Design and statistical modelling of fusogenic magnetoliposomes production for a potential antibacterial application

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The growing inefficiency of several classes of antibiotics against pathogenic bacteria, due to resistance mechanisms, is emerging as a major concern worldwide. Regarding this issue, nanotechnology is starting to provide efficient strategies to combat bacterial infections [1], [2]. Recently, superparamagnetic iron oxide nanoparticles (SPIONs) have attracted attention, mainly because of their magnetic properties. Already used in nanomedicine SPIONs have recently showed antibacterial properties through magnetic hyperthermia [2], [3]. Nonetheless, since SPIONs are very small in size and tend to aggregate, toxicity effects, such as obstruction of blood vessels and sequestration in several body systems, represent an important drawback of these particles [4].
In this work, the encapsulation of SPIONs inside fusogenic liposomes was performed, not only to reduce toxicity, but also to achieve a targeted therapy against bacteria. A production method of DOPE:DPPC:CHEMS (4:2:4) vesicles encapsulating SPIONs was designed. Performed lipid mixing assays, using FRET, showed the fusogenic ability of the nanosystem with large unilamellar vesicles, mimicking bacterial cell membranes. Furthermore, cytocompatibility assays revealed that the encapsulation of SPIONs decrease their cytotoxicity against fibroblasts. PEGylation was then carried out, in order to increase stability, as well as prolong liposomes *in vivo* circulation time, using a Box-Behnken design. Statistically relevant equations to model size and the polydispersity index behaviour were obtained (Figure 1), leading to an optimized formulation with mean size of 182 nm and polydispersity index of 0.202, with an associated encapsulation efficiency around 66%.

REFERENCES

[1] S. Singh *et al., International Journal of Nanomedicine,* vol. 14 (2019) pp. 2301–2325
[2] R. M. Pinto, F. A. Soares, S. Reis, C. Nunes, and P. Van Dijck, *Frontiers in Microbiology*, vol. 11 (2020), p. 952
[3] A. B. Seabra, M. T. Pelegrino, and P. S. Haddad, *Nanostructures for Antimicrobial Therapy: Nanostructures in Therapeutic Medicine Series*, Elsevier (2017) pp. 531–550
[4] R. M. Patil *et al.*, *Biochemistry and Biophysics Reports,* vol. 13 (2018) pp. 63-72

FIGURES

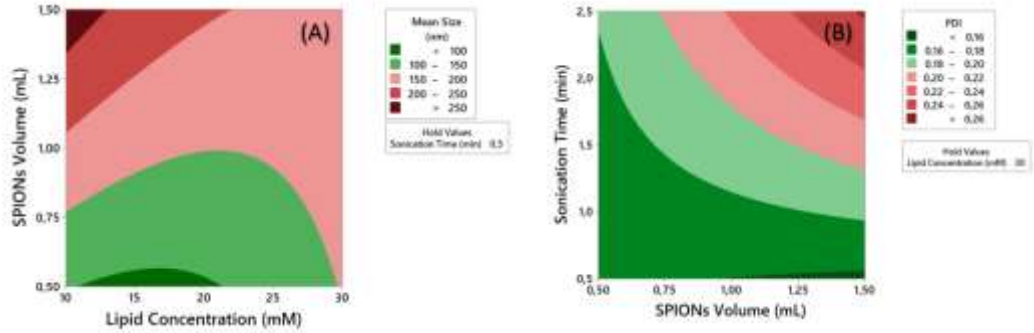

Figure 1: Contour plots of (A) PDI vs sonication time (min) and SPIONs volume (mL) and (B) mean size (nm) vs SPIONs volume (mL) and lipid concentration (mM).