Drug Delivery and Translational Research
https://doi.org/10.1007/s13346-021-01055-9

ORIGINAL ARTICLE

Appraisal of fluoroquinolone-loaded carubinose-linked hybrid nanoparticles for glycotargeting to alveolar macrophages

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Accepted: 20 August 2021

Abstract

There is a curious case in Alveolar macrophages (AM), the frontline defence recruits that contain the spread of all intruding bacteria. In response to *Mycobacterium tuberculosis (M.tb),* AM either contain the spread or are modulated by *M.tb* to create a region for their replication. The *M.tb* containing granulomas so formed are organised structures with confined boundaries. The limited availability of drugs inside AM aid drug tolerance and poor therapeutic outcomes in diseases like tuberculosis. The present work proves the glycotargeting efficiency of levofloxacin (LVF) to AM. The optimised formulation developed displayed good safety with 2% hemolysis and a viability of 61.14% on J774A.1 cells. The physicochemical characterisations such as Fourier-transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA) proved that carubinose linkage was accomplished and LVF is entrapped inside carubinose-linked hybrid formulation (CHF) and hybrid formulation (HF) in amorphous form. The transmission electron microscopy (TEM) images revealed a core–shell structure of HF. The particle size of 471.5 nm estimated through dynamic light scattering (DLS) is enough to achieve active and passive targeting to AM. The nanoparticle tracking analysis (NTA) data revealed that the diluted samples were free from aggregates. Fluorescence-activated cell sorting (FACS) data exhibited excellent uptake via CHF (15 times) and HF(3 times) with reference to plain fluorescein isothiocyanate (FITC). The pharmacokinetic studies revealed that CHF and HF release the entrapped moiety LVF in a controlled manner over 72 h. The stability studies indicated that the modified formulation remains stable over 6 months at $5 \pm 3^{\circ}C$. Hence, hybrid systems can be efficiently modified via carubinose to target AM via the parenteral route.

Keywords Hybrid nanoparticles · Carubinose · Flow cytometry · Macrophage targeting · Thermal analysis · NTA analysis

Introduction

Tuberculosis (TB) is the frontrunner in the infectious disease group. It possessed the highest mortality rate in 2019, with 1.4 million deaths and 10 million new cases. *Mycobacterium tuberculosis (M.tb)*, a bacillus spread from an infected individual with active TB during coughing, is the leading cause of tuberculosis. About $1/4^{th}$ of the world's population is affected by it. It can be pulmonary or extrapulmonary. BCG, the only vaccine for TB, was discovered 100 years ago [1]. Search for an effective drug to overcome the side effects (of existing medications) and improve efficiency is still on. $1/4^{th}$ population is still affected by TB and research is ongoing makes up a solid ground for further investigations. The severity of the situation is evident because a disease with a vaccine in place and a standard dosage regimen retains top mortality rates year after year. Pulmonary TB occurs when the lungs are afflicted by *M.tb*.

Alveolar macrophages (AM) form the first line of defence for all incoming particulate matter through the nasal route and, in process, clears them through phagocytosis. AM, the prominent warriors of the body's defence mechanism, are transformed to harbour the bacteria or promote pro-inflammatory milieu in the lungs leading to progression of inflammatory diseases like chronic obstructive pulmonary disease (COPD)

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