BBCE

Summer School 2024

Biomaterials Erlangen

FAU FRIEDRICH-ALEXANDER UNIVERSITÄT ERLANGEN-NÜRNBERG FACULTY OF ENGINEERING

HORIZON 2020

Teaming Phase 2

Baltic Biomaterials Centre of Excellence

Book of Abstracts

BBCE Summer School 2024

14-18 October 2024

Erlangen, Germany

Organized by Marcela Arango-Ospina, Zoya Hadzhieva and Prof. Aldo R. Boccaccini

(Institute of Biomaterials, FAU)

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 857287

BBCE

Summer School 2024

Biomaterials Erlangen

FAU FRIEDRICH-ALEXANDER UNIVERSITÄT ERLANGEN-NÜRNBERG FACULTY OF ENGINEERING

HORIZON 2020

Teaming Phase 2

Baltic Biomaterials Centre of Excellence

Physically crosslinked calcium phosphates containing hydrogels

Betija Grinberga[1,2], **Dagnija Loca**[1,2]

[1] Institute of Biomaterials and Bioengineering, Faculty of Natural Sciences and Technology, Riga Technical University, Pulka 3, Riga LV-1007, Latvia

[2] Baltic Biomaterials Centre of Excellence, Headquarters at Riga Technical University, Riga, Latvia

The design of multifunctional hydrogels based on bioactive hyaluronic acid (HA) and antibacterial ε-poly-L-lysine (ε-PL) is a promising tool for treating bone infections like osteomyelitis. Electrostatic interactions between the negatively charged carboxyl groups of HA and the positively charged amino groups of ε-PL result in physically crosslinked injectable hydrogels, eliminating the need for toxic crosslinking agents [[1],2].

In the current research, HA/ε-PL hydrogels were modified with calcium phosphates - hydroxyapatite (HAp, Ca/P molar ratio of 1.67) and calcium deficient hydroxyapatite (CDHAp, Ca/P molar ratio of 1.5) to mimic the composition of the natural bone. Multiple compositions were prepared (CaP:(HA/ ε-PL) ratios 50:50, 60:40, 70:30) and characterized for their physico-chemical, mechanical, rheological, and antimicrobial properties.

Obtained results showed that the lowest gel fraction value (indicating the degree of crosslinking) was found for 50:50 CaP:(HA/ε-PL) composite hydrogels (~86% for both HAp and CDHAp), while 60:40 CaP: (HA/ ε-PL) exhibited the best mechanical properties, cross-linking and stability in cell culture media. The 70:30 CaP:(HA/ε-PL) composite hydrogels did not show antimicrobial efficacy, whereas 60:40 CaP: (HA/ ε-PL) had the best antimicrobial activity.

To determine the best hydrogel composition for future biomedical applications, further exploration of their influence on cellular behaviour and tissue regeneration is needed.

References

[1] K. Salma-Ancane, A. Sceglovs, E. Tracuma, J.K. Wychowaniec, K. Aunina, A. Ramata-Stunda, V. Nikolajeva, D. Loca. Effect of crosslinking strategy on the biological, antibacterial and physicochemical performance of hyaluronic acid and ε-polylysine based hydrogels. Int J Biol Macromol, **2022**, 208, 995-1008.

[2] R. Sikkema, B. Keohan, I. Zhitomirsky. Hyaluronic-Acid-Based Organic-Inorganic Composites for Biomedical Applications. Mater., **2021**, 14, 4982.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 857287

HORIZON 2020

Teaming Phase 2

Baltic Biomaterials Centre of Excellence

Acknowledgement

This project has received funding from the European Union's Horizon 2020 research and innovation programme Baltic Biomaterials Centre of Excellence (BBCE) under grant agreement No 857287.

