.

DSP loading



DSP release



CONCLUSIONS

❖**Multicomponent polymer network comprising poly(ethylene glycol) and poly(dimethyl acrylamide) segments, as well as corresponding IPN based on cross-linked poly(N-isopropylacrylamide) are promising new platforms for dexamethasone sodium phosphate (DSP) delivery.**

❖**Both CPN and IPN show high DSP loading efficiency. The amount of DSP loaded in the network could be easily controlled by the concentration of drug aqueous solution.**

❖**Drug release profiles prove the feasibility of potential dermal application for developed new DSP carriers.**

Постер 7

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

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INTRODUCTION

Aripiprazole (APZ) is an atypical antipsychotic used in the treatment of schizophrenia and bipolar disorders. However, APZ is poorly soluble in water and this limits it's broad application. Many studies are focused on improving APZ solubility in water with the aid of polymeric carriers. Our goal is to design nanogel system able to form an inclusion complex with APZ and thus to improve its solubility in aqueous media and ensure a favorable release profile of the drug.
This work describes the development of novel nanogel carriers comprising β-cyclodextrin (β-CD) moieties as a platform for controlled delivery of APZ.

SYNTHESIS OF β-CD

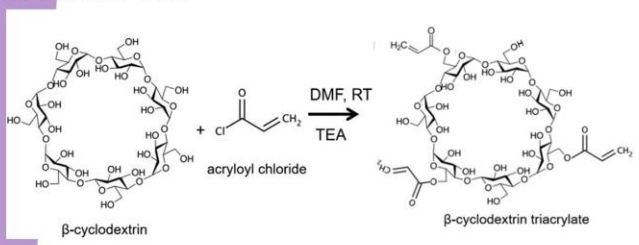

Figure 1. Synthetic scheme of β-CD-Ac$_3$ preparation.

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.

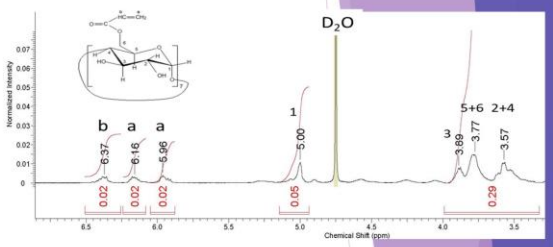

Figure 2. Proton NMR spectrum of β-CD-Ac$_3$ in D$_2$O

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 crosslinking agent with three reactive groups was synthesized.

SYNTHESIS OF NANOGELS

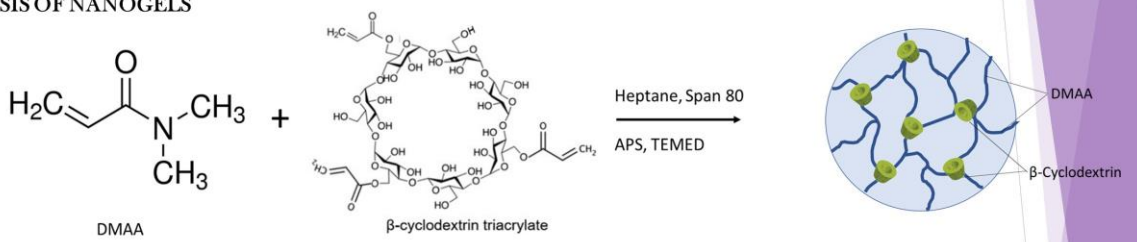

Figure 3. Synthetic scheme of poly(N,N-dimethylacrylamide)/β-cyclodextrin nanogel fabrication.

The nanogels were synthesized as follows: Span 80 (surfactant) was dissolved in heptane (oil phase), while APS, TEMED, β-CD-Ac$_3$ and DMAA were dissolved in water (aqueous phase). The two solutions were mixed under stirring to form an emulsion. The reaction was carried out for 20 h at RT to afford the nanogel. Next, the heptane was removed via evaporation, and the Span 80 was extracted with methylene chloride. After that, a dialysis was performed to purify the product. The sample was frozen, and water was removed by freeze drying.

CHARACTERISATIONS OF NANOGELS

SAMPLE CODE	DMAA/β-CD-Ac3 FEED RATIO	DMAA/β-CD-Ac3 CALCULATED	YIELD (%)	D_h (nm)	ζ (mV)
CC06	5:1	5.26:0.74	93.6 %	325 ± 25	-37 ± 2
CC08	1:1	1.3:0.7	72.4 %	321 ± 44	-31 ± 3

The amount of β-CD-Ac$_3$ in the nanogels were estimated indirectly based on the inclusion of phenolphthalein in the β-CD cavities (phenolphthalein method).

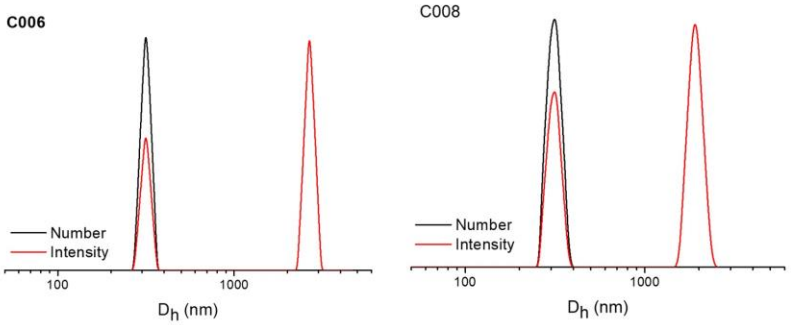

Figure 4. Size distribution plots of nanogels.

DLS measurement proved that the particles obtained are nano-sized. ELS measurements revealed a negative surface charge (sample concentration – 1 mg/ml).

CONCLUSIONS AND PERSPECTIVES

Novel nanogels were 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 network was proven by the phenolphthalein method. The nano size of the particles was confirmed by performing measurements on a Zetasizer (DLS and ELS). In forthcoming experiments, the nanogels will be loaded with aripiprazole. The drug loading efficiency of the carrier and the release profile are yet to be explored.

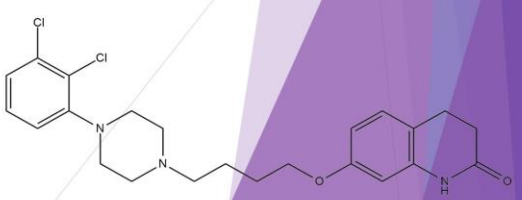

Figure 5. Structural formula of Aripiprazole.

ACKNOWLEDGEMENT: The authors thank the INFRAMAT project for the research equipment that was used in this investigation.

Постер 8

ТРИНАДЕСТА НАУЧНА СЕСИЯ „МЛАДИТЕ УЧЕНИ В СВЕТА НА ПОЛИМЕРИТЕ“

2 юни 2022 година, ИП-БАН, гр София, ул. Академик Георги Бончев 103

ПОЛУЧАВАНЕ НА ФОСФОРСЪДЪРЖАЩИ ПОЛИМЕРНИ ДОБАВКИ НА ОСНОВАТА НА РЕЦИКЛИРАН ПЕТ

***Симона Захова**, Ивелина Цачева, Кольо Троев, Виолета Митова*

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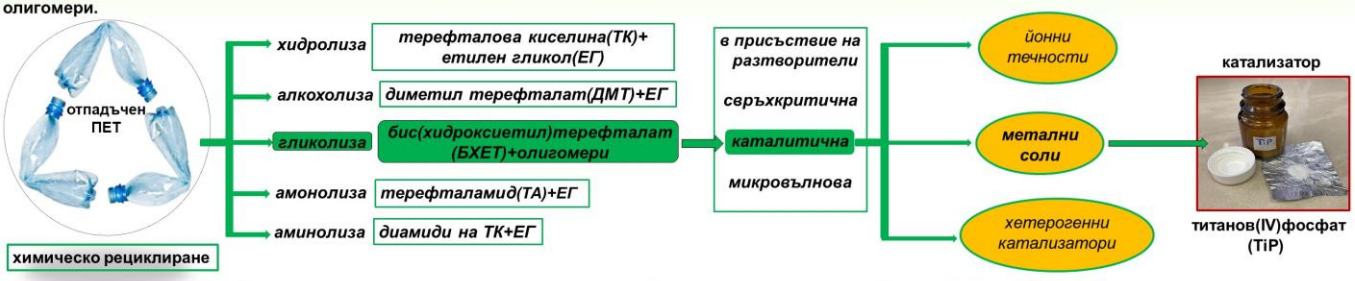
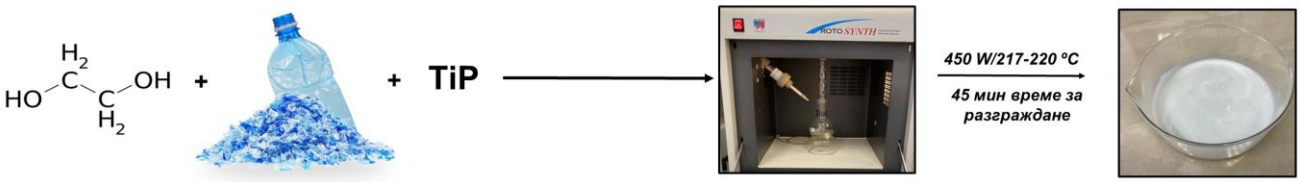
В настоящата ера на глобализация, пластмасата е неразделна част от нашето ежедневие. Най-често използваните полимери не са биоразградими, следователно проблемите свързани със замърсяването са неизбежни. Сред тях, значителен дял заема полиетилен терефталатът (ПЕТ) поради широката му употреба като опаковъчен материал за храни и напитки. До 2025 година се очаква световното търсене на полимера да достигне 22,36 милиона тона (Pint Week, Англия, 2020 година „Thu future of PET packaging“), а според доклад от 2019 година (Taniguchi) само 28,4% от общото производство на ПЕТ е било рециклирано в бутилки, фолиа и влакна, а останалите генерирани в отпадъци. За разрешаване на този проблем изследователи и технолози фокусират усилията си върху рециклиране на отпадъчен ПЕТ в продукти с висока добавена стойност. Химическото разграждане на полиестера представляват чист и рентабилен метод за опазване на околната среда. В зависимост от вида на химическия агент, ПЕТ деполимеризира напълно до основни мономери и олигомери.



