

# Impact of Different Zwitterionic Surfaces on the Performance of Lipid-Based Nanocarriers

Antonio Lopalco<sup>1</sup>

Antonio Spennacchio<sup>1</sup>, Angela Assunta Lopodota<sup>1</sup>, Nunzio Denora<sup>1</sup>, Andreas Bernkop-Schnürch<sup>2</sup>

<sup>1</sup> University of Bari Aldo Moro, Department of Pharmacy-Pharmaceutical Sciences, 4, Orabona, Bari, Italy

<sup>2</sup> University of Innsbruck, Department of Pharmaceutical Technology, Institute of Pharmacy, Center for Chemistry and Biomedicine, 6020 Innsbruck, Austria

[antonio.lopalco@uniba.it](mailto:antonio.lopalco@uniba.it)

Nano-sized carriers are known to overcome many of the current limitations in drug delivery, especially if you consider delivery via various mucosal surfaces. These surfaces are located in cavities that present harsh conditions to the delivery systems. Up to now, these delivery systems mostly relied on PEG-based surfactants to navigate those conditions and pass biological barriers [1]. However, PEG-based surfactants face notable limitations such as immunogenicity or oxidative degradation, which strengthen the need for an alternative surface character of nano-sized drug carriers.

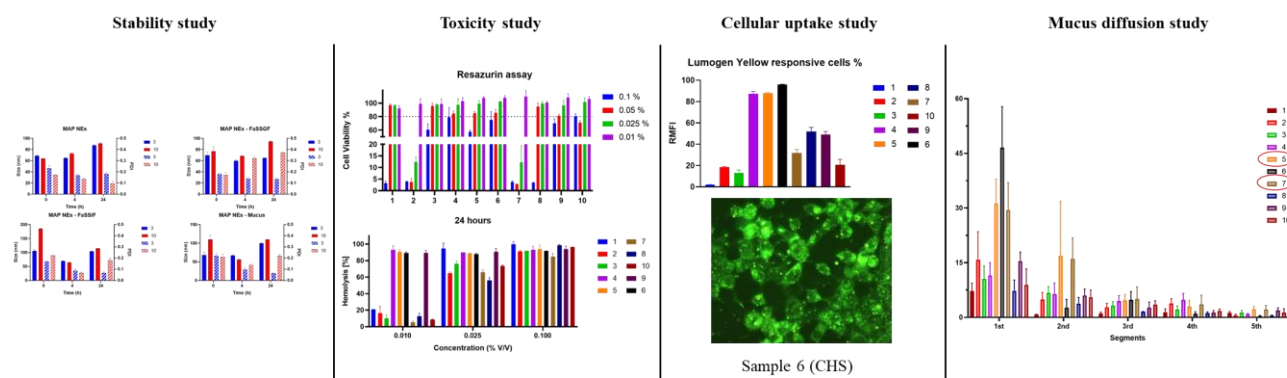
Recently, zwitterionic surfactants have emerged as a potential alternative to PEG-based surfactants [2]. Despite the promising results so far, their performance on biological barriers and the impact of their zwitterionic surface structures remains unknown.

This work evaluates key parameters, including physical stability in biorelevant fluids, toxicity, mucus diffusion, and cellular uptake, to assess whether these structural differences among zwitterionic surfactants translate into variations in performance (Figure 1). Furthermore, efforts have been made to elucidate the underlying mechanisms driving any observed differences, providing critical insights for expanding knowledge about zwitterionic surfaces. The results provide valuable new insights for prospective drug delivery in the field of nanoscience and help shaping novel delivery applications.

## References

- [1] F. Veider, P. Knoll, A.M. Jörgensen, D. Stengel, A. Bernkop-Schnürch, Oral drug delivery: Influence of mucus on cellular interactions and uptake of lipid-based nanocarriers in Caco-2 cells, *Acta Biomater* 167 (2023) 416–424.
- [2] D. Stengel, B.H. Demirel, P. Knoll, M. Truszkowska, F. Laffleur, A. Bernkop-Schnürch, PEG vs. zwitterions: How these surface decorations determine cellular uptake of lipid-based nanocarriers, *J Colloid Interface Sci* 647 (2023) 52–64. <https://doi.org/10.1016/j.jcis.2023.05.079>.

## Figures



**Figure 1:** Evaluation of Nano-emulsions for stability in HEPES buffer and simulated gastrointestinal fluids, toxicity in Caco-2 cells and hemolysis assay, cellular uptake via flow cytometry and fluorescence microscopy, and mucus diffusion in the rotating tube assay (from left to right).