NanoPharma

Towards Topical Transdermal Chemoprevention with Hyaluronic Acid–Functionalized Nanocarriers

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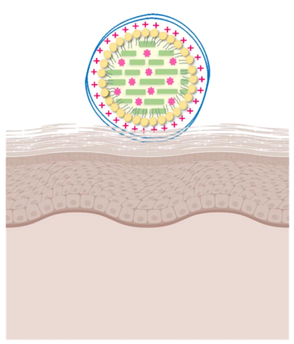
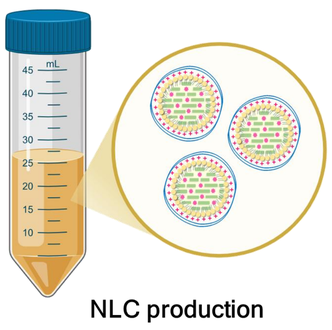
INTRODUCTION

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer-related death among women

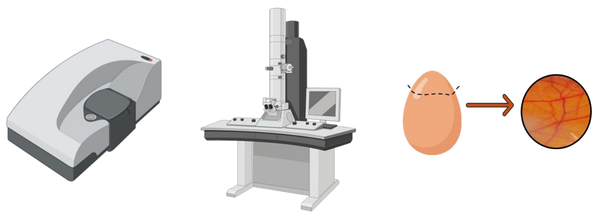


Nanostructured lipid carriers (NLC) functionalized with hyaluronic acid emerge as a promising platform for topical-transdermal chemoprevention. This approach enables delivery of fenretinide to breast tissue, achieving high local drug concentrations through a non-invasive, safe, and patient-friendly strategy.

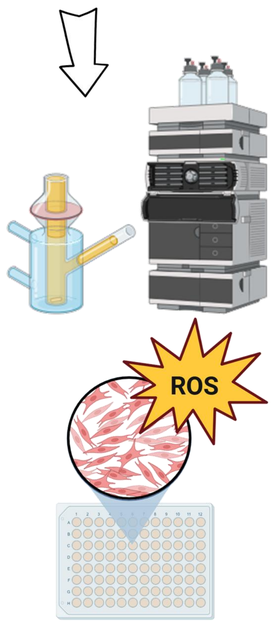
METHODS



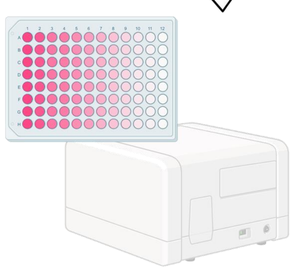
NLC production



1. Characterization by dynamic light scattering and transmission electron microscopy, Irritation potential by HET-CAM.



2. Evaluation of the effect of NLC composition in skin penetration with/without microneedles, using Franz diffusion cell model.



3. Effect of NLC coating on cell viability on breast cancer and keratinocyte cell lines.

4. Effect of fenretinide encapsulation on ROS production.

CONCLUSION

The optimized HA-coated NLC-TR formulation demonstrated excellent physicochemical properties, enhanced skin penetration, and significant increase the cytotoxicity activity against triple-negative breast cancer cells. This platform emerges as a strategy for a safe and effective transdermal platform for breast cancer treatment, reducing systemic exposure and improving patient adherence.

ACKNOWLEDGMENTS

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RESULTS

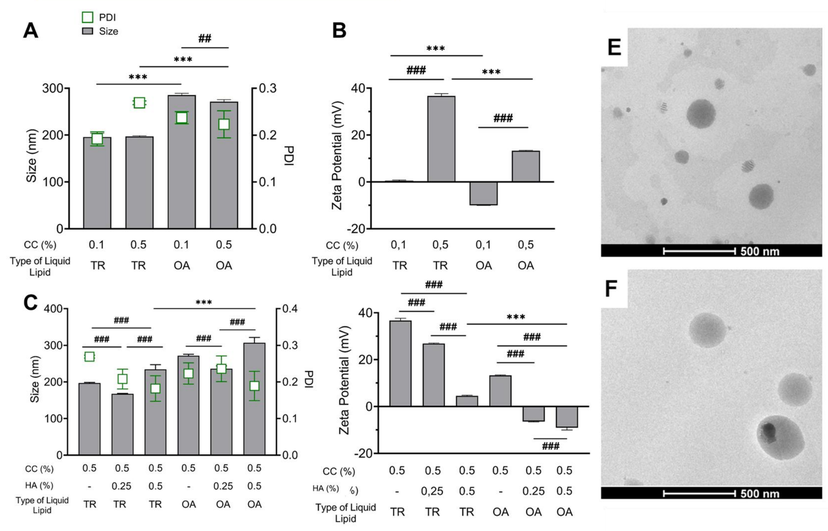

Figure 1. Physicochemical and morphological aspects of NLCs after the addition of cetylpyridinium chloride (CC) and coating of the particles with hyaluronic acid (HA).