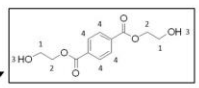
Гликолизата и свързаните с нея процеси допринасят за по-устойчива ПЕТ икономика.

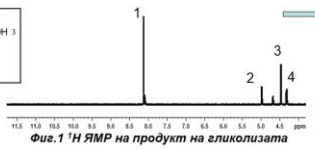
Микровълнова гликолиза на ПЕТ /TiP катализатор и охарактеризиране на получения продукт

Гликолизата е проведена в микровълнов реактор Roto Synth при молно отношение ПЕТ/ЕГ 1:2,77 и 0,2% TiP (спрямо масата на ПЕТ).



- ✓ *61,7%БХЕТ (ГПХ анализ)*
- ✓ *58,13% БХЕТ (УВ анализ)*

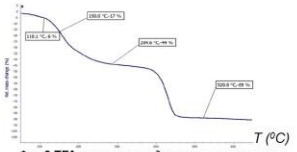




Фиг.1 ^{1}H ЯМР на продукт на гликолизата

- ✓ 61,01% БХЕТ
- ✓ 26,11% димери
- ✓ 12,88 % тримери и др. олигомери

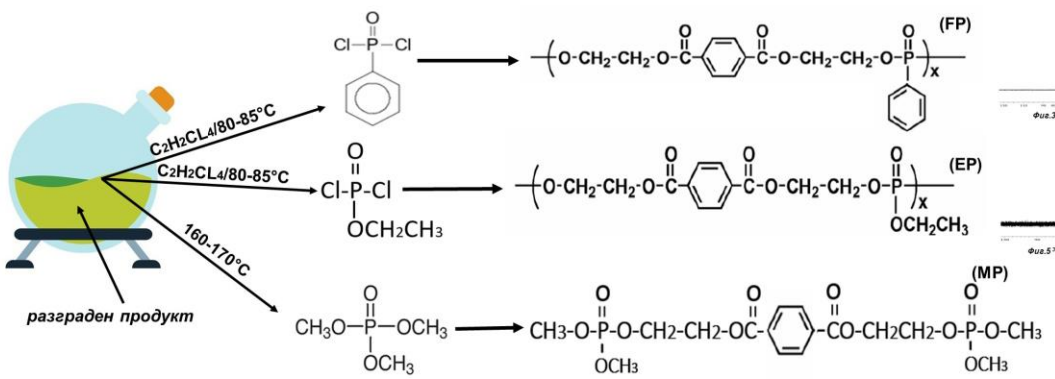
БХЕТ мономер
+
димери
+
тримери
+
други олигомери

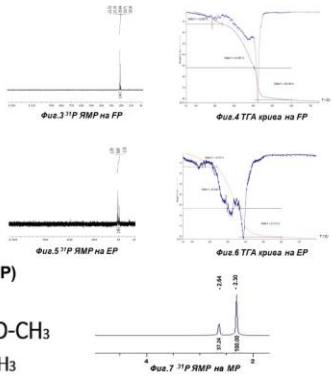


Фиг.2 ТГА крива на продукта на гликолизата

- ✓ *От 110°C до 285°C - загуба на съединения с ниски мол. маси, като ЕГ*
- ✓ *От 380°C до 450°C - загуба на маса от разграждането на продуктите на гликолизата*

Получаване на фосфорсъдържащи продукти на основата на получения разграден продукт





Фиг.3 ^{31}P ЯМР на FP

Фиг.4 ТГА крива на FP

Фиг.5 ^{31}P ЯМР на EP

Фиг.6 ТГА крива на EP

Фиг.7 ^{31}P ЯМР на MP

Изводи:

- При използване на малък излишък ЕГ при процеса на гликолиза се постига добре дефиниран разграден продукт и се елиминира нуждата от рециклиране на големи количества ЕГ, което допълнително оптимизира процеса.
- Разградният продукт от ПЕТ гликолизата може да бъде 100% оползотворен.
- Процесът на рециклиране може да бъде оптимизиран до 45 мин време за реакция.
- Получените фосфорсъдържащи продукти биха могли да имат потенциално приложение, като забавители на горене при влагането им като добавка към ПЕТ.

Постер 9

Enhanced adsorption capacity of modified MCM-48 and SBA-15 silicas

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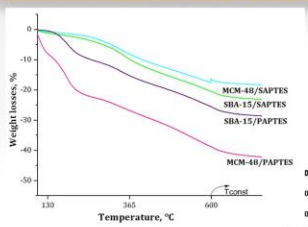
SBA-15 and MCM-48 mesoporous silicas were modified with functionalized triethoxysilanes by post synthesis method thus indroducing on the pore surface polar N- and P-containing groups. The physicochemical characteristics of the adsorbent samples were studied by nitrogen physisorption, UV-Vis spectroscopy and TG measurements. The adsorption capacity of CO_2 was measured in dynamic CO_2 adsorption regime. Higher capacity for CO_2 adsorption was determined for the modified materials in comparison to the initial ones. Values of 4.2-4.6 mmol/g were achieved for the MCM-48 modified adsorbent. A slight decrease about 5 % in CO_2 adsorption capacities was registered for the modified silicas in three adsorption/desorption cycles indicating their high performance stability.

CHARACTERIZATION OF THE MODIFIED MCM-48 AND SBA-15 MESOPOROUS SILICAS



TG profiles of the SAPTES and PAPTES-modified material.

N_2 adsorption/desorption isotherms of the initial and the SAPTES and PAPTES modified materials.

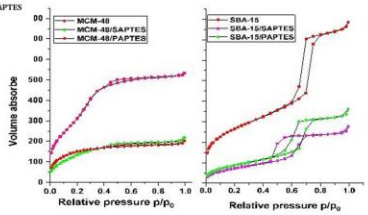


Table 1: Textural properties of the synthesized materials obtained and the content of the grafted functional moieties.

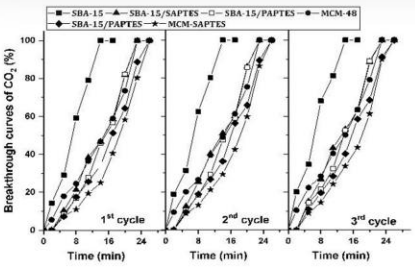
Sample name	S_{BET} (m^2/g)	Pore volume (cm^3/g)	Pore diameter (nm)	Content of the grafted groups, %
MCM-48	1235	0.83	2.4	-
MCM-48/SAPTES	439	0.35	3.1	19.07
MCM-48/PAPTES	516	0.31	3.1	42.42
SBA-15	926	1.22	6.8	-
SBA-15/SAPTES	318	0.56	6.6	23.25
SBA-15/PAPTES	265	0.43	5.6	28.85

The greater amount of PAPTES incorporated in the mesoporous silicas could be explained with its bulk molecule and the peculiarities of the matrix structure.

The isotherms of the parent and the modified MCM-48 exhibit a sharp increase at a relative pressure between p/p_o= 0.2-0.4, which is associated with capillary condensation of nitrogen in the channels. It is also an indication of narrow pore size distribution. The isotherms of the MCM-48 samples are reversible and do not show any hysteresis loop. The isotherms of the SBA-15 samples are of type IV with a hysteresis loop at 0.6-0.7 relative pressure, typical for SBA-15 structure.

A decrease of the textural parameters, such as surface area and total pore volume of the modified samples, was registered. Significant decrease in the S_{BET} and pore volume was observed after modification of SBA-15 and MCM-48 with both modifying agents. The SBA-15/PAPTES showed higher decreased of surface area and pore volume than that in the case of SAPTES. Probably, this is due to the more bulky structure of PAPTES compared to SAPTES. MCM-48/PAPTES displayed textural parameters similar to those of MCM-48/SAPTES. The strong effect of the post-synthetic treatment on the textural parameters of both MCM-48 modifications was due to the partial deterioration of the three-dimensional structure of the MCM-48 silica with small pore sizes around 2.4 nm during the modification procedure. The significant decrease of surface area and pore volume of MCM-48/SAPTES and MCM-48/PAPTES is probably due to the total pore blocking of some pores with grafted groups.