BBCE

Summer School 2024

Biomaterials Erlangen

FAU FRIEDRICH-ALEXANDER UNIVERSITÄT ERLANGEN-NÜRNBERG FACULTY OF ENGINEERING

HORIZON 2020

Teaming Phase 2

Baltic Biomaterials Centre of Excellence

The Impact of *IL1B rs1143634* and *DEFB1 rs11362* variants on Periodontitis Risk in Phenylketonuria and Type 1 Diabetes Mellitus Patients in a Latvian Population

Darta Elizabete Emulina [1,2*,†], Iveta Abola [1,2,†], Anda Brinkmane [1], Aleksejs Isakovs [2], Ingus Skadins [3], Georgijs Moisejevs [2,4], Linda Gailite [2] and Madara Auzenbaha [2,3,5]

[1] Department of Conservative Dentistry and Oral Health, Riga Stradins University, LV-1007 Riga, Latvia; (D.E.E.); (I.A.); (A.B.)

[2] Scientific Laboratory of Molecular Genetics, Riga Stradins University, LV-1007 Riga, Latvia; (D.E.E.); (I.A.); (A.I.); (G.M.); (L.G.); (M.A.)

[3] Department of Biology and Microbiology, Riga Stradins University, LV-1007 Riga, Latvia; (I.S.); (M.A)

[4] Jekabpils Regional Hospital, LV-5201 Jekabpils, Latvia; (G.M)

[5] Clinic of Medical Genetics and Prenatal Diagnostics, Children's Clinical University Hospital, LV-1004 Riga, Latvia; (M.A.)

† These authors contributed equally to this work

Objectives: Periodontitis is a multifactorial disease that affects approximately 11% of the global population. The objective of this study was to examine whether, among individuals with phenylketonuria and type 1 diabetes mellitus, those with the *IL1B rs1143634* and/or *DEFB1 rs11362* genetic variants exhibit a higher periodontitis risk compared to healthy controls. Materials and methods: 43 phenylketonuria patients (aged 12–53), 28 type 1 diabetes mellitus patients (aged 11–40), and 63 healthy controls (aged 12–53) were included. The evaluation of periodontitis risk was conducted using the Silness–Löe plaque index, the Greene–Vermillion index, and an assessment for the necessity of calculus removal. Genetic variants *rs1143634* and *rs11362* were genotyped from salivary samples using restriction length polymorphism analysis. Results: The *DEFB1 rs11362* variant was associated with higher Silness–Löe and Greene–Vermillion index scores in phenylketonuria patients (p = 0.011 and p = 0.043, respectively). The *IL1B rs1143634* variant was associated with lower calculus removal necessity in type 1 diabetes

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 857287

mellitus patients (p = 0.030). Clinical examination showed the worst oral hygiene index scores for PKU patients. PKU patients also reported the least consistent tooth brushing and flossing habits. Conclusions: Genetic associations between *DEFB1 rs11362* and *IL1B rs1143634* variants and oral hygiene indices were observed in the PKU and T1DM groups, suggesting that genetic factors may contribute to periodontal health differences in these populations. Further research with a larger sample size is needed to confirm these findings and develop targeted oral health interventions.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 857287

Summer School 2024

HORIZON 2020

Teaming Phase 2

Baltic Biomaterials Centre of Excellence

Evaluation of calcium phosphate biomaterials: Enhancing the reliability of *in vitro* cytotoxicity analysis

I. Kovrlija[1,2], K. Menshikh[3], H. Abreu[3], O. Marsan[4], C. Rey[4], C. Combes[4], L. Rimondini[3], J. Locs[1,2], D. Loca[1,2]

[1] Institute of Biomaterials and Bioengineering, Faculty of Natural Sciences and Technology, Riga Technical University, Pulka 3, Riga LV-1007, Latvia

[2] Baltic Biomaterials Centre of Excellence, Headquarters at Riga Technical University, Riga, Latvia

[3] Center for Translational Research on Autoimmune and Allergic Disease—CAAD, Department of Health Sciences, Università del Piemonte Orientale, 28100 Novara, Italy

[4] CIRIMAT, Toulouse INP, Université Toulouse 3 Paul Sabatier, CNRS, Université de Toulouse, ENSIACET, 4 allée Emile Monso, 31030 Toulouse cedex 4, France

As highly effective and reliable materials, calcium phosphates have been heavily utilized and investigated in the field of regenerative medicine. However, despite being highly biocompatible and osteogenic they still exhibit inconsistencies in basic cytotoxicity evaluations. The generalized approach, typically starting with cytocompatibility evaluation using the ISO 10993-5 standard as a reference (cell metabolic activity should exceed 70 % in extract tests) may not accurately reflect the material's behaviour when in direct contact with cells.

