ABSTRACT

Bacterial adhesion and encrustations are the major problem that can lead to the infection of implanted urological stents. In this present study, kanamycin-chitosan nanoparticles (KMCSNPs) and ciprofloxacin-loaded genipin cross-linked chitosan/heparin nanoparticles were prepared and immobilized on the surface of a polyurethane ureteral stent (PUS) to prevent urinary bacterial infection and encrustations. Chitosan nanoparticles (CSNPs) were synthesized by ionotropic gelation method with sodium tripolyphosphate as a cross linker in the presence of different pH condition. To achieve maximum drug loading efficiency, KMCSNPs were prepared with different polymer/drug ratios. The maximum KM entrapment of 92.32% with loading efficiency of 32.85% was achieved using 1:1 (w/v) drug/polymer in pH 4.5. The particle size, surface charge, bond interaction, and morphology of KMCSNPs were characterized by dynamic light scattering, Fourier transform infrared spectroscopy, and scanning electron microscopy. Analysis showed dispersed spherical shaped particles with a ζ-average of 225 nm and a zeta potential of +35 mV. The antibacterial property of KMCSNPs by Kirby-Bauer disk agar diffusion showed relatively large the zone of inhibition compared to KM. Further flow cytometry analysis was carried out to determine the antibacterial activity. KMCSNPs were immobilized on the PUS surface by covalent immobilization techniques. The KMCSNPs surface-modified PUS (KMCSNPs@PUS) was characterized using attenuated total reflectance Fourier transform infrared spectroscopy, field emission scanning electron microscopy, and energy dispersive X-ray spectroscopy. Similarly, Ciprofloxacin loaded genipin cross-linked chitosan/heparin nanoparticles were prepared (CIPRO-GP-CS/HepNPs) by ionic gelation. The nanoparticles were optimized under different ratios of CIPRO, genipin,
chitosan and heparin. The physiochemical characteristics were analyzed using FTIR, DLS, FESEM and EDAX. The synthesized particles had a spherical shape with z-average of 250 nm and zeta potential +32 mV with maximum 45.5 % drug loading efficiency. The antibacterial activity of the CIPRO-GP-CS/HEPNPs was evaluated against *Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *S. aureus* which showed that it is 4 to 8 times better than KMCSNPs antibacterial activity. The CIPRO-GP-CS/HEPNPs covalently immobilized on the PUS surface. The CIPRO-GP-CS/HEPNPs@PUS was characterized using ATR-FTIR, goniometer, FESEM, and EDAX. The CIPRO-GP-CS/HEPNPs@PUS showed significantly increased antibacterial activity against *Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* relative to the surface of unmodified PUS and KMCSNPs@PUS. Encrustation study results showed that the CIPRO-GP-CS/HEPNPs@PUS have no encrustation on the PUS surface after 1 month treatment, whereas KMCSNPs@PUS failed to protect the PUS from encrustations. *In vitro* drug release at artificial urine demonstrated that the CIPRO-GP-CS/HEPNPs exhibited a sustained release which fitted Higuchi model and KMCSNPs fitted Korsmeyer-Peppas model. Finally, *in vitro* biocompatibility test was conducted which resulted in both KMCSNPs and CIPRO-GP-CS/HEPNPs have no significant cytotoxicity to the L929 mouse fibroblast cells. In conclusion, our finding concludes that CIPRO-GP-CS/HEPNPs@PUS can be efficiently used as urological medical device to prevent bacterial adhesion and encrustations.