CHITOSAN NANOPARTICLES AS DRUG DELIVERY SYSTEM FOR CEPHALEXIN AND ITS ANTIMICROBIAL ACTIVITY AGAINST MULTIIDRUG RESISTENT BACTERIA

Mona El Assal ,MONA IBRAHIM EL-ASSAL1, NAGWAN GALAL EL MENOFY2*

Associat Professor of Pharmaceutics at Pharmaceutics and Pharmaceutical Technology department at FUE University.

Abstract

ABSTRACT Objective: The evolution of antimicrobial resistance is a universal obstacle that necessities the innovation of more effective and safe antimicrobial alternatives with synergistic properties. The purpose of this study was to investigate the possible improvement of cephalexin antimicrobial treatments by loading into chitosan-based nanoparticles, then evaluate their antibacterial and antibiofilm activities as well as determination of its cytotoxicity. Methods: Chitosan nanoparticles (CSNPs) were prepared by ionic gelation method. Parameters were studied to optimize the particle size of CSNPs including pH, stirring rate, homogenization and ultra-sonication time. Size was measured by transmission electron microscope (TEM) and Zeta sizer, morphology seen by scanning electron microscope (SEM). Entrapment efficiency, drug loading and drug content were calculated. Stability of both plain and loaded chitosan Nano-carriers, Drug release and Kinetics also compatibilities were studied. Antimicrobial activity of CSNPs and cephalexin loaded CSNPs were evaluated against 4 Gram-positive and 4 Gram-negative standard and clinical isolates by microdilution method, also assessment of antibiofilm activity of both formulas was investigated against two biofilm producers clinical isolates by tube assay in addition to determination of their cytotoxicity by MTT(3-(4, 5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay. Results: Chitosan nanoparticles and its loaded antibiotics proved compatible combination with small Zeta size, suitable Zeta potential, maximum EE% and drug-loading capacity, sustained controlled release properties followed diffusion kinetic model and six month stability studies. Cephalexin loaded CSNPs showed better antimicrobial activity than plain CSNPs. Synergistic effects were found against S. aureus (ATCC 25923), B. subtilis (ATCC 9372), S. epidermidis, E. faecalis, P. aeruginosa (ATCC 29853) in addition to two carbapenem resistant isolates k. pneumoniae and E. coli. Also cephalexin loaded CSNPs exhibited antibiofilm activity against E. faecalis clinical isolate. Even though, cephalexin loaded CSNPs exhibited significant antibacterial activity, it showed less toxicity against mammalian cells, it had IC50 equal to 231.893 and did not exhibit any cytotoxicity against the WI-38 fibroblast cells at concentration 23.4 Conclusion: Cephalexin loaded CSNPs possessed good stability and sustained release effect in addition to its antimicrobial, antibiofilm activities and reduced cytotoxicity