Rifampicin-loaded lipid nanoparticles to improve tuberculosis treatment: an active targeting approach

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Tuberculosis is a major global health problem of overwhelming proportions [1]. The current treatment is associated with several adverse-effects and noncompliance to therapy [2]. The development of nanodelivery systems represents an interesting alternative for the delivery of anti-tuberculosis drugs to the target site of infection, as an attempt to reduce the required dose, to minimize the side effects, and to enhance patients' compliance [3]. Thus, this work aims to develop a mannosylated nanostructured lipid carrier (NLC) loaded with rifampicin, to improve tuberculosis treatment. An active targeting strategy was used and the nanoparticles were characterized in terms of size, polydispersity, zeta potential, surface morphology, encapsulation efficiency, and in vitro drug release. Effects on cell viability were tested using primary mouse bone marrow-derived macrophages (BMDM), and the anti-mycobacteria activity of the nanofORMulations was evaluated using Mycobacterium avium-infected BMDM. The nanoparticles developed exhibited a size of about 315 nm, and polydispersity below 0.2. The drug encapsulation efficiency was higher than 90%, and its release was sensitive to pH. The mannosylated NLCs showed efficient uptake by BMDM. Further, rifampicin-loaded mannosylated NLCs were more efficient in inducing a decrease of intracellular growth of mycobacteria. The overall results support that mannosylated NLCs constitute a promising strategy for the delivery of rifampicin selectively to macrophages. Moreover, although in vivo studies are required to validate the clinical potential of these nanoparticles, the results obtained are a promising proof-of-concept, and demonstrate, albeit in vitro, the applicability of the nanofORMulations developed.

This may ultimately open up new avenues in the fight against the world’s deadliest infectious disease.

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References

Figure

Figure 1. Schematic representation of the active targeting approach used in the present study. Mannosylated nanostructured lipid carriers loaded with rifampicin (M-NLCs-RIF) were developed to target macrophages, the main site of tuberculosis infection.