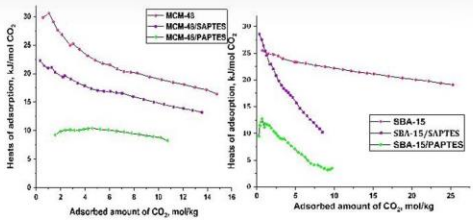
CARBON DIOXIDE ADSORPTION MEASUREMENTS UNDER DYNAMIC AND STATIC CONDITIONS



CO_2 breakthrough curves of the prepared materials under dynamic conditions with 3 % CO_2/N_2

CO_2 adsorption experiments were performed under dynamic conditions in a flow system. The sample (0.40 g adsorbent) was dried at 150 °C for 1 h, and 3 vol.% CO_2/N_2 at a flow rate of 30 mL/min was applied for the experiments. The gas was analyzed online by GC NEXIS GC-2030 ATF with 25 m PLOT Q capillary column.

Under static conditions CO_2 adsorption measurements were measured at 0 °C with AUTOSORB iQ-MP-AG surface area and pore size analyzer (from Quantachrome). Transformation of the primary adsorption data was performed by the Quantachrome software.



Heats of adsorption for the initial and modified SBA-15 and MCM-48 materials

MCM-48 grafted with PAPTES or SAPTES residues displayed:

- greater amounts of CO_2 absorbed than the initial ones;
- the CO_2 capture is due to the physisorption process;
- three adsorption cycles showed similar adsorption performance of the initial and the modified silicas;
- significant effect of the matrix structural characteristics;
- enhanced adsorbent performance via appropriate modification. Grafting of PAPTES or SAPTES onto the silica surface afforded polar adsorption sites and changes in the textural characteristics that synergistically increased the CO_2 adsorption capacities of the silica material to levels obtained for modifications with amines. In certain applications it could be an advantage accounting the lower temperatures needed for CO_2 desorption (40°C).

Table 2. CO2 adsorption in dynamic conditions on the studied samples

Sample	Adsorption of CO_2, mmol/g (1 cycle)	Adsorption of CO_2, mmol/g (2 cycle)	Adsorption of CO_2, mmol/g (3 cycle)
MCM-48	2.50	2.40	2.40
MCM-48/SAPTES	4.60	4.50	4.45
MCM-48/PAPTES	4.20	4.00	4.05
SBA-15	1.30	1.30	1.30
SBA-15/SAPTES	2.50	2.40	2.40
SBA-15/PAPTES	2.80	2.75	2.70

Contrariwise, MCM-48 varieties display relatively homogeneous distribution of the modified adsorption sites on the matrix pore surface.

The results presume stronger interaction of the CO_2 molecules with the grafted Schiff base residues. However the CO_2 adsorption capacities achieved with the PAPTES modified adsorbents are similar to that of the SAPTES grafted materials. The partial pore blocking effect of PAPTES resulted in the restricted diffusion of CO_2 molecules and its effective capture in the pore volume of the matrix. The obtained results are consequence of a balance between the matrix textural parameters and the functional and structural features of the modifying agents.

CONCLUSIONS: The modified MCM-48 and SBA-15 mesoporous silicas displayed high adsorption capacity, low energy consumption for CO_2 desorption and performance stability. Adsorbents with such parameters could be considered in certain applications .

Acknowledgement: This study is supported by the Bulgarian Ministry of Education and Science under the National Scientific Program EPLUS: Low Carbon Energy for the Transport and Domestic Use, grant agreement D01-361/17.12.2020.

Постер 10

Hybrid porous silica – biopolymer carriers for target delivery of Curcumin

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[2]Faculty of Pharmacy, Medical University of Sofia, 1000 Sofia, Bulgaria
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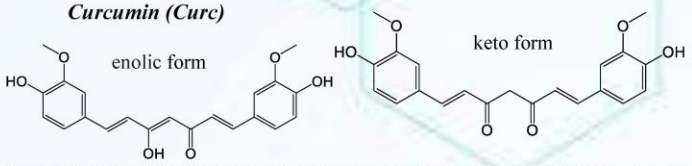
Introduction

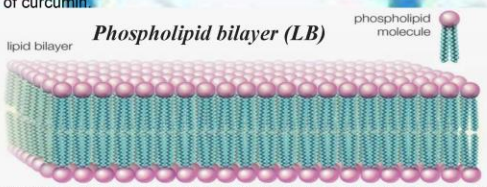
In the present study mesoporous silica nanoparticles with embedded magnetic particles and sizes around 80 nm were prepared. Curcumin loading in mesoporous silica was realized by a post-synthesis impregnation procedure. The loaded particles were additionally modified by surface coating with a phospholipid bilayer of a thickness of around 5 nm changing the surface charge of the carrier from negative to positive, which enables the efficient attachment to cells, increasing the probability of cellular uptake. The non-loaded, curcumin loaded and their surface-coated counterparts were characterized by XRD, N2 physisorption, thermal analysis, TEM, and ATR-FTIR. A comparative study on the antiproliferative effect of curcumin loaded into the mesoporous carrier and lipid-coated vs. free drug was performed on a panel of three human cell lines. On the basis of the obtained results, it can be concluded that obtained hybrid magnetic silica-lipid particles are promising carriers of curcumin.

Curcumin (Curc)



Curcumin ((1E,6E)-1,7-Bis(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione) has been widely used as a traditional medicine for centuries. Due to its low toxicity and pharmacological activity, its application in the treatment of various diseases such as cancer, inflammatory diseases, diabetes etc., has been the focus of extensive studies.

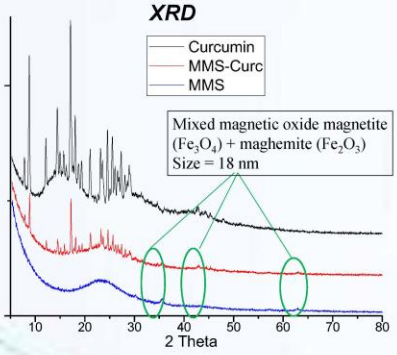
Phospholipid bilayer (LB)



Encapsulating a drug in lipid-coated carriers can lead to increased solubilization and absorption, resulting in enhanced bioavailability, possible attachment to cells, and increasing cellular uptake.

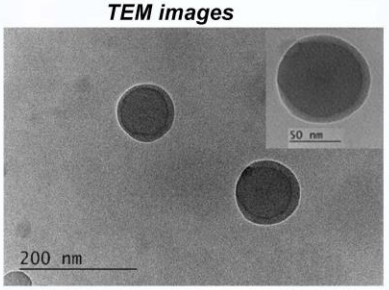
Characterization

XRD



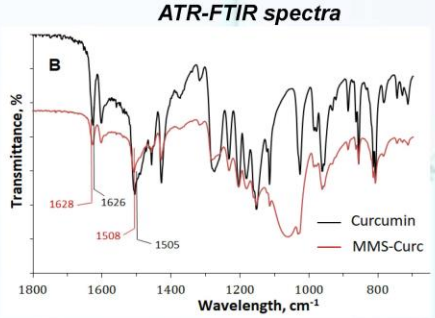
The reflections in the diffractogram of the curcumin-loaded sample are characterized with much lower intensity than the pure curcumin, indicating that only a small amount of it can be found on the particles' surface or into interparticle voids, which means that curcumin is generally loaded into the pores of the support.

TEM images



Uniform spherical particles with size around 80-90 nm, coated with thin phospholipid bilayer ~5 nm

ATR-FTIR spectra



Upon drug loading small shifts of bands related to keto-enol moiety can be observed: from 1626 cm^{-1} to 1628 cm^{-1} and from 1505 cm^{-1} to 1508 cm^{-1}. These shifts imply weak interactions between the silica surface groups and curcumin, as well as preservation of the keto-enolic form.

Loading efficiency and content of the phospholipids

The exact amount of the loaded bioactive compound was evaluated by thermogravimetric analysis, and it was found to be 30%. This result proved the higher loading capacity of the obtained porous support and the efficiency of the applied loading technique. After the coating of the loaded silica particles with the lipid bilayer, the observed weight loss was 38% means that the coating was successful and it results in 8 w.% lipids of the prepared delivery system.

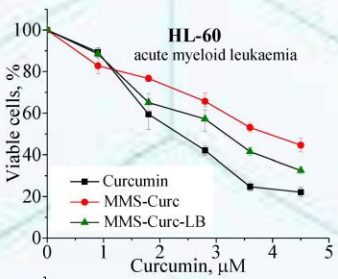
Textural characteristics

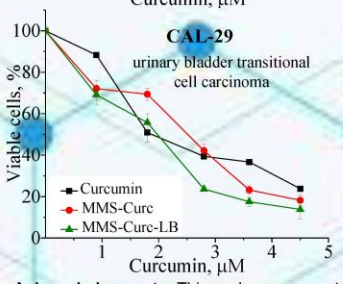
Sample	BET (m^2/g)	Pore volume (cc/g)	Pore diameter[a] (nm)
MMS	820	0.53	3.1
MMS-Curc	444	0.29	3.1

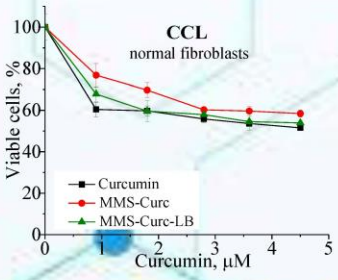
Surface charge

The zeta potential of the non-coated MMS particles was negative (-12.5± 1.2) whereas the positive value (9.2 ± 1.2) was measured for particles coated by lipid layer. A positive charge of the obtained delivery system is preferred to enable efficient attachment to cells, increasing the probability of cellular uptake.