To evaluate cytocompatibility dependence on various experimental setups and material-cell interactions, amorphous calcium phosphate, α-tricalcium phosphate, hydroxyapatite, and octacalcium phosphate were tested (0.1 mg/mL to 5 mg/mL) with core cell lines of bone microenvironment: mesenchymal stem cells, osteoblast-like, and endothelial cells [1]. Physicochemical properties were analyzed both before and after contact with cells. Post-assay, materials identified as ‘cytotoxic’ underwent further investigation using a modified Annexin-V apoptosis assay to accurately determine cell death.

The obtained results showed that indirect cell-material contact following ISO standards had satisfactory cell metabolic activities, but direct contact tests at physiological concentrations revealed decreased metabolic activity and viability.

Obtained findings offer valuable guidelines for handling powder biomaterials, to better assess their biological effectiveness and avoid false negatives generally linked with traditional ISO standard approach.

This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 857287

HORIZON 2020

Teaming Phase 2

Baltic Biomaterials Centre of Excellence

Acknowledgements

This project has received funding from the European Union's Horizon 2020 research and innovation programme Baltic Biomaterials Centre of Excellence (BBCE) under grant agreement No 857287.

References

[1] Kovrlija I., K. Menshikh, H. Abreu, A. Cochis, L. Rimondini, O. Marsan, C. Rey, C. Combes, J. Locs, D. Loca, Challenging Applicability of ISO 10993-5 for Calcium Phosphate Biomaterials Evaluation: Towards More Accurate In Vitro Cytotoxicity Assessment, Biomaterials Advances, 160, 213866, 2024.

BBCE

Summer School 2024

Biomaterials Erlangen

FAU FRIEDRICH-ALEXANDER UNIVERSITÄT ERLANGEN-NÜRNBERG FACULTY OF ENGINEERING

HORIZON 2020

Teaming Phase 2

Baltic Biomaterials Centre of Excellence

Genus Vaccinium Fruit Extracts as a source of antioxidants: Quantitative Comparison Against Common Polyphenols

Daniela Paula Prudņikova[1,2], **Ance Bārzdiņa**[1,2]

[1]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Rīga Stradiņš University, Rīga, Latvia

[2]Baltic Biomaterial Centre of Excellence, Headquarters at Rīga Technical University, Rīga, Latvia

Bilberry extracts are highly valued for their health benefits, particularly their anti-inflammatory and antioxidative properties, as well as their positive effects on vascular health and glucose regulation. [1] They contain a range of phytochemicals, including phenolic acids, anthocyanins, and flavanols.[2] However, it is crucial to evaluate whether these beneficial properties are consistent across all *Vaccinium* genus fruit extracts, including highbush blueberries. This study aimed to compare the antioxidative properties of extracts from highbush blueberries and bilberries, analyze their polyphenolic composition, and compare their antioxidant properties to common polyphenol standards. The antioxidative activity was evaluated using the DPPH radical scavenging assay, with IC50 values calculated for both extracts. The IC50 values for highbush blueberry extracts ranged from 2.19 to 4.44 mg/mL, while bilberry extracts demonstrated lower values of 0.52 to 0.84 mg/mL, indicating that bilberry extracts possess stronger antioxidative activity. UHPLC-MS/MS analysis identified several phenolic acids, such as chlorogenic acid, caffeic acid and more. Although the IC50 values for both highbush blueberry and bilberry extracts were relatively higher than the polyphenol standards, which ranged from 11.2 to 88.9 µg/mL, these fruits could serve as valuable sources of polyphenols for optimizing the use of natural antioxidants in drug delivery.

