Taylor & Francis
Taylor & Francis Group

Annals of Medicine

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/iann20

Layer-by-layer coated silicone-based soft contact lens hydrogel for diclofenac sustained release

Diana Silva, Hermínio C. de Sousa, Maria Helena Gil, Carmen Alvarez-Lorenzo, Benilde Saramago & Ana Paula Serro

To cite this article: Diana Silva, Hermínio C. de Sousa, Maria Helena Gil, Carmen Alvarez-Lorenzo, Benilde Saramago & Ana Paula Serro (2021) Layer-by-layer coated silicone-based soft contact lens hydrogel for diclofenac sustained release, Annals of Medicine, 53:sup1, S22-S23, DOI: 10.1080/07853890.2021.1896898

To link to this article: https://doi.org/10.1080/07853890.2021.1896898

Published online: 28 Sep 2021.

Table 1. Effect of the LP content on the properties of the Chi containing CPC.

LP content (%)	Initial setting time (min)	Final setting time (min)	Compressive strength (MPa)	Hardness (HV)	Injectability (%)
30	6.5	7.5	9.53±1.00	10.56±1.27	Not injectable
38	11.5	14	9.49±0.80	13.25±1.38	30.65±2.28
42	12.25	15.25	7.66±0.56	12.21±0.55	91.04±0.71
50	24	32	0.83±0.20	2.48±0.62	a)

a) Not tested because the setting times and mechanical properties do not suit clinical applications.

the cytotoxicity of the commercial CPC was assessed using MG63 and NIH/3T3 cell lines following the ISO 10993-5 guidelines.

Results: As shown in Table 1, increasing the LP content from 30% to 50% increased the initial setting time from 6.5 min to 24 min, and the final setting time from 7.5 min to 32 min. Concerning the resistance to compression, it was lowered from 9.53 ± 1.00 MPa to 0.83 ± 0.20 MPa. Regarding materials' hardness, it decreased by 77%. Injectability measurements showed that only 38% and 42%LP formulations could be injected. Nonetheless, while 38%LP formulation presented an injectability of 31 ± 2%, 42%LP formulation showed an injectability of 91 ± 1%. As for the addition of HPMC, for 38%LP formulation an initial setting time of 6.5 min and a final setting time of 10.5 min were measured, and for 42%LP formulation 12 min and 14.5 min, respectively. The mechanical properties presented similar values regardless the added polymer. Moreover, the formulations containing HPMC presented 69 ± 6% injectability for 38%LP and 94 ± 1% for 42%LP. Finally, when in contact with extracts of the commercial CPC for 24 h, the studied cell lines presented viability greater than 75% when compared to unexposed cells.

Discussion and conclusions: Our study shows that LP content has a significant impact on the CPC studied properties. Effectively, for 38 and 42%LP the setting times, resistance to compression and hardness of the materials assume suitable values for their use as trabecular bone defect fillers. For the Chi CPC, 42%LP formulation is ~200% more injectable than the 38%LP one. Even though the replacement of Chi by HPMC does not affect the mechanical properties significantly, HPMC itself seems to promote injectability, increasing it by 126%. Finally, the commercial CPC does not show a cytotoxic effect under the conditions of this assay.

CONTACT M. Reis marta.m.reis18@gmail.com

Acknowledgements

The authors acknowledge Fundação para a Ciência e Tecnologia for funding through the unit projects UID/QUI/00100/2019, UID/BIM/04585/2019 and UID/EMS/50022/2019 from CQE, CiiEM and IDMEC.

References

[1] Zhang J, Liu W, Schnitzler V, et al. Calcium phosphate cements for bone substitution: chemistry, handling and mechanical properties. Acta Biomater. 2014;10(3):1035–1049.

[2] O'Neill R, et al. Critical review: injectability of calcium phosphate pastes and cements. Acta Biomater. 2017;50:1–19.

DOI: 10.1080/07853890.2021.1896897

Layer-by-layer coated silicone-based soft contact lens hydrogel for diclofenac sustained release

Diana Silva[a], Hermínio C. de Sousa[b], Maria Helena Gil[b], Carmen Alvarez-Lorenzo[c], Benilde Saramago[a] and Ana Paula Serro[a,d]

[a]CQE, Instituto Superior Técnico, Universidade de Lisboa, Lisboa, Portugal; [b]CIEPQPF, Departamento de Engenharia Química, Universidade de Coimbra, Coimbra, Portugal; [c]Departamento de Farmacología, Farmacia y Tecnología Farmacéutica, R + D Pharma Group (GI-1645), Facultad de Farmacia and Health Research Institute of Santiago de Compostela (IDIS), Universidade de Santiago de Compostela, Santiago de Compostela, Spain; [d]Centro de Investigação Interdisciplinar Egas Moniz (CiiEM), Egas Moniz Cooperativa de Ensino Superior, Caparica, Portugal

