**ABSTRACT**

**Aim:** The current research was aimed at formulating and optimizing polymeric nanoparticles of clarithromycin (an antibacterial agent) in terms of particle size, entrapment efficiency, in vitro release behaviors and antibacterial efficiency against S. Pneumoniea.

**Methods:** Clarithromycin loaded polymeric nanoparticles are prepared using chitosan (low molecular weight) by ionic gelation method and Poly (lactide –co-glycolic acid) (50:50 monomer ratio) by emulsification solvent evaporation and nanoprecepitation method. Tripolyphosphate used as a cross linker and polyvinyl alcohol, poloxamer- 188 as stabilizers. Carbapol, Poloxmer-188 and Tween 80 were added as co-stabilizer and co-surfactant respectively. Clarithromycin –β-cyclodextrin complex was prepared and incorporated into chitosan nanoparticles. Minitab 17 statistical software was employed to create general full factorial design. NPs were characterized in terms of surface morphology, particle size and distribution, zeta potential, encapsulation efficiency, clarithromycin release profile and antibacterial activity. The antibacterial activity of nanoparticles against S. Pneumoniea was evaluated by calculation of minimum inhibitory concentration and zone of inhibition. Drug-excipient compatibility study by FTIR and DSC revealed no possible interactions.

**Results:** The chitosan nanoparticles prepared under optimal condition of 0.25% chitosan concentration, 0.5% TPP concentration with 1:1 volume ratio had particle size of 424.9 ±2.91 and 452.91± 1.98 nm diameter, with %EE of 47.5±1.69 and 59±3.14% for F1 and F1/CD respectively. Clarithromycin –β-cyclodextrin complex loaded chitosan nanoparticles showed good particle size with increased encapsulation efficiency when compared to chitosan nanoparticles. PLGA nanoparticles prepared by nanoprecipitation yielded nanoparticles with better physicochemical properties than emulsion solvent evaporation technique. PLGA nanoparticle prepared under optimal condition of 125 mg PLGA yields 89.5±2.17% encapsulation, particle size of 319.5±17.6 nm for 1.5% PVA and 88±0.8% encapsulation, particle size of 176.5±7.6 nm for 1.5% P-188 by nanoprecepitation method. Use of a co-surfactant in PLGA nanoparticles altered particle size and in vitro release pattern. Use of a co-stabilizer altered the entrapment of drug, and stability of formulation. Drug release studies of clarithromycin loaded nanoparticles was carried out for 72 h. In vitro release profile of clarithromycin from nanoparticles follows biphasic release pattern: initial burst release followed by slow release. Kinetic modelling of in vitro release showed that both chitosan and PLGA nanoparticles were more linear towards Korsmeyer-Peppas and n value for most of the formulations was found to be less than 0.5 indicating fickian diffusion mode. The MIC values for both F1 and F1/CD were found to be 16 μg/ml and 8 μg/ml for F24 formulation. When the clarithromycin nanoparticles were tested against the S. Pneumoniae, they effectively inhibit the microbial growth. SEM analysis of optimized nanoparticles revealed that, nanoparticles are discrete and almost spherical in shape. Stability study results showed that there were no significant change in physical appearance and drug release profile at refrigerator condition for selected formulations. The optimized formulations were selected for in vivo studies in rats. in vivo results revealed that when compared with pure drug, the formulated nanoparticles showed better results upon intra treacheal administration. Amount of drug released from F24 formulations was slow when compared to F1 and F1/CD. F1/CD showed increased drug release upto 24% at 45 min. From the results, we observed an increased drug release upon using cyclodextrin. F24 formulation sustained drug release, due to mucoadhesiveness and viscosity of carbapol.

**Conclusion:** Clarithromycin in the form of nanoparticles not only improves the physicochemical characteristics of the drug, but also improves its antibacterial activity. Key words: Clarithromycin, chitosan nanoparticles, β-cyclodextrin complex, PLGA nanoparticles, antibacterial activity.

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