Acknowledgements

The authors acknowledge the access to the infrastructure and expertise of the BBCE—Baltic Biomaterials Centre of Excellence (European Union's Horizon 2020 research and innovation programme under the grant agreement No. 857287).

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 857287

HORIZON 2020

Teaming Phase 2

Baltic Biomaterials Centre of Excellence

References

1. Kalt W, Cassidy A, Howard LR, Krikorian R, Stull AJ, Tremblay F, Zamora-Ros R. Recent Research on the Health Benefits of Blueberries and Their Anthocyanins. Adv Nutr. 2020 Mar 1;11(2):224-236. doi: 10.1093/advances/nmz065. PMID: 31329250; PMCID: PMC7442370.

2. Gibson L, Rupasinghe HP, Forney CF, Eaton L. Characterization of Changes in Polyphenols, Antioxidant Capacity and Physico-Chemical Parameters during Lowbush Blueberry Fruit Ripening. Antioxidants (Basel). 2013 Oct 15;2(4):216-29. doi: 10.3390/antiox2040216. PMID: 26784460; PMCID: PMC4665526.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 857287

Summer School 2024

HORIZON 2020

Teaming Phase 2

Baltic Biomaterials Centre of Excellence

Development of doxorubicin/octacalcium phosphate drug delivery systems

Marta Laizane[1,2], Ilijana Kovrlija[1,2], Janis Locs[1,2], Dagnija Loca[1,2]

[1] Institute of Biomaterials and Bioengineering, Faculty of Natural Sciences and Technology, Riga Technical University, Pulka 3, Riga LV-1007, Latvia

[2] Baltic Biomaterials Centre of Excellence, Headquarters at Riga Technical University, Riga, Latvia

e-mail: marta.laizane@rtu.lv

Octacalcium phosphate (OCP) is an osteoconductive material that promotes bone regeneration [1]. Its structure of interconnected apatite and water layers make it a promising candidate for drug delivery (DDS). Doxorubicin (DOX), a common chemotherapy drug, is effective but heavily associated with systemic toxicity. Doxorubicin/octacalcium phosphate (DOX-OCP) DDS could offer an alternative option for osteosarcoma treatment.

In this study, α-tricalcium phosphate and 1-20 theoretical DOX wt% were synthesized *in situ* to obtain DOX-OCP. DOX-OCPs physico-chemical properties were characterized by X-Ray Diffraction (XRD) and Fourier Transform Infrared Spectroscopy (FTIR). To confirm whether DOX was incorporated into the OCP during in situ synthesis or simply adsorbed onto the surface, OCP was added to a DOX solution and stirred for 24 hours. Determination of DOX release kinetics from both systems was performed with Ultraviolet–visible spectroscopy (UV-VIS).

The obtained results showed that >10 theoretical DOX wt% inhibited the formation of OCP phase. The incorporation of DOX into OCP structure was evident from physico-chemical characterization: XRD maxima at 4.7, 9.4, and 9.7 2Θ° shifted to lower angles and FTIR absorbance bands at 1111 and 464 cm^{-1} became more pronounced. Moreover, the release kinetics between the *in situ* synthesized DOX-OCPs and the adsorbed DOX-OCPs differed substantially.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 857287

HORIZON 2020

Teaming Phase 2

Baltic Biomaterials Centre of Excellence

Acknowledgements

The authors acknowledge financial support from the European Union's Horizon 2020 research and innovation programme under the grant agreement No. 857287 (BBCE – Baltic Biomaterials Centre of Excellence).

References

[1] Kovrlija, I., Locs, J., Loca D., Octacalcium phosphate: Innovative vehicle for the local biologically active substance delivery in bone regeneration. *Acta Biomater.*, **2021**, *135*, 27–47.

Summer School 2024

HORIZON 2020

Teaming Phase 2

Baltic Biomaterials Centre of Excellence

A method for quantification of hormones and vitamins using LC-MS.