ABSTRACT

Introduction: Soft contact lenses (SCLs) constitute a promising vehicle for ocular drug delivery due to their biocompatibility, prolonged contact with the eye and general acceptance. Soaking in the drug solution is the simplest method to load the drug into the SCLs. However, it usually does not ensure a controlled drug release, compatible with the therapeutic needs. Thus, additional approaches, such as the application of coatings on the SCLs that constitute a barrier to the drug release, have been tried to achieve that purpose [1]. The main goal of this work is to investigate the possibility

of using a layer-by-layer (LbL) coating strategy, with alginate, chitosan and hyaluronic acid (ALG/CHI/HA) to get a controlled release of diclofenac from silicon based hydrogels.
Materials and methods: A lab-made silicon-based hydrogel intended for SCLs was loaded by soaking with the anti-inflammatory (diclofenac, DCF) and coated layer-by-layer (LbL) by immersion in solutions of alginate, chitosan and hyaluronic acid. Material properties such as transmittance, wettability, ionic permeability and swelling were studied. Drug release experiments were carried out under sink conditions (3 mL NaCl aqueous solution 130 mM, 36 °C, 180 rpm stirring). The coating stability and lysozyme-coating interaction was evaluated by quartz crystal microbalance with dissipation (QCM-D). A mathematical model was applied to predict the *in vivo* efficacy of the coated lenses. Chorioallantoic membrane (HET-CAM) tests were carried out to predict potential ocular irritation.
Results: The coating did not impair the studied physico-chemical properties, relevant for the application of the material in SCLs. HET-CAM tests did not suggest any potential for ocular irritation of both uncoated and coated samples. QCM-D data revealed the stability of the deposited layers and no adsorption of the protein. DCF release kinetics was controlled by the presence of the coating. The DCF concentration profile in the tear fluid estimated from the mathematical model predicts values above the half maximal inhibitory concentrations (IC_{50}) for cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) during more than 2 weeks, for the coated hydrogels, while for the uncoated such levels are only expected in the first day of release.
Discussion and conclusions: ALG/CHI/HA LBL coated silicon hydrogels present adequate properties to be used in DCF releasing SCLs. They reveal an antifouling behaviour against lysozyme, one of the most abundant protein in lacrimal fluid. *In vitro* studies suggest that such system has potential to be used in the production of efficient therapeutic SCLs.

CONTACT Diana Silva dianacristinasilva@tecnico.ulisboa.pt

Acknowledgements

To Fundação para a Ciência e a Tecnologia for Diana Silva PhD Grant (PD/BD/114088/2015), and funding through the unit projects UID/QUI/00100/2019 for CQE and UID/BIM/04585/2019 for CiiEM, and the research project (STReoSTRAT) PTDC/CTM-BIO/3640/2014. This work was also partially funded by Spanish MINECO (SAF2017-83118-R), Agencial Estatal de Investigación (AEI) and FEDER.

Reference

[1] Silva D, Sousa HC, Gil MH, et al. Antibacterial layer-by-layer coatings to control drug release from soft contact lenses material. Int J Pharma. 2018;553(1–2):186–200.

DOI: 10.1080/07853890.2021.1896898

Nanoencapsulation as a novel delivery approach for therapeutic applications of gla-rich protein (GRP)

Nuna Araújo[a], Carla Viegas[a,b], Jorge F. Pontes[a,c], Catarina Marreiros[a], Pedro Raimundo[d], Anjos L. Macedo[e], António Alves de Matos[f], Ana Grenha[a,c], Cees Vermeer[f] and Dina Costa Simes[a,b]

[a]Centre of Marine Sciences, University of Algarve, Algarve, Portugal; [b]GenoGla Diagnostics, CCMAR, University of Algarve, Algarve, Portugal; [c]Centre for Biomedical Research, University of Algarve, Algarve, Portugal; [d]Departamento de Ciências Biomédicas e Medicina, Universidade do Algarve, Algarve, Portugal; [e]UCIBIO-REQUIMTE, Departamento de Química, Faculdade de Ciências e Tecnologia, Universidade NOVA de Lisboa, Caparica, Portugal; [f]Centro de Investigação Interdisciplinar Egas Moniz (CiiEM), Egas Moniz Cooperativa de Ensino Superior, Caparica, Almada, Portugal; [g]Maastricht University, Maastricht, The Netherlands

ABSTRACT
Introduction: Gla rich protein (GRP) is a vitamin K dependent protein, shown to function as an inhibitor of pathological calcification and as an anti-inflammatory agent, with potential therapeutic use for age-related diseases such as osteoarthritis (OA) [1,2]. OA is a leading cause of disability and morbidity in the older population and constitutes a major worldwide challenge for our health system. Presently, there are no drugs approved that can prevent, stop, or even restrain progression of OA. GRP has been shown to be able to lower inflammation and mineralisation processes in the articular tissue. Chitosan/tripolyphosphate (TPP) nanoparticles were selected for this study due to their biocompatibility, biodegradability and capacity to overcome the problem of low solubility of GRP in physiological conditions. This study aims to produce and characterise chitosan/TPP nanoparticles as GRP-delivery vehicles and test its anti-inflammatory potential in human macrophages.