BIOCOMPATIBLE POLYMERS-COATED LIPOSOMES TO AMELIORATE ANTIBIOTIC VAGINAL DELIVERY

Sara Lugli[1], C. Foschi, M. Scafa, M. L. Bolognesi, T. Cerchiara, B. Luppi, F. Bigucci, A. Abruzzo
[1] Dept of Pharmacy and Biotechnology, University of Bologna, Via San Donato 19/2, Bologna, 40127, Italy.

Vaginal infections affect millions of women during their lifetime, causing significant distress for patients and representing a relevant burden to the health care system. Conventional antibiotic oral dosage forms generally determine a poor drug accumulation at the site of infection, leading to the need for multiple administrations and increasing the rate of antimicrobial resistance [1]. Nanocarriers, like liposomes (LPs) coated with mucoadhesive polymers, could ensure an increased residence time of the drug inside the vaginal cavity and control its release over time, thus promoting its accumulation on infected mucosae [2]. In this study, azithromycin (AZT)-containing LPs, coated with two biocompatible polymers, chitosan (CS) and hyaluronic acid (HA), were developed with the final aim of controlling drug release and increasing drug retention time in the vaginal mucosae.
Egg yolk phosphatidylcholine (PC), cholesterol (CHOL) and AZT were employed for LPs preparation through the thin film hydration method followed by French-Press extrusion [3]. Then, for LP coating, solutions of CS or HA, separately dissolved in lactate buffer, were mixed with LPs suspension (1:1 v/v). The formulations' size, polydispersity index (PDI), zeta potential, stability and encapsulation efficiency were measured. *In vitro* drug release was assessed at neutral pH, mimicking the conditions of the infected vagina, and at pH 4.5, the physiological value, while mucoadhesion ability was investigated by evaluating the interaction between LPs and mucin. Results demonstrated that coated LPs were characterized by a size increase compared to the uncoated LPs, because of the presence of polymer on the LP surface. All formulations presented a low PDI value, which indicated good sample homogeneity. The zeta potential switched from negative values for uncoated LPs to positive values for CS coated LPs, due to the ability of CS positive charges to interact with the negative charges on LPs surface. Concerning HA, the superficial charge of LPs was not significantly altered, probably due to the different nature of the interaction between HA and LPs. All formulations were stable and allowed to obtain a good encapsulation efficiency. Among all the formulations, CS coated LPs allowed us to achieve better drug release control than the uncoated ones, at both pH values. Moreover, CS coated LPs showed the best mucoadhesive properties thanks to the interaction between CS and the anionic residues of mucin. The obtained results highlighted that CS coated LPs could be considered a promising platform, able to increase the residence time of antibiotic molecules inside the vaginal cavity and to control its release over time. The selected formulation allows adequate local drug concentrations to be achieved, with the final goal of improving treatment efficacy.

Key words: *liposomes, azithromycin, chitosan, hyaluronic acid, vaginal infections*

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