Gentamicin loaded niosomes: antimicrobial activity against uropathogenic *Escherichia coli* strains

Linda Maurizi[a], Jacopo Forte[b], Maria Pia Conte[a], Antonietta Lucia Conte[a], Maria Gioia Fabiano[b], Maria Grazia Ammendolia[c], Carlo Zagaglia[a], Catia Longhi[a]

[a]Department of Public Health and Infectious Diseases, Microbiology Section, "Sapienza" University of Rome, Rome, Italy; [b]Department of Drug Chemistry and Technologies, "Sapienza" University of Rome, Rome, Italy; [c]National Center of Innovative Technologies in Public Health, Italian National Institute of Health, Rome, Italy.

Urinary tract infections (UTIs) are the most frequent community and hospital-acquired infections. Uropathogenic *Escherichia coli* (UPEC) is the major causative agent of UTIs [1]. UPEC initially colonize the human host adhering to the bladder epithelium and invade urothelial epithelial cells, where they can replicate forming compact aggregates of intracellular bacterial communities (IBCs) and persist establishing quiescent intracellular bacterial reservoirs (QIRs) [2]. It has been shown as intravesical instillations of gentamicin (GM), a broad-spectrum antibiotic that exhibits a concentration-dependent activity and a post-antibiotic effect, reduce the frequency of UTIs. Despite this, the oral GM administration is not effective due to low bioavailability and poor penetration into cells [3]. To improve the therapeutic drug efficacy, the use of nanocarriers like niosomes, as drug-delivery sistems, received particular attention. Niosomes are drug delivery systems, composed by surfactant, self-assembled, stable and non-immunogenic [4]. In particular, the components employed for the preparations are Tween 85 and Span 80 and empty and loaded with gentamicine niosomes are prepared and characterized. This work aimed to evaluate the ability of niosomes to increase both the intracellular concentration of GM and the effect against persistent intracellular UPEC strains isolated from a patient with recurrent UTIs. In this work a deep physical-chemical characterization was carried out as well as stability over time/biological media and drug entrapment efficiency. Moreover, thanks to the niosomes intimate structure, both lipophilic and hydrophilic moiety-drugs, have been loaded inside the nanocarriers (co-loading of GM and Nile Red), to better evaluate the intracellular uptake. The internalization of these samples occurred in T-24 bladder cells already after 7 hours of contact. To assess a potential anti invasive activity, non-cytotoxic and non-bactericidal concentrations of GM loaded niosomes were tested during the infection step of *E. coli* in T-24 cells. The decrease in invasion rates leads us to hypothesize a release of the antibiotic inside the cell. In conclusion, we can speculate that the delivery of antibiotic by niosomes may be very promising but some aspects need to be elucidated for a potential application in the therapeutic field.

[1] E. Serretiello, V. Folliero, et al., *Int J Microbiol*. **2021**, 2021, 1-10.
[2] K. Sharma, V.V. Thacker, et al., *Cell Rep.* **2021**, 36, 109351.
[3] A. Pietropaolo, P. Jones, et al., *Curr Urol Rep*. **2018**, 19, 78.
[4] C. Marianecci, L. Di Marzio, et al., *Adv Colloid Interface Sci.* **2014**, 205,187–206.