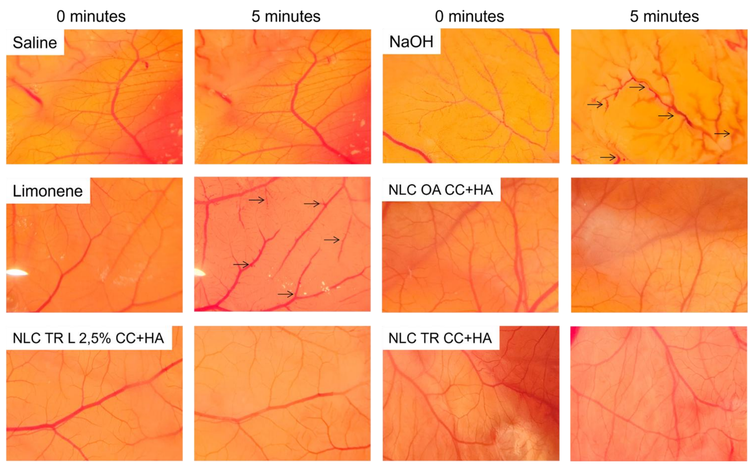

Figure 2. Irritation potential assessment by HET-CAM assay. The investigated reactions were hemorrhage, lysis, and/or coagulation.

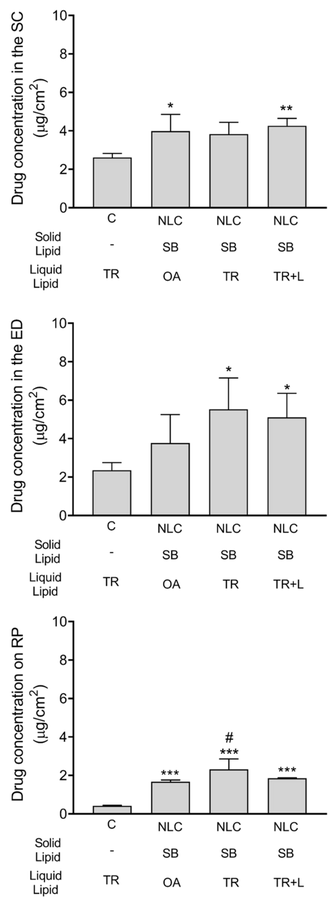

Figure 3. Influence of the liquid lipid used in the composition of NLCs on the penetration of fenretinide into the stratum corneum (SC), epidermis+dermis (ED), and receptor phase (RP). * $p < 0.03$ for the difference from the control; # $p = 0.01$ for the difference between NLCs.

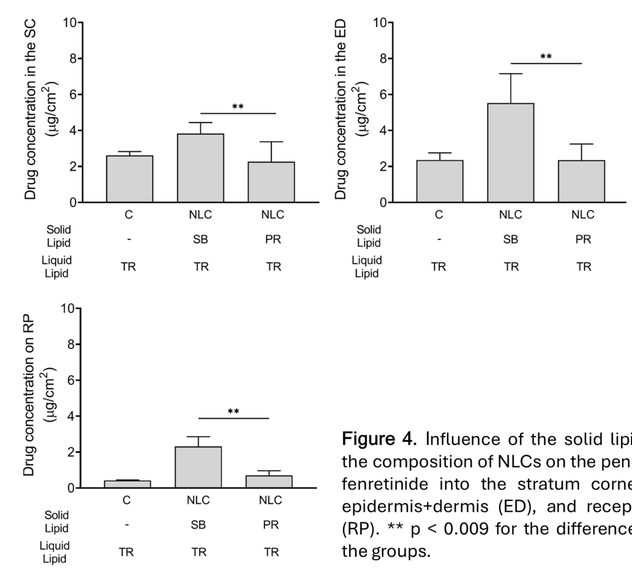

Figure 4. Influence of the solid lipid used in the composition of NLCs on the penetration of fenretinide into the stratum corneum (SC), epidermis+dermis (ED), and receptor phase (RP). ** $p < 0.009$ for the difference between the groups.

