World Academy of Science, Engineering and Technology
International Journal of Pharmacological and Pharmaceutical Sciences
Vol:15, No:07, 2021

Mannose-Functionalized Lipopolysaccharide Nanoparticles for Macrophage-Targeted Dual Delivery of Rifampicin and Isoniazid

Authors : Mumuni Sumaila, Viness Pillay, Yahya E. Choonara, Pradeep Kumar, Pierre P. Kondiah

Abstract : Tuberculosis (TB) remains a serious challenge to public health globally, despite every effort put together to curb the disease. Current TB therapeutics available have proven to be inefficient due to a multitude of drawbacks that range from serious adverse effects/drug toxicity to inconsistent bioavailability, which ultimately contributes to the emergence of drug-resistant TB. An effective 'cargo' system designed to cleverly deliver therapeutic doses of anti-TB drugs to infection sites and in a sustained-release manner may provide a better therapeutic choice towards winning the war against TB. In the current study, we investigated mannose-functionalized lipopolysaccharide hybrid nanoparticles for safety and efficacy towards macrophage-targeted simultaneous delivery of the two first-line anti-TB drugs, rifampicin (RF) and isoniazid (IS). RF-IS-loaded lipopolysaccharide hybrid nanoparticles were fabricated using the solvent injection technique (SIT), incorporating soy lecithin (SL) and low molecular weight chitosan (CS) as the lipid and polysaccharide components, respectively. Surface-functionalized nanoparticles were obtained through the reaction of the aldehyde group of mannose with free amine functionality present at the surface of the nanoparticles. The functionalized nanocarriers were spherical with average particle size and surface charge of 107.83 nm and +21.77 mV, respectively, and entrapment efficiencies (EE) were 53.52% and 69.80% for RF and IS, respectively. FTIR spectrum revealed high-intensity bands between 1663 cm^{-1} and 1408 cm^{-1} wavenumbers (absent in non-functionalized nanoparticles), which could be attributed to the C=N stretching vibration produced by the formation of Schiff's base (–N=CH–) during the mannosylation reaction. In vitro release studies showed a sustained-release profile for RF and IS, with less than half of the total payload released over a 48-hour period. The nanocarriers were biocompatible and safe, with more than 80% cell viability achieved when incubated with RAW 264.7 cells at concentrations 30 to 500 µg/mL over a 24-hour period. Cellular uptake studies (after a 24-hour incubation period with the murine macrophage cells, RAW 264.7) revealed a 13- and a 9-fold increase in intracellular accumulation of RF and IS, respectively, when compared with the unformulated RF+IS solution. A 6- and a 3-fold increase in intracellular accumulation of RF and IS, respectively, were observed when compared with the non-functionalized nanoparticles. Furthermore, fluorescent microscopy images showed nanoparticle internalization and accumulation within the RAW 264.7 cells, which was more significant in the mannose-functionalized system compared to the non-functionalized nanoparticles. The overall results suggested that the fabricated mannose-functionalized lipopolysaccharide nanoparticles are a safe and promising platform for macrophage-targeted delivery of anti-TB therapeutics. However, in vivo pharmacokinetic/pharmacodynamics studies are required to further substantiate the therapeutic efficacy of the nanosystem.

Keywords : anti-tuberculosis therapeutics, hybrid nanosystem, lipopolysaccharide nanoparticles, macrophage-targeted delivery

Conference Title : ICPSR 2021 : International Conference on Pharmaceutical Sciences and Research
Conference Location : Toronto, Canada
Conference Dates : July 19-20, 2021