Breaking the barrier - Efficient topical drug delivery using responsive polymers

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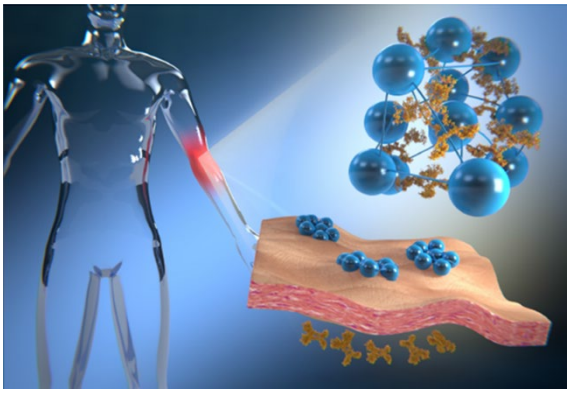
The term nanogel (NG) refers to nanometer-sized crosslinked polymeric networks that reveal intrinsic properties ideal for biomedical applications, i.e. high water content, soft nature, cell and tissue compatibility, and excellent water dispersability/solubility. Therefore, NGs are commonly developed as drug carriers which shrink or swell significantly by expelling or absorbing large amounts of water, and selectively release their cargo in response to external stimuli. Among such stimuli, temperature is attractive because of its simple accessibility and easy applicability, both in vitro and in a biological environment.[1] In this context, our group has developed several thermoresponsive NGs as drug delivery systems based on hyperbranched polyglycerol as a macro-crosslinker and different thermoresponsive polymers such as poly(N-isopropylacrylamide),[2] poly(oligo ethylene glycol methacrylate),[3] and thermoresponsive poly(glycidil ether).[4] Their biocompatibility, together with the possibility of fine tuning their size and responsive modality, makes them ideal candidates for various therapeutic and diagnostic approaches, particularly for topical drug delivery.



Topical administration permits targeted, sustained delivery of therapeutics to human skin. Delivery to the skin however is limited to lipophilic molecules with molecular weight of typically < 500 Da, capable of crossing the stratum corneum. Nevertheless, there are indications that protein delivery may be possible in barrier deficient skin, a condition found in several inflammatory skin diseases such as psoriasis and atopic dermatitis, and in congenital diseases like autosomal recessive congenital ichthyosis. Here, the synthesis, characterization, and potential application in topical protein delivery of thermoresponsive NGs is presented. The delivery of proteins such a Transglutaminase,[1,2b] Etanercept,[4b] Ovalbumin,[5] and the CRISPR-Cas 9 complex will be discussed as models for protein replacement therapy, antiinflamatory treatment, needle-free vaccination, and gene edition, respectively.

References:

[1] a N. Tiwari, et al. Angew. Chem. Int. Ed. 2022, 61, e202107960; b J. Bergueiro, M. Calderón. Macrom. Bioscience 2015, 15, 183-199; c M. Molina, M. Calderón et al., Chem. Soc. Rev. 2015, 44, 6161-6186.

[2] a M. Molina, S. Wedepohl, M. Calderón, Nanoscale 2016, 8, 5852–5856; b R. Plack et al., J. Investig. Derm. 2019, 139, 1191-1195; c H. Wang et al., Small 2024, 20, 2311166

[3] a M. Asadian-Birjand et al., Polym. Chem. 2015, 6, 5827-5831; b M. Asadian-Birjand et al., Macromol. Bioscience 2016, 1432−1441; c F. Rancan, M. Calderón et al., J. Control. Release 2016, 228, 159–169.

[4] a M. Giulbudagian, M. Calderon et al., Polym. Chem. 2014, 5, 6909-6913; b M. Giulbudagian, M. Calderón et al., Theranostics 2018, 8, 450-463; c M. Giulbudagian, M. Calderón et al., Nanoscale 2018, 10, 469-479.

[5] A.S. Sonzogni, M. Calderón, R. J. Minari et al., Biomacromolecules 2018, 19, 4607–4616.

ABOUT THE SPEAKER

Marcelo Calderón is an Ikerbasque Research Professor at POLYMAT, the Basque Center for Macromolecular Design and Engineering, from 2019. He received a Bachelor degree in Chemistry in 2003 and a Ph.D. degree in Chemical Sciences in 2007, both from the National University of Córdoba, Argentina. He was progressively a post-doctoral fellow, a Junior Group Leader focused in the area of NanoScale and an Assistant Professor at the Institute for Chemistry and Biochemistry, Freie Universität Berlin from 2007 to 2018.

Professor Calderón today is leader of the Responsive Polymer for Therapeutics Group at POLYMAT. He was highlighted as 'Emerging Investigator' by the Royal Society of Chemistry journals Chemical Communications (2015) and Journal of Material Chemistry B (2017). He was the recipient of the Arthur K. Doolittle Award in 2010 (American Chemical Society, Polymer Materials: Science and Engineering Division), the Cesar Milstein Fellowship in 2011 (Ministry of Science, Technology and Productive Innovation, Argentina), the NanoMatFutur Grant for Young Scientists from the German Ministry of Science in 2012, a Beca Leonardo of the BBVA Foundation in 2025, and the Manuel Laborde Werlinden Award in 2024. He completed his bachelor and doctoral studies with fellowships from the YPF Foundation and the Research Council of Argentina (CONICET), respectively.

Professor Calderón's research on smart polymers for medicine has been recognized with several national and international grants, with a total sum above 9 millon €. He has more than 170 publications in peer-reviewed journals, more than 20 conference proceedings, 4 book chapters and 2 patents. He is frequently reviewer of the American Chemical Society, Royal Society of Chemistry, Elsevier, Wiley, amongst others.

His group research activities have focused toward the development of polymer based nanomaterials that are able to sense environmental triggers and respond to them at the site of action as novel therapeutic and diagnostic approaches for novel efficient materials suitable on nanomedicine. The materials synthesized by the group were successfully used for imaging, tumor ablation by hyperthermia, capture and quantification of circulating tumor cells (CTCs), wound healing, and dermal/mucosal drug delivery.