MTT-dye reduction assay







Cell line	CCL	HL-60	CAL-29
Sample	IC_{50} (μM)		
MMS	n.d.	n.d.	n.d.
Curcumin	n.d.	2.3	0.18
MMS-Curc	n.d.	3.9	0.25
MMS-Curc-LB	n.d.	3.2	0.19

Conclusions:
Mesoporous silica particles of size around 80 nm with embedded magnetic nanoparticles were successfully prepared. Curcumin loading in the silica support was achieved by post synthesis impregnation procedure. Lipid layer of 5 nm was formed around the silica nanoparticles changing the surface charge of the carrier from negative to positive favoring the interaction with the cells, and assisting particles dispersibility. A comparative study on the antiproliferative effect of the loaded curcumin vs. free drug was performed on a panel of three human cell lines. On the basis of the obtained results it can be concluded that the coated silica particles are appropriate carriers for curcumin delivery system with targeting function.

Acknowledgements: This work was supported by the Bulgarian Ministry of Education and Science under the National Research Program "Young scientists and postdoctoral students" approved by DCM # 577/17.08.2018, project "Delivery systems for biologically active natural compounds on the basis of novel organic-inorganic carriers ".

Постер 11

Synthesis of grafting agents for modification of egg shell membrane (ESM)

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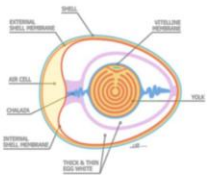
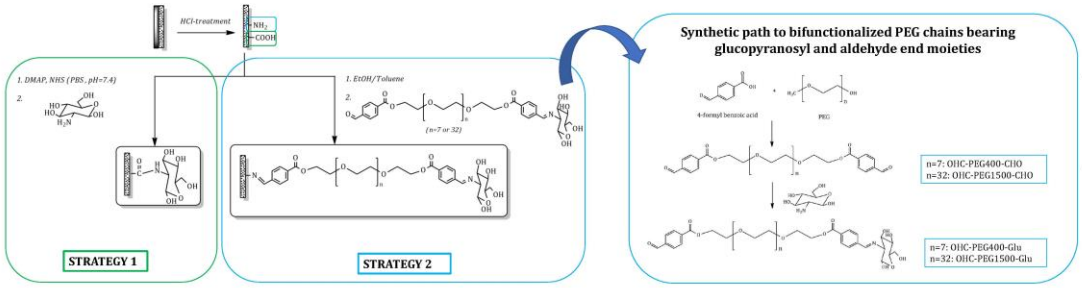
Introduction

Recently the reuse of Eggshell membranes (ESM) separated from the eggshell has become a focus of many investigations targeting specific applications. Being an abundant industrial and household byproduct ESM present inexpensive, environmentally friendly and nontoxic material readily available for use. Studies reported application of naked ESM in wound dressing, cell culture, or adsorption of heavy metals. Besides its unique mechanical and filtering properties, the ESM surface is rich in functional groups susceptible to further modifications.

In the current study two modification pathways were applied to enrich the ESM surface with glucopyranosyl units. The one was based on the reaction of activated surface carboxylic groups with glucosamine and the other approach exploited the reactivity of the surface amino groups for grafting poly(ethylene glycol) (PEG) chains bearing end glucopyranosyl and benzaldehyde moieties.



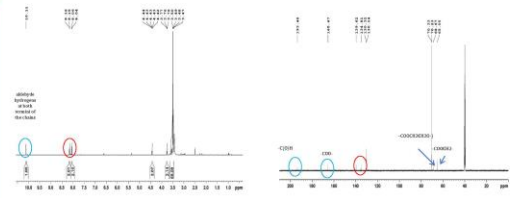
Synthetic procedures and methods



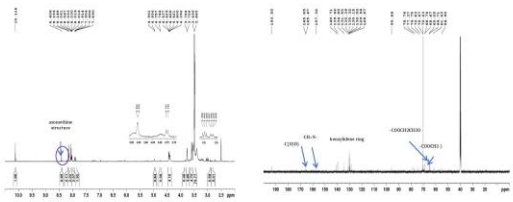
- The functionalization of the PEGs was evidenced by ^{1}H and ^{13}C NMR spectral data.
- The modified ESMs were characterized applying FT-IR, SEM and BET.

Results

STRATEGY 2

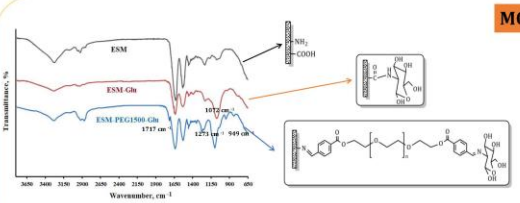


^{1}H NMR (left) and ^{13}C NMR (right) spectra of dialdehyde terminated PEG1500 (OHC-PEG1500-CHO) in DMSO-d6.



^{1}H NMR (left) and ^{13}C NMR (right) spectra of PEG1500 terminated with aldehyde and glucose moieties (OHC-PEG1500-Glu) in DMSO-d6.

MODIFICATIONS OF ESM



FTIR spectra of ESM, ESM-Glu and ESM-PEG1500-Glu.

Degree of grafting and glucopyranosyl units content of the modified ESMs.

Sample	Degree of grafting to ESM (%)	Glucopyranosyl units content (mmol g^{-1} ESM)
ESM-Glu	37.50	2.22
ESM-PEG400-Glu	74.47	0.92
ESM-PEG1500-Glu	26.32	0.14

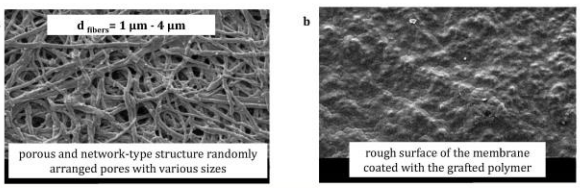
- Degree of grafting: mESM2-mESM1; HPLC measurement
- Glucopyranosyl units content: gravimetric determination and calculation

TEXTURAL PROPERTIES OF THE ESMs

BET-Analysis of modified ESMs

Sample	S_{BET} ($m^2 g^{-1}$)	Total pore volume ($cm^3 g^{-1}$)	
ESM	14.500 ± 2.380	0.0430 ± 0.0073	
ESM-Glu	0.274 ± 0.108	0.0092 ± 0.0038	→ in the pores
ESM-PEG400-Glu	1.644 ± 0.439	0.0056 ± 0.0016	→ partially in the pores/on the surface
ESM-PEG1500-Glu	12.859 ± 2.873	0.0071 ± 0.0021	→ on the surface

SEM images of (a) ESM-Glu and (b) ESM-PEG1500-Glu.



Conclusion

- ✓ Both strategies lead to a considerably high degree of grafting (content of glucopyranosyl units: 2.33 mmol - 0.14 mmol per 1 g ESM);
- ✓ The modification of ESM affects its textural characteristics: $\downarrow S_{BET}$; $\downarrow V_{\text{total pore}} = f\uparrow(M_{\text{grafted reactant}})$
- ✓ The protein and bacteria recognition properties of the modified ESMs can be further investigated.

Acknowledgement

NATIONAL PROGRAMME „POST-DOCTORAL STUDENTS" Funded by the Bulgarian Ministry of Education and Science (MES)

Постер 12

ТРИНАДЕСТА НАУЧНА СЕСИЯ „МЛАДИТЕ УЧЕНИ В СВЕТА НА ПОЛИМЕРИТЕ“

2 юни 2022 година, ИП-БАН, гр София, ул. Академик Георги Бончев 103

INSTITUTE of POLYMERS BULGARIAN ACADEMY OF SCIENCES

ИНСТИТУТ ПО ОРГАНИЧНА ХИМИЯ С ЦЕНТЪР ПО ФИТОХИМИЯ Българска Академия на науките

SILICA NANOPARTICLES DERIVED FROM AGRARIAN WASTES

Ioanna Veleva[1], Oyundari Tumurbaatar[2], Hristina Lazarova[2], Margarita Popova[2], Violeta Mitova[1] and Neli Koseva[1]

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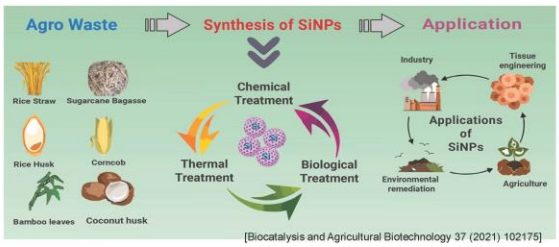
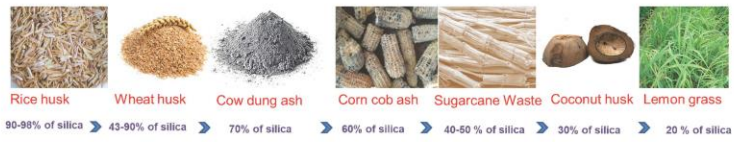
Silica nanoparticles (NPs) have diverse applications in the field of medicine, supercapacitors, batteries, optical fibers and concrete materials, because silica nanoparticles have tunable physical, chemical, optical and mechanical properties. In most applications, high-purity silica comes from synthetic organic precursors, yet this approach could be costly, polluting and non-biocompatible.