Nikola Gabriela Matusevica[1,2], **Kajetan Nierychlewski**[3], **Maros Mastrak**[3], **Kristaps Klavins**[1,2]

[1]Institute of Biomaterials and Bioengineering, Faculty of Natural Sciences and Technology, Riga Technical University, Riga, Latvia

[2]Baltic Biomaterials Centre of Excellence, Headquarters at Riga Technical University, Riga, Latvia

[3]Physikit, Berlin, Germany

Hormones and vitamins are essential for organisms to function, so it is crucial in medical assays to acquire their precise concentrations, usually from plasma, serum, and blood. Dried blood spots (DBS) has emerged as a simple and minimally invasive method for blood collection. [1] Liquid chromatography coupled with mass spectrometry is analytical method that is widely used for quantitative and qualitative hormone and vitamin measurements. However, due to the different chemical structures and properties of hormones and vitamins, it is challenging to measure them using a single LC-MS analysis method. [2]

In this study, the goal was to develop a multi-analyte LC-MS/MS method for absolute quantification of 20 crucial hormones and vitamins in DBS samples. The analysis was performed on Agilent 1290 Infinity II Liquid UHPLC system coupled to SCIEX 7500 Triple Quadrupole Mass spectrometer. The separation was carried using ACQUITY UPLC HSS T3 (2.1x100 mm, 1.8 um) column. The mobile phase consisted of A - water with 0.2 mM NH4 fluoride and B - MeOH with 0.2 mM NH4 fluoride, gradient elution was applied with the total analysis time of 10 min. The developed LC-MS/MS method provides a fast and reliable analysis for 20 compounds in DBS samples.

Acknowledgements

This project has received funding from the European Union's Horizon 2020 research and innovation program Baltic Biomaterials Centre of Excellence (BBCE) under grant agreement No 857287.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 857287

References

[1] C.S.L.B. Jana Verstraete, «Dried blood microsample-assisted determination of vitamins: Recent developments and challenges,» *Trends in Analytical Chemistry,* vol. 132, 2020.

[2] V.H. E.N. R.V. M.Č. F.V.P.F. David Kahoun, «Development and validation of an LC-MS/MS method for determination of B vitamins and some its derivatives in whole blood,» *PLOS ONE, vol. 17,* 2022.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 857287

Summer School 2024

HORIZON 2020

Teaming Phase 2

Baltic Biomaterials Centre of Excellence

Effect of PEGylation of IGF-1-containing Liposomes on Gingival Mesenchymal Stem Cell Differentiation

Dana Galkina[1,2], **Arita Dubnika**[1,2]

[1] Institute of Biomaterials and Bioengineering, Faculty of Natural Sciences and Technology, Riga Technical University, Pulka 3, Riga LV-1007, Latvia

[2] Baltic Biomaterials Centre of Excellence, Headquarters at Riga Technical University, Riga, Latvia

Liposomes have been used for drug delivery for many years, with membranes composed of phospholipid bilayers surrounding an internal aqueous core [1]. Insulin-like growth factor-1 (IGF-1) can be encapsulated into the aqueous core of liposomes, enabling sustained release.

Gingival mesenchymal stem cells (GMSCs) are non-hematopoietic adult stem cells capable of osteogenic, chondrogenic, and adipogenic differentiation, making them ideal for treating various pathologies [2]. This study aims to investigate how PEGylation of IGF-1-containing liposomes affects GMSC differentiation for potential use in regenerative therapies, such as repairing small bone defects.

To minimize liposome aggregation, PEGylation was performed using 1,2-distearoyl-sn-glycero-3-PE/polyethylene glycol (DSPE-PEG) to modify the liposome surface [3]. Liposomes composed of DSPC and DSPC with DSPE-PEG were synthesized via thin-film hydration, with IGF-1 added in phosphate buffered saline (PBS) solution during the hydration process.

Dynamic light scattering (DLS) analysis revealed that DSPE-PEG had minimal impact on liposome size without IGF-1 (DSPC: 660 ± 70 nm, PEGylated: 640 ± 120 nm). However, PEGylation significantly reduced the size of IGF-1-loaded liposomes (DSPC: 1430 ± 210 nm, PEGylated: 310 ± 20 nm).

