proceedings

MDPI

Abstract

Synthesis and Characterization of a Novel Nanomicellar System Pluronic-PEI Suitable for Gene and Drug Co-Delivery in Cancer Therapy †

Cátia Domingues [1,2,3], Ivana Jarak [1], Carla Varela [4,5], Elisiário Tavares [4,5], Fernanda Roleira [4,5], Carmen Alvarez-Lorenzo [6], Angel Concheiro [6], Rui de Carvalho [7,8], Francisco Veiga [1,2], Marília Dourado [3,9,10] and Ana Figueiras [1,2,*]

1 Laboratory of Pharmaceutical Technology, Faculty of Pharmacy, Pólo III Campus—Health Sciences, University of Coimbra, Azinhaga de Santa Comba, 3000-548 Coimbra, Portugal; cdomingues@ff.uc.pt (C.D.); jarak.ivana@gmail.com (I.J.); fveiga@ci.uc.pt (F.V.)
2 LAQV, REQUIMTE, Faculty of Pharmacy, Pólo III Campus—Health Sciences, University of Coimbra, Azinhaga de Santa Comba, 3000-548 Coimbra, Portugal
3 Institute for Clinical and Biomedical Research (iCBR) Area of Environment Genetics and Oncobiology (CIMAGO), Faculty of Medicine, Pólo III Campus—Health Sciences, University of Coimbra, Azinhaga de Santa Comba, 3000-548 Coimbra, Portugal; mdourado@ff.uc.pt
4 Laboratory of Pharmaceutical Chemistry, Faculty of Pharmacy, Pólo III Campus—Health Sciences, University of Coimbra, Azinhaga de Santa Comba, 3000-548 Coimbra, Portugal; carlalvarela@gmail.com (C.V.); etavares@ff.uc.pt (E.T.); froleira@ff.uc.pt (F.R.)
5 CIEPQPF, Centre for Chemical Processes Engineering and Forest Products, Pólo I Campus, University of Coimbra, 3004-504 Coimbra, Portugal
6 Departamento de Farmacología, Farmacia y Tecnología Farmacéutica, I+D Farma (GI-1645), Facultad de Farmacia and Health Research, Institute of Santiago de Compostela (IDIS), Universidade de Santiago de Compostela, 15782 Santiago de Compostela, Spain; carmen.alvarez.lorenzo@usc.es (C.A.-L.); angel.concheiro@usc.es (A.C.)
7 Center for Innovative Biomedicine and Biotechnology (CIBB), Pólo I Campus, University of Coimbra, 3004-504 Coimbra, Portugal; rac@uc.pt
8 LAQV, REQUIMTE, Department of Life Sciences, Faculty of Sciences and Technology, Pólo I Campus, University of Coimbra, 3004-504 Coimbra, Portugal;
9 Center for Health Studies and Research of the University of Coimbra (CEISUC), Faculty of Medicine, Pólo III Campus—Health Sciences, University of Coimbra, Azinhaga de Santa Comba, 3000-548 Coimbra, Portugal
10 Center for Studies and Development of Continuous and Palliative Care (CEDCCP), Faculty of Medicine, Faculty of Medicine, Pólo III Campus—Health Sciences, University of Coimbra, Azinhaga de Santa Comba, 3000-548 Coimbra, Portugal
* Correspondence: rfigueiras@ff.uc.pt
† Presented at the 1st International Electronic Conference on Pharmaceutics, 1–15 December 2020; Available online: https://iecp2020.sciforum.net/.

Citation: Domingues, C.; Jarak, I.; Varela, C.; Tavares, E.; Roleira, F.; Alvarez-Lorenzo, C.; Concheiro, A.; de Carvalho R.; Veiga, F.; Dourado, M.; et al. Synthesis and Characterization of a Novel Nanomicellar System Pluronic-PEI Suitable for Gene and Drug Co-Delivery in Cancer Therapy. *Proceedings* **2021**, *78*, 36. https://doi.org/10.3390/IECP2020-08795

Published: 1 December 2020

Abstract: Polyethyleneimine (PEI) is a synthetic cationic polymer recognized as a non-viral gene carrier with high transfection efficiency. However, cytotoxicity issues limit its use. Pluronic block-copolymers conjugated with PEI have demonstrated promising results for multiparametric target gene/drug co-delivery in cancer with reduced side effects. The goal of this work was to synthesize and characterize a novel nanosystem Pluronic L121-PEI for gene/drug co-delivery. For this purpose, hydroxyl groups from Pluronic were activated using acryloyl chloride leading to the synthesis of a diacrylate intermediate, which was further conjugated with PEI. FTIR and ^{1}H-NMR spectroscopy were used for structural characterization. Particle size, polydispersity index (PDI) and zeta potential were assessed by dynamic and electrophoretic light scattering, respectively. A fluorescent pyrene probe was used to evaluate the critical micellar concentration (CMC). A hemolysis experiment was performed to estimate the in vitro biocompatibility of the nanosystem. FTIR analysis showed that Pluronic diacrylate was successfully synthetized as a new band around 1730 cm^{-1} (C=O bond) appears. Its conjugation with PEI was confirmed by the presence of a band between 3380 and 3390 cm^{-1} (N–H bond). ^{1}H-NMR results showed characteristic proton peaks from Pluronic (-CH3 at δ1.1

ppm) and from PEI (-CH2-CH2NH- between δ2.7–3.4 ppm) and the molar ratio Pluronic–PEI was 1:2. The nanoparticles' hydrodynamic diameter was ca. 125 nm with a PDI below 0.250, and a charge nearby +30 mV. The CMC was around 50 μg/mL. The hemolysis ratio of a 5 mg/mL nanomicellar solution was less than 5%. A novel Pluronic L121-PEI was successfully synthesized, which was able to self-assemble in aqueous solution leading to the formation of biocompatible cationic polymeric micelles. Their small size is suitable for tumor-targeting and as they are positively charged they can be also valuable for gene delivery. Overall, this new nanosystem could be a promising multiparametric nanoapproach for gene/drug co-delivery in cancer therapy.

Keywords: cancer therapy; gene/drug co-delivery; Pluronic L121; polyethyleneimine; nanosystems

Funding: This work received financial support from PT national fund (FCT/MCTES, Fundação para a Ciência e Tecnologia and Ministério da Ciência, Tecnologia e Ensino Superior) through the projects UIDB/50006/2020, co-financed by European Union (FEDER under the Partnership Agreement PT2020). It was also supported by the grant FCT, PTDC/BTM-MAT/30255/2017(POCI-01-0145-FEDER-030255), from the Portuguese Foundation for Science and Technology (FCT) and the European Community Fund (FEDER) through the COMPETE 2020 program.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: For more detailed information please take a look at our presentation: https://sciforum.net/manuscripts/8795/slides.pdf.

References

1. Da Domingues, C.S.C.; Serambeque, B.P.; Laranjo Cândido, M.S.; Marto, C.M.M.; de Veiga, F.J.B.; Sarmento Antunes Cruz Ribeiro, A.B.; Figueiras, A.R.R.; Botelho, M.F.R.; de Dourado, M.A.R.F. Epithelial-mesenchymal transition and microRNAs: Challenges and future perspectives in oral cancer. *Head Neck* **2018**, doi:10.1002/hed.25381.
2. Domingues, C.; Alvarez-Lorenzo, C.; Concheiro, A.; Veiga, F.; Figueiras, A. Nanotheranostic Pluronic-Like Polymeric Micelles: Shedding Light into the Dark Shadows of Tumors. *Mol. Pharm.* **2019**, *16*, 4757–4774, doi:10.1021/acs.molpharmaceut.9b00945.