[Biocatalysis and Agricultural Biotechnology 37 (2021) 102175]

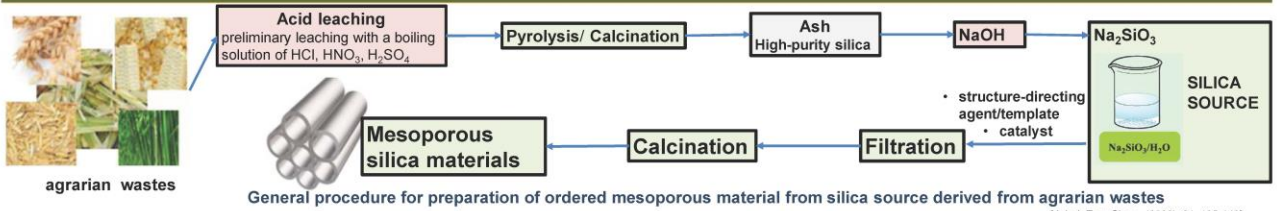
NATURAL AND RENEWABLE SOURCES OF SILICA AND SILICON NPs

Natural and renewable sources are ideal materials for the preparation of silica nanoparticles. They can be effectively obtained from various agrarian sustainable bio-resources (rice husk ash, sugar-cane, coffee husk, wheat husk and corn cob ash), which are often disposed of. Using green and sustainable techniques can help eliminate or reduce laborious/complicated procedures and reduce the environmental contaminants to obtain advanced materials for high-tech applications.



Silica content of ashes from agrarian sustainable bio-resources

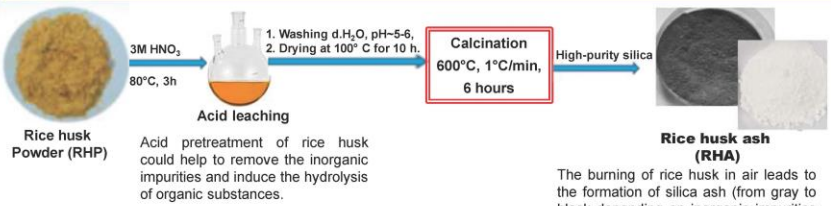
SYNTHETIC ROUTE FOR PREPARATION OF NANOSTRUCTURED MESOPOROUS MATERIALS BASED ON AGRARIAN WASTES



General procedure for preparation of ordered mesoporous material from silica source derived from agrarian wastes

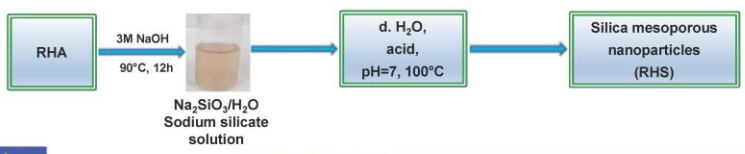
[J. Ind. Eng. Chem. (2020), 81, 135-143]

SILICA MESOPOROUS NANOPARTICLES FROM RICE HUSK POWDER

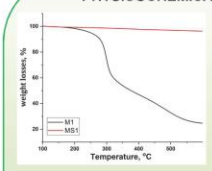


Acid pretreatment of rice husk could help to remove the inorganic impurities and induce the hydrolysis of organic substances.

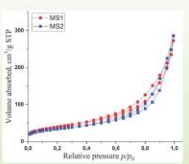
The burning of rice husk in air leads to the formation of silica ash (from gray to black depending on inorganic impurities and unburned carbon amounts).



PHYSICOCHEMICAL CHARACTERIZATION



TG profiles of the acid treated RHP(M1) and RHS(MS1)



N_2 adsorption/desorption isotherms of the RHS

TEM images of RHS

CONCLUSIONS: 1. Silica nanoparticles were successfully synthesized by applying rice husk as a precursor.
2. The acid pretreatment of rice husk removed the inorganic impurities and induced the hydrolysis of organic substances, ensuring high purity (97 wt. %) of the obtained silica powder.
3. The applied procedure for treatment of rice husk resulted in the preparation of silica nanoparticles with a high specific surface area.

Acknowledgement: This study is supported by the Centre of Competence “Sustainable utilization of bio-resources and waste of medicinal and aromatic plants for innovative bioactive products”, BG05M2OP001-1.002-0012-C01.

ЕВРОПЕЙСКИ СЪЮЗ ЕВРОПЕЙСКИ ФОНД ЗА РЕГИОНАЛНО РАЗВИТИЕ

НАУКА И ОБРАЗОВАНИЕ ЗА ИНТЕЛИГЕНТЕН РАСТЕЖ

Постер 13

SOFIA UNIVERSITY
ST. KLIMENT OHRIDSKI
est. 1888

FACULTY OF CHEMISTRY AND PHARMACY

Solid lipid nanoparticles as vehicles for quinine delivery- synthesis and characterization

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2. *Laboratory of Pharmaceutical technology and biopharmacy, Faculty of chemistry and pharmacy, Sofia University "St. Kliment Ohridski", 1, J. Bourcheir blvd., 1164- Sofia, Bulgaria;*

I. Introduction

Solid Lipid Nanoparticles (SLN) are defined as drug carriers in the submicron size range made of biocompatible and biodegradable lipids solid at room and body temperature. The drug of interest for the present study is quinine- it remains an important anti-malarial drug almost 400 years after its effectiveness was first documented. However, its continued use is challenged by its poor tolerability, poor compliance with complex dosing regimens, and limited roads for administration in human body. The advantages of incorporation of quinine in SLN were investigated.

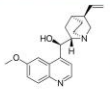

Fig. 1 Quinine molecule

II. Methods

Novel SLN[1,2] (CellInject™), patented as carrier system with unique mechanism of drug release were used to encapsulate quinine. For synthesis of SLNs was applied the phase inversions technique (PIT). The technique is based on change in the properties of polyoxyethylated surfactants with temperature shift. The hydrophillic-lipophillic balance (HLB) value of surfactants defined by Griffin is valid at 25 °C. At this temperature the hydrophilic parts of the SAC molecules are hydrated to a certain degree. An increase in temperature causes dehydration of the ethoxy- groups. As a result the molecule lipophilicity rises with corresponding decrease in HLB value. At a certain point the affinity of the SAC to the aqueous and lipid phase is equal - this temperature is defined as the phase inversion temperature.

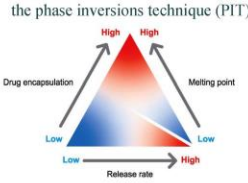

Fig. 2 Supposed relationship between melting point, release rate and drug encapsulation

This particulate state is characterized by very low surface tension and presence of complex structures in the system. If the temperature is further increased the SAC's affinity to the lipid phase becomes higher enough to stabilize emulsions of W/O type (*Figure 3*). If cooled back the system goes inversely through the same processes. Due to the specific properties of the system around the PIT very small particles are formed just below that temperature.

The intrinsic properties of the lipids and surfactants are essential to the process.

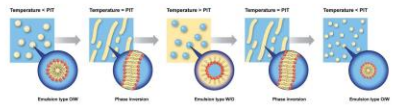

Fig. 3. Phase inversions of hot emulsion with variations of the temperature above and below PIT

Solid lipid nanoparticles outmatch other nanoparticles by important parameters:

- ***Better stability*** compared to the liposomes due to their rigid core that is solid at room and body temperatures
- ***Lower toxicity*** and ***better tolerability*** as an alternative to polymeric systems, which is considered to correlate with biodegradable nature of the lipid carrier.

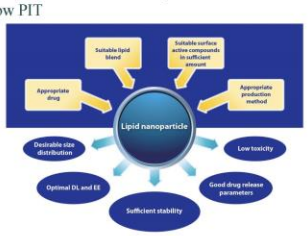

Fig. 4 SLNs advantages

Important advantage of SLN to the conventional dermal forms is improved dermal uptake after topical application and high accumulation in skin *in vivo*.

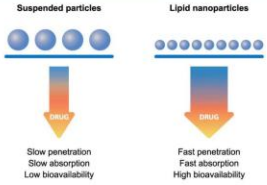

Fig. 5 Occlusion depends on particles size. Smaller particles have more tight distribution on the skin than the bigger ones.

