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CHITOSAN-COATED LIPOSOMES FOR AZITHROMYCIN VAGINAL DELIVERY

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Female reproductive tract-related infections affect millions of women each year, causing significant distress for patients. Conventional vaginal dosage forms can fail in controlling mucosal infections, due to inadequate drug accumulation at infection site [1]. Nanocarriers, like liposomes (LPs), have shown peculiar properties, like the ability to increase drug solubility and to control its release. Furthermore, LP-coating with mucoadhesive polymers could assure an increased drug residence time and promote its accumulation on infected vaginal mucosae, thus improving treatment efficacy [2]. In this context, chitosan (CS) represents one of the most employed mucoadhesive polymers, thanks also to its biodegradability and antimicrobial activity. Within this study, azithromycin (AZT)-containing liposomes, coated with CS, were developed with the final aim to obtain formulations able to increase drug retention time in the vaginal cavity and to improve its antimicrobial effect.
LPs were composed of phosphatidylcholine from egg yolk (PC), cholesterol (CHOL) (70:30 w/w) and AZT (3 mg/mL) and obtained using the thin film hydration method followed by French-Press extrusion [3]. Then, a 2 mg/mL solution of low viscosity CS in lactate buffer was mixed with LP suspension (1:1 v/v), to ensure LPs coating. After their preparation, LPs were characterized for their dimensions, polydispersity index (PDI), zeta potential, stability and encapsulation efficiency. Finally, *in vitro* drug release was assessed using the Franz-cells apparatus 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. Un-coated and coated LPs showed sizes equal to 460 ± 18 nm and 921 ± 90 nm, respectively and a PDI around 0.3. The zeta potential value switched from extremely negative values (-45.2 ± 0.1 mV) for un-coated LPs to positive values (+6.8 ± 0.4 mV) for coated LPs, confirming the ability of CS to adhere to the liposomal surface. Un-coated and coated LPs were stable and allowed to obtain encapsulation efficiency equal to 54.2% ± 8.1% and 41.2% ± 8.1%, respectively. The CS-coated LPs showed a controlled drug release compared to the un-coated LPs both at neutral and acidic pH, thanks to polymer ability to slow down the drug diffusion. Finally, CS-coated LPs showed an increase in mucoadhesion with respect to the un-coated LPs, as consequence of the interaction between CS and the anionic residues of mucin. In conclusion, the coating of LP with CS allowed to obtain nanocarriers able to efficiently encapsulate AZT and to control its release over time as well as to adhere to mucin. This result could contribute to reach adequate local concentrations of the drug over the time and to facilitate a prolonged topical therapy, thus reducing the dosage and the administration frequency.

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