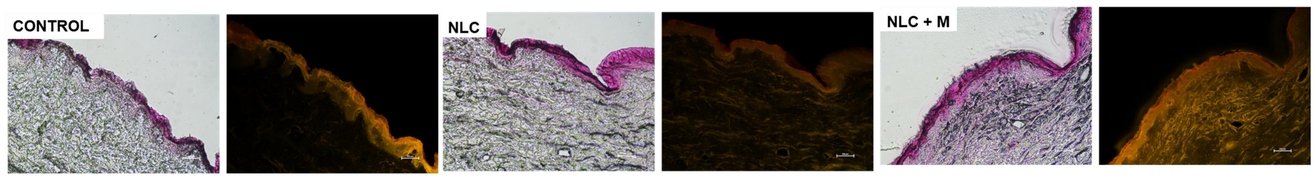

Figure 5. Distribution of the fluorescent agent Rhodamine B in the skin, as a model of distribution of lipophilic agents mediated by NLC alone or in association with microneedling (NLC+M).

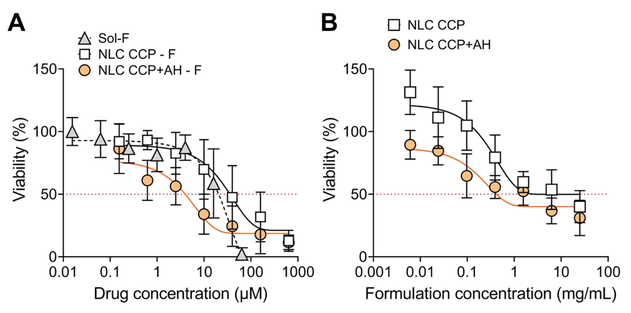

Figure 6. Influence of treatment on the viability of MDAMB-231 cells treated for 48 h. (A) Cell viability as a function of fenretinide concentration (µM); (B) Cell viability as a function of the concentration of empty NLC dispersion, with and without HA coating (mg/mL);

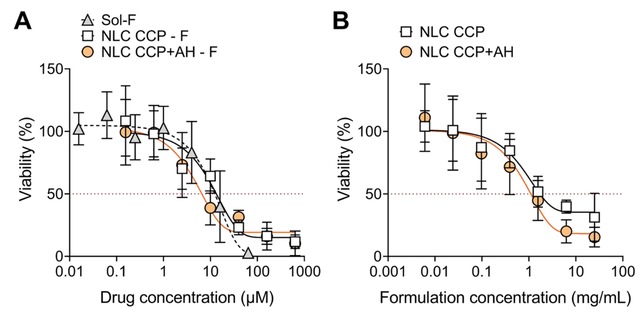

Figure 7. Influence of treatment on the viability of MCF-7 cells treated for 48 h. (A) Cell viability as a function of fenretinide concentration (µM); (B) Cell viability as a function of the concentration of empty NLC dispersion, with and without HA coating (mg/mL);

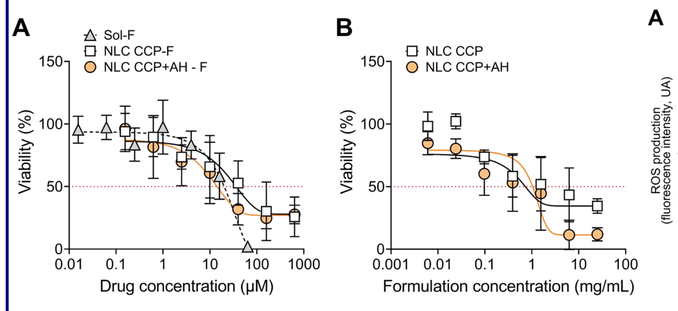

Figure 8. Influence of treatment on the viability of HaCat cells treated for 48 h. (A) Cell viability as a function of fenretinide concentration (µM); (B) Cell viability as a function of the concentration of empty NLC dispersion, with and without HA coating (mg/mL);

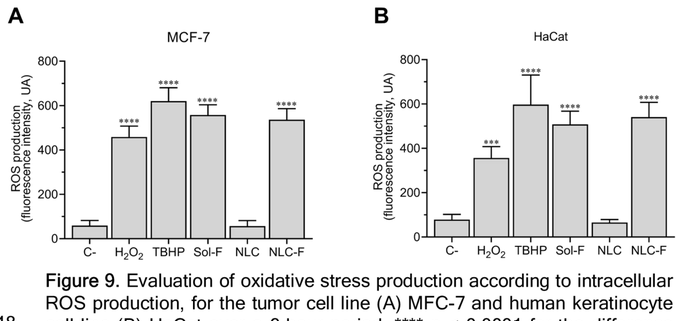

Figure 9. Evaluation of oxidative stress production according to intracellular ROS production, for the tumor cell line (A) MFC-7 and human keratinocyte cell line (B) HaCat over a 6-hour period. **** $p < 0.0001$ for the difference between positive controls and NLCs with the negative control. UA: Arbitrary unit.