III. Results

Characterization	CellInject™ solid lipid nanoparticle
Size (nm)	32.8
Polydispersity	0.399
Z potential (mV)	-18.5

Table 1. *Size, polydispersity and z-potential of tested SLNs [1,2] dispersions.*

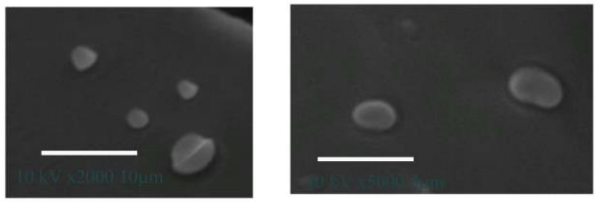

Fig. 6 SEM images of SLNs at 2000x and 5000x magnification

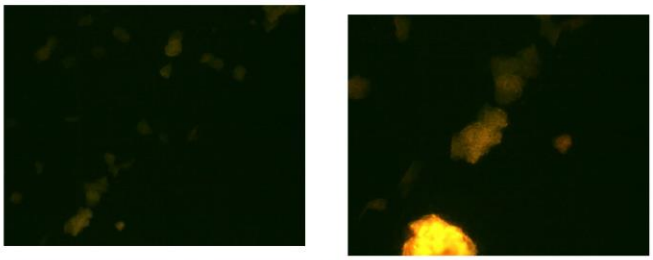

Fig. 7 Fluorescence microscope images of aggregates of loaded SLNs at 10x and 20x magnification

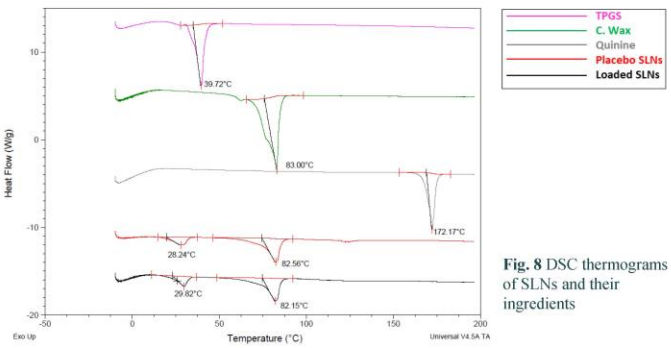

Fig. 8 DSC thermograms of SLNs and their ingredients

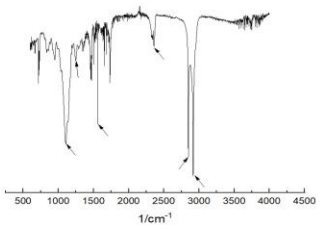

Fig. 9 FTIR spectra of SLNs loaded with quinine

IV. Conclusion

The innovative technology for formulation SLNs as a drug carrier, demonstrates excellent properties to encapsulate efficiently quinine in therapeutic doses, forming stable and biocompatible dispersions.

References:

[1] C. Tzachev, Solid lipid nanoparticle for intracellular release of active substances and method for production the same, *WO2019116062*

[2] C. Tzachev, Mucoadhesive dispersion nanoparticle system and method for production the same, *WO2020053609*

Acknowledgement: This work was kindly funded by National Science Fund. Project № КП-06-ДО02/2//08.07.2021г.

Novel hybrid materials obtained via polymer-controlled calcium phosphate formation

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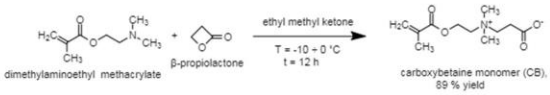
[3] Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences, Acad. G. Bonchev Str., Bl. 9, 1113 Sofia, Bulgaria

Aim of the study

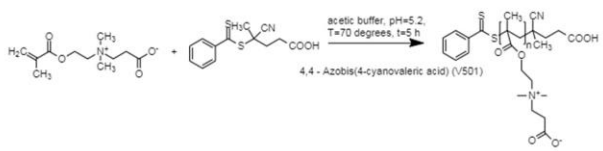
This study aims to develop and characterize new hybrid materials based on linear polycarboxybetaine (PCB) and in situ deposed calcium phosphates as materials able to enhance the teeth biomineralization.

1. Synthesis of linear PCB via RAFT polymerization

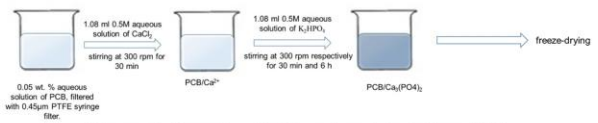
➢ ***Synthesis of carboxybetaine nonomers (CB)***



➢ ***Synthesis of linear PCB via RAFT polymerization***



2. Formation of calcium phosphate in linear PCB



Scheme 1: Formation of calcium phosphate in linear PCB

3. Results

3.1. Molecular weight of linear PCB

Sample	Mw (Da)	Mn (Da)	Mw/Mn
PCB	90420	75200	1.2 (±7.432 %)

Table 1. Weight-average molecular weight (Mw), number-average molecular weight (Mn) and polydispersity index (Mw/Mn) of PCB as estimated by GPC

3.2. Dynamic light scattering

	0.05 wt.% PCB	0.05 wt.% PCB + 0.5M $CaCl_2$	PCBCaP-0
Hydrodynamic diameter [nm]	12 ± 2 nm	30 ± 4 nm	125 ± 5 nm

Table 2. Hydrodynamic diameter of linear PCB as well as its hybrid materials.

3.3. Attenuated Total Reflectance Infrared spectroscopy (ATR-IR)

Lack of shift of the two characteristic bands of –COOH groups (1722 cm^{-1} (vC=O) and 1589 cm^{-1} in PCB-CaP-0 and PCBCaP-6 spectrum as compared to pure PCB. Vibrations appropriated to the formation of CaP between 900 and 1200 cm^{-1} are missing in the PCB-CaP-0 and PCBCaP-6.

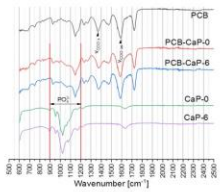


Figure 1. ATR-IR spectrums of PCB, PCB with in situ formed CaP matured for 0 and 6 h, respectively, and neat CaP matured for 0 and 6 h (the characteristic region for PO_4^{3-} vibrations in CaP between 900 and 1200 cm^{-1} is bordered with red lines).

3.4. X-Ray study

PCB-CaP is crystallographically amorphous due to the lack of CaP crystal peaks in the X-ray diffractograms. The crystal peaks denoted with * and # are due to the side products such as KCl and NaCl.

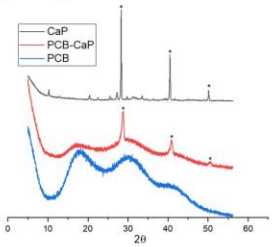


Figure 2. XRD powder diffractograms of neat PCB, hybrid PCB-CaP-0 and neat CaP-0.

3.3. Scaninng Electron Microscopy with Energy-Dispersive X-ray Spectroscopy

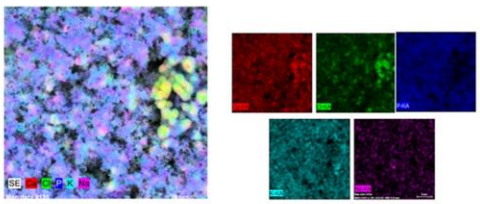


Figure 3. SEM image of CaP-0 and mapping elemental analysis for the same sample.

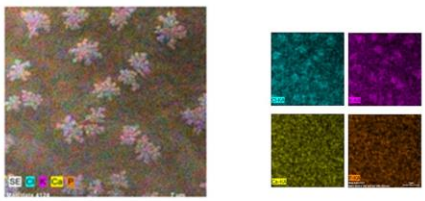


Figure 4. SEM image of PCBCaP-0 and mapping elemental analysis for the same sample.

The results from SEM with EDX analysis demonstrate the even distribution of the inorganic phase within the polymeric matrix. The size of the obtained calcium phosphate particles is uniform and in the nano meter range.

3.4. Differential scanning calorimetry (DSC)

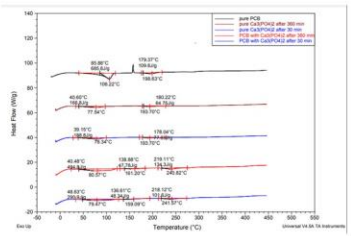


Figure 5. DSC thermograms of PCB, PCBCaP-0 and PCBCaP-6 hours.

Conclusions:

Linear PCB was synthesized and used for the first time to obtain a new hybrid material based on PCB and calcium phosphates (PCB/CaP). The potential of this new hybrid material for dental remineralization will be tested.

Acknowledgement: The authors are grateful for financial support of project KP- 06-H49/6-27.11.2020.

Постер 15

СОФИЙСКИ УНИВЕРСИТЕТ „СВ. КЛИМЕНТ ОХРИДСКИ“
Факултет по химия и фармация

Контролирана промяна на формата на двуслоен полимерен хидрогел посредством външни стимули

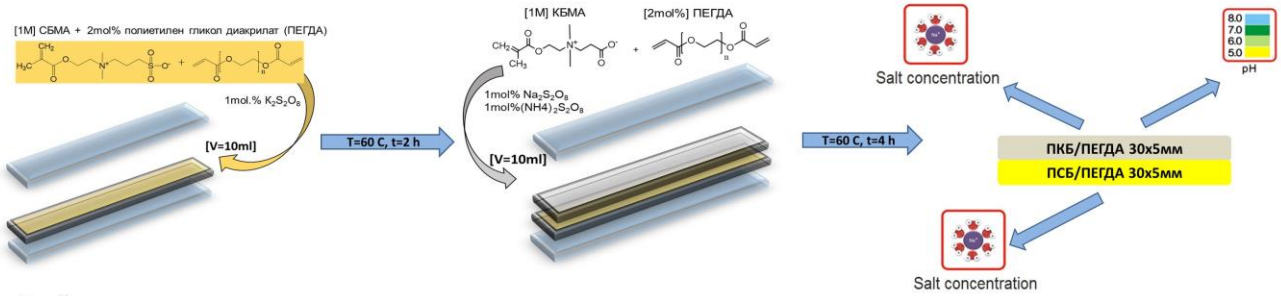
Николай Петров, Констанс Русева, Елена Василева

Абстракт

Полицвитерйонните хидрогелове са полимерни мрежи с еднакъв брой странични вериги в мономерните звена. Всяка една верига е носител на положителна амино група и отрицателен противойон. Кулоновото взаимодействие между зарядите обуславя способността на хидрогеловете да откликват на физични или химични промени в заобикалящата ги среда. Получен е ПЦв хидрогел съставен от два слоя – поликарбоксибетаин (ПКБ) и полисулфобетаин (ПСБ), който притежава свойството да променя формата си. Целта е да се изследва поведението на хидрогела при промяна на pH и солевата концентрация във водна среда. Възможностите за вариране дебелината на слевете, профила на гела и степента на омрежване предполага различна кинетика и форма на огъване, а биосъвместимостта на ПКБ и ПСБ разширява спектъра от възможни приложения.