Future experiments will assess the effect of PEGylation on IGF-1 release kinetics and GMSC differentiation to optimize therapeutic potential.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 857287

References

[1] A. C.-P. E. N. Diana Guimarães, «Design of liposomes as drug delivery system for therapeutic applications,» *International Journal of Pharmaceutics, vol*. 601, 2021.

[2] J. J. S. D. T. Yuanyuan Peng, «Gingival mesenchymal stem cells: Biological properties and therapeutic applications,» *Journal of Oral Biology and Craniofacial Research, vol*. 14, nr. 5, pp. 547-569, 2024.

[3] P. C. G. H. S. a. H. J. P. Ji Young Yu, «Post-Processing Techniques for the Improvement of Liposome Stability,» *Pharmaceutics, vol*. 13, nr. 7, p. 1023, 2021.

Acknowledgements

This project has received funding from the European Union's Horizon 2020 research and innovation programme Baltic Biomaterials Centre of Excellence (BBCE) under grant agreement No 857287.

This research has received funding from the M-era.Net 2 project INJECT-BIO under agreement No. ES RTD/2020/14

Summer School 2024

HORIZON 2020

Teaming Phase 2

Baltic Biomaterials Centre of Excellence

Alginate-based inks for 3D bioprinting

L. Dauge[1,2], J. Vecstaudza[1,2] , J. Locs[1,2]

[1]Institute of Biomaterials and Bioengineering, Faculty of Natural Sciences and Technology, Riga Technical University, Pulka 3, Riga LV-1007, Latvia

[2]Baltic Biomaterials Centre of Excellence, Headquarters at Riga Technical University, Riga, Latvia

Three-dimensional (3D) bioprinting is a promising approach in biomaterial technology. The 3D building blocks are often hydrogel-based inks, which need to be printed into structures with high resolution. Alginate is frequently used as a biocompatible hydrogel [1], but the low viscosity makes it unsuitable for obtaining stable 3D structures. In this study, we observed how variations in biopolymer concentration, additives, and printing parameters influenced the final product.

The printing precision was characterised using the spreading ratio and the deposition accuracy of the inks. Three parallel lines were printed each time and the data for the calculations was obtained with *ImageJ* software. All compositions contained alginate, gelatine and glycerin. The printing tips used were conical and needle type, both 22G.

Obtained results showed that the optimal ink composition contained at least 3 w/v% alginate, in combination with 10 w/w% gelatine and at least 25 w/w% glycerin. If the alginate concentration was <10 w/v%, the print precision was higher with the needle tip, but if the concentration was ≥10 w/v%, the conical tip performed better. Optimal printing speed was 30–35 mm/s.

Evaluation of the compositional parameters laid the foundation for further research on addition of other bioactive additives and cellular components.

Acknowledgement

This project has received funding from the European Union's Horizon 2020 research and innovation programme Baltic Biomaterials Centre of Excellence (BBCE) under grant agreement No 857287.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 857287

HORIZON 2020

Teaming Phase 2

Baltic Biomaterials Centre of Excellence

References

[1] Piras, C. C., Smith, D. K. *J. Mater. Chem. B,* 2020, **8**, 8171

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 857287

Summer School 2024

HORIZON 2020

Teaming Phase 2

Baltic Biomaterials Centre of Excellence

Sulfoxides at the Forefront: Enhancing Chemical Processes and Biomedical Innovation

Mahuya Pakhira[1,2], **Antons Sizovs**[1,2]

[1]Latvian Institute of Organic Synthesis, Riga, Latvia, LV-1006; [2]Baltic Biomaterials Centre of Excellence, Headquarters at Riga Technical University, Riga, Latvia, LV-1007.