Ключови думи: Полицвитерйон, полимерен хидрогел, двуслоен хидрогел, промяна на форма

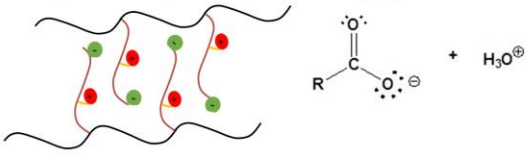
Структура и получаване



Свойства

pH-чувствителност

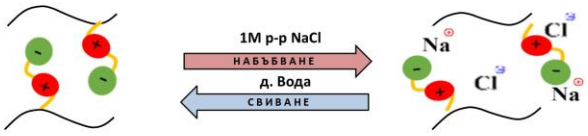
При pH стойности на средата по-високи от pKa на карбоксилната група, тя дисоциира до карбоксилатен анион и наблюдаваме клъстерна полицвитерйонна структура.



При pH стойности на средата ниски от pKa, карбоксилатният анион се протонира до карбоксилна група, като в структурата на гела настъпват електростатични сили на отблъскване между амино групите и той набъбва.

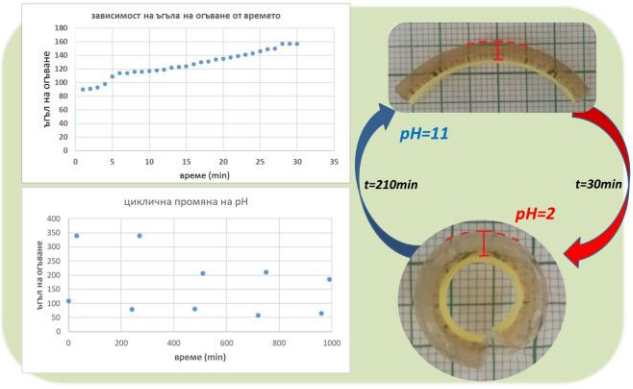
Солева чувствителност

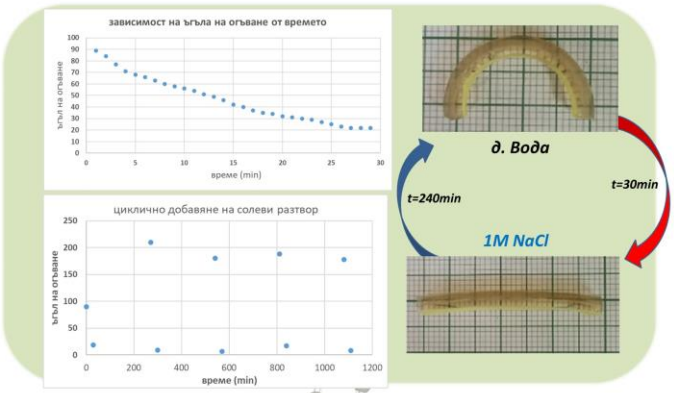
Когато хидрогелът е потопен в дестилирана вода, той запазва полицвитерйонната си структура, характеризираща се с електростатични сили на привличане между противойоните



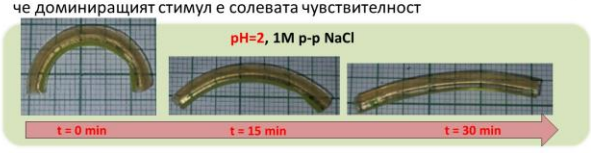
В присъствие на солеви разтвор, дисоциираните йони се привличат от карбоксилатния анион и положителната амино група, в резултат на което, зарядите в страничните групи намаляват и гелът набъбва

Резултати - влиянието на двата фактора върху способността на единия или на двата слоя да набъбват, водят до контолирано огъване или изправяне на хидрогела





Комбинирането на двата фактора, които карат ПКБ да набъбват показва, че доминиращият стимул е солевата чувствителност



Дискусия- успешно бе получен ПКБ/ПСБ двуслоен хидрогел, който притежава свойството да променя формата си при промяна на pH и солевата концентрация във водната среда. Процесът на огъване/изправяне е обратим и възвръщането на първоначалната форма на хидрогела е контролируем процес

Постер 16

Нови електроовлакнени материали от полимлечна киселина и производно на хитозана и 8-хидроксихинолина: Получаване, охарактеризиране и противотуморна активност

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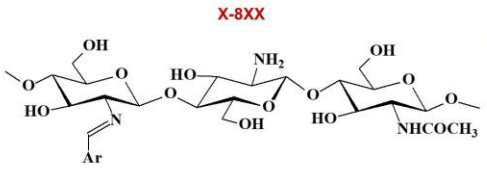
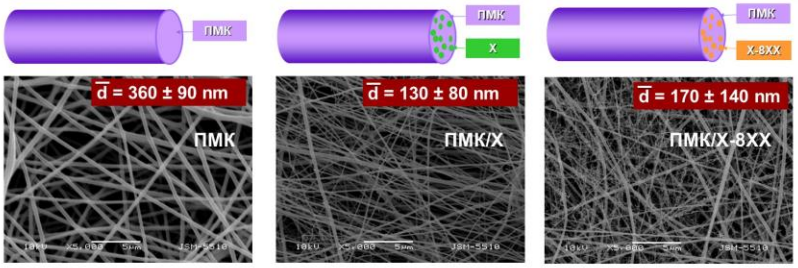
Ароматните хетероциклени съединения от групата на 8-хидроксихинолина притежават ценни биологични свойства – антибактериални, антимикотични, противотуморни, антиоксидантни и др. Целта на настоящето изследване е да се получат чрез електроовлакняване нови влакнести материали от полимлечна киселина (ПМК) и производно на хитозана и 8-хидроксихинолина (Х-8ХХ). Цели се да бъде оценена и *ин витро* противотуморната активност на получените влакнести материали спрямо HeLa клетки от рак на шийката на матката.

Схематично представяне и СЕМ микрографии на влакнестите материали

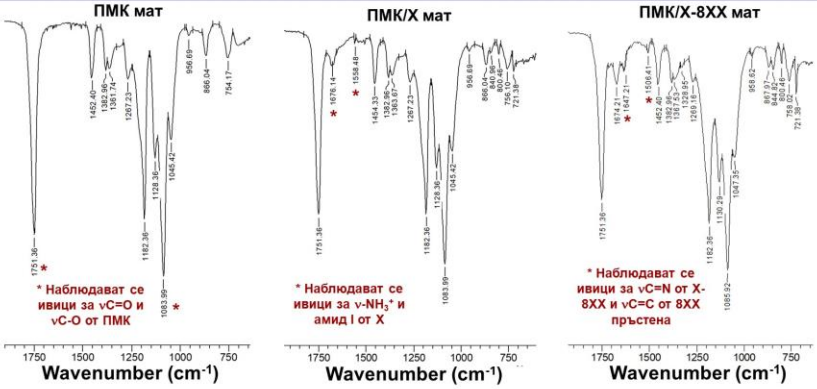


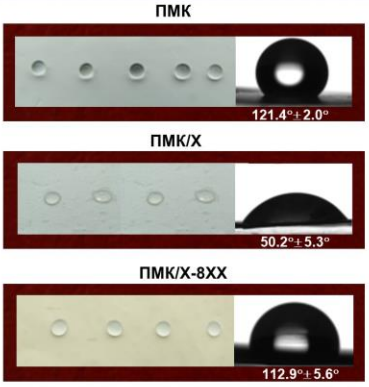
$Ar = C_9H_7NO$

антимикробна и противотуморна активност



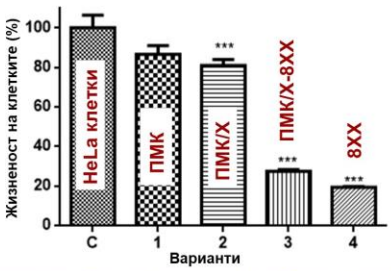
ИЧ спектри и ъгъл на омокряне



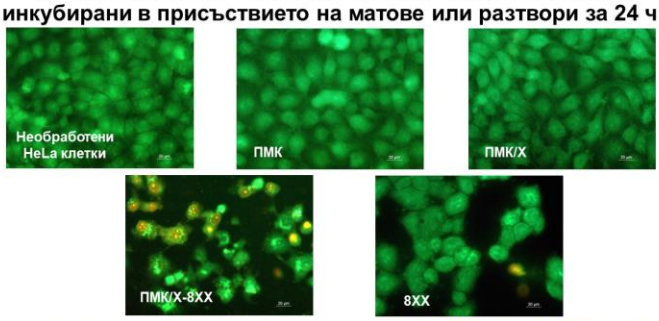


Противотуморна активност на влакнестите материали

Жизненост на HeLa ракови клетки, тествана чрез MTT метод за 72 ч инкубиране с различни варианти



Флуоресцентни микрографии на HeLa ракови клетки, двойно оцветени с акридин оранж и етидиев бромид, инкубирани в присъствието на матове или разтвори за 24 ч



Заключение: За първи път бяха успешно получени нови влакнести материали от ПМК и Х-8ХХ чрез едноетапно електроовлакняване. Охарактеризирани са структурата, морфологията и хидрофилно-хидрофобните отнасяния на получените матове. Материалите проявяват висока цитотоксичност спрямо HeLa клетки от рак на шийката на матката. Тези свойства правят получените влакнести материали перспективни кандидати за локално приложение при лечение на ракови заболявания, представляващи сериозен проблем за здравеопазването.

Благодарност: Авторите изказват благодарност на ФНИ (Договор КП-06-Н39/13 от 09.12.2019 г.) за финансовата подкрепа.

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Постер 17

Non-phospholipid conjugate of poly(2-isopropyl-2-oxazoline) for design of surfactant vesicles

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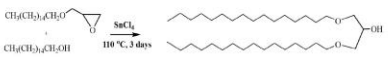
The development of a wide spectrum of nanoscale technologies is beginning to change the scientific landscape in terms of disease diagnosis, treatment, and prevention. In the field one of the fastest growing areas in the modern pharmaceutical nanoscale science and technology is targeted drug delivery. The practical realization of this concept is possible thanks to recent advances in nanotechnology. Among the array of nanoscale drug carriers, niosomes attract increasing scientific interest as promising drug delivery systems. They are composed of nonionic surfactants and cholesterol and offer several advantages as vesicles for drug encapsulation, codelivery of lipophilic/water insoluble and hydrophilic compounds, biocompatibility, low-immunogenicity, stability (physical, chemical and osmotic) and controlled release and targeting properties. By adding appropriately designed conjugates, the membranes of niosomes can be modified. This strategy offers many possibilities for fabricating highly effective carriers which, in addition, can release the incorporated drugs in a controlled manner. In this regard, a non-phospholipid conjugate of poly(2-isopropyl-2-oxazoline) was synthesized using "click" chemistry reaction and characterized in detail. Novel noisome formulations using various surfactants and a poly(2-isopropyl-2-oxazoline) non-phospholipid conjugate were prepared.

Keywords: click chemistry, niosomes, poly(2-isopropyl-2-oxazoline)s

Synthesis and characterization of mono-azide terminated DHP-N_3 macroagent

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

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



Scheme 1. The epoxide ring opening reaction.

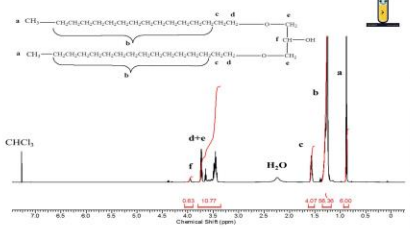
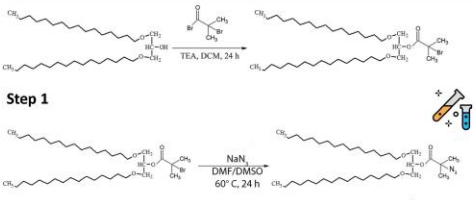


Figure 1. ^{1}H NMR spectrum of the purified DHP-OH product.

2. Two step procedure involving esterification of the primary hydroxyl end groups of DHP with 2-bromoisobutyryl bromide and reaction with sodium azide.



Scheme 2. Synthesis of azide terminated DHP.

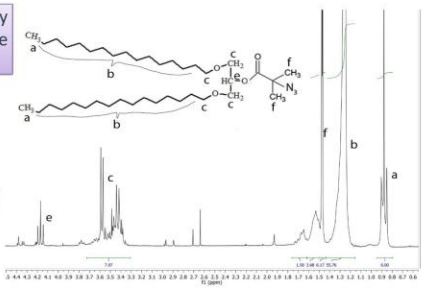
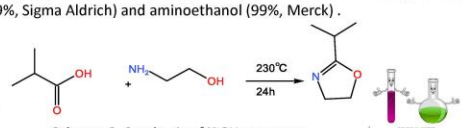


Figure 2. ^{1}H NMR spectrum of the mono-azide functionalized DHP.

Synthesis of mono-alkyne functional poly(2-isopropyl-2-oxazoline) (PiPOX-C≡CH) macroagent

1. Synthesis of 2-isopropyl-2-oxazoline (iPOX).

2-isopropyl-2-oxazoline (iPOX) was synthesized from isobutyric acid (99%, Sigma Aldrich) and aminoethanol (99%, Merck) .



Scheme 3. Synthesis of iPOX monomer.

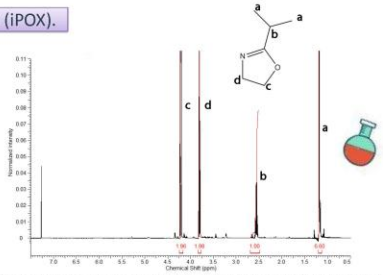
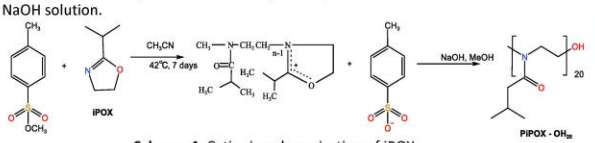


Figure 3. ^{1}H NMR spectrum of the purified iPOZ monomer.

2. Cationic polymerization of 2-isopropyl-2-oxazoline (iPOX).

Poly(2-isopropyl-2-oxazoline) bearing end hydroxyl functionality was obtained via cationic polymerization of 2-isopropyl-2-oxazoline initiated by methyl p-tosylate. Hydroxyl functionality was introduced by treating the reaction mixture with a methanolic NaOH solution.



Scheme 4. Cationic polymerization of iPOX.

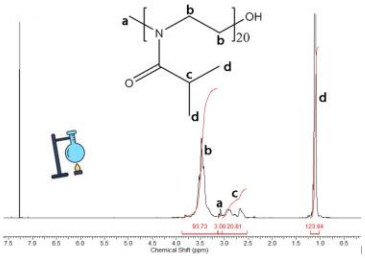
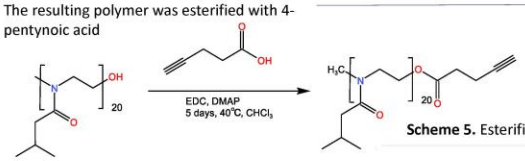


Figure 4. ^{1}H NMR spectrum of the purified PiPOX-OH.

3. Esterification of PiPOX-OH.

The resulting polymer was esterified with 4-pentynoic acid



Scheme 5. Esterification of PiPOX-OH.

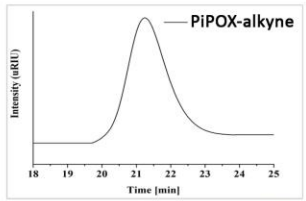


Figure 6. GPC chromatogram of the mono-alkyne functional poly(2-isopropyl-2-oxazoline) (PiPOX-C≡CH) macroagent (RI trace, THF).

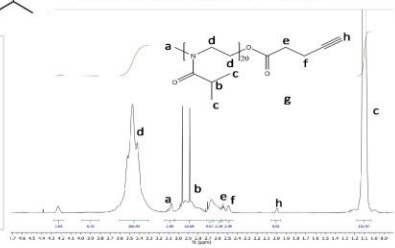
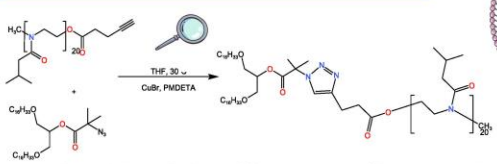


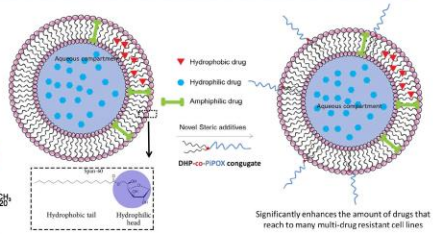
Figure 5. ^{1}H NMR spectrum of the mono-alkyne functional poly(2-isopropyl-2-oxazoline) (PiPOX-C≡CH) macroagent.

Synthesis of DHP-co-PiPOX conjugate

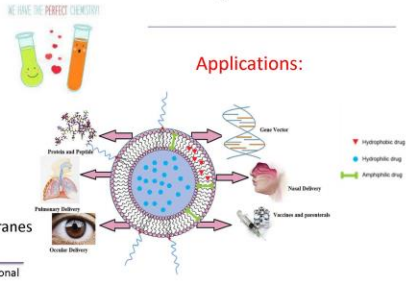


Scheme 6. General scheme of the preparation of the DHP-co-PiPOX conjugate via cooper catalyzed azide-alkyne "click" coupling reaction.

Preparation of novel noisome formulations



Scheme 7. Preparation and modification of niosomes membranes by adding DHP-co-PiPOX conjugate .



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