Sulfoxides are increasingly recognized for their versatility across a wide range of scientific applications due to their unique chemical and physical properties [1,2]. Sulfoxide derivatives have demonstrated utility in asymmetric synthesis and catalysis, providing efficient routes for producing chiral compounds in chemical processes [3]. The versatility of the sulfoxide group also extends to environmental applications, including the design of new solvents and reagents with reduced toxicity [4]. The polar nature of the sulfoxide group, coupled with its ability to form hydrogen bonds, allows for enhanced solubility, stability, and biocompatibility and making them ideal for constructing delivery systems that efficiently transport therapeutic nucleic acids, such as DNA or RNA, into target cells [5]. Their ability to stabilize active compounds and modify pharmacokinetics makes them valuable in the development of pharmaceuticals and prodrugs. Sulfoxide-based materials can be engineered into polymers or nanoparticles, which offer protective environments for nucleic acids, preventing degradation by nucleases and enhancing cellular uptake [6]. The expanding influence of sulfoxides in gene therapy highlights their potential to transform therapeutic delivery, paving the way for better clinical results in various biomedical domains.

Acknowledgements

Authors acknowledge support by the Gints Smits group of the Latvian Institute of Organic Synthesis and financial support from the European Union's Horizon 2020 research and innovation programme under the grant agreement No. 857287 (BBCE – Baltic Biomaterials Centre of Excellence).

References

[1]M. C. Carreño, Chem. Rev. 1995, 95, 1717-1760.

[2] I. Fernández, N. Khiar, Chem. Rev. 2003, 103, 3651-3706.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 857287

[3] N. Khiar, S. Werner, S. Mallouk, F. Lieder, A. Alcudia, I. Fernández, J. Org. Chem. 2009, 74, 6002-6009.

[4] J. Wei, Z. Sun, Org. Lett. 2015, 17, 5396-5399.

[5] D. Işık et.al Biomater. Sci., 2021, 9, 712.

[6] D. Işık, E. Quaasb, D. Klinger Polym. Chem., 2020, 11, 7662.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 857287

Summer School 2024

HORIZON 2020

Teaming Phase 2

Baltic Biomaterials Centre of Excellence

Ultra-High Molecular Weight PEG-Based Polymers for Enhanced Cancer Nanotherapy

Mingjia Chen[1,2], **Antons Sizovs**[1,2,*]

[1]Latvian Institute of Organic Synthesis, LV-1050, Riga, Latvia

[2]Baltic Biomaterials Centre of Excellence, Headquarters at Riga Technical University, LV-1007 Riga, Latvia

The application of nanomedicine in cancer therapy via the Enhanced Permeability and Retention (EPR) effect has been widely explored for its potential drug delivery. However, significant variability in the EPR effect across different cancer types and among individuals has limited its therapeutic success. Bottleneck brush PEG-based polymers have demonstrated potential in cancer therapy, but synthesizing Ultra-high Molecular Weight (UHMW) PEG-based polymers is challenging, and controlling a defined molecular weight adds further complexity.[1, 2] To address this, we synthesized a series of UHMW bottleneck brush PEG-based polymers, achieving number-average molecular weights exceeding 1 million. Our synthetic approach ensures precise control over molecular weight distribution, facilitating reproducible and uniform nanoparticle formation. These polymers self-assemble into highly stable nanoparticles, exhibiting robust resistance to opsonization and prolonged systemic circulation. Nanoparticles of different sizes displayed considerable differences in tumor accumulation and retention. This study demonstrates the crucial role of bottleneck brush PEG-based polymers in advancing EPR-based cancer therapies by offering enhanced control over nanoparticle properties and improving the predictability of therapeutic outcomes.

Acknowledgements

The authors acknowledge financial support from the European Union's Horizon 2020 research and innovation programme under the grant agreement No. 857287 (BBCE – Baltic Biomaterials Centre of Excellence) and Latvian Council of Science grant lzp-2021/1-0593.

References

1. Zhang, X. and Y. Dai, *Recent development of brush polymers via polymerization of poly (ethylene glycol)-based macromonomers*. Polymer Chemistry, 2019. **10**(18): p. 2212-2222.
2. Klimkevicius, V. and R. Makuska, *Successive RAFT polymerization of poly (ethylene oxide) methyl ether methacrylates with different length of PEO chains giving diblock brush copolymers*. European Polymer Journal, 2017. **86**: p. 94-105.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 857287