Monocyte-targeted delivery to immune cells using Modified Polysaccharide particles

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Tuberculosis (TB) has now surpassed AIDS as the leading cause of death from infectious diseases.¹ Despite the progress achieved in global TB control, eradication and treatment has been significantly jeopardised by the HIV epidemic and emergence of multidrug-resistant TB.²,³ Targeting of pyrazinoic acid (PCA) to monocytes infected with tubercle bacilli might potentially assist the treatment of chronic TB by delivering higher doses of intracellular PCA To do this, we conjugated PCA to the Modified Polysaccharide particles (MPI) through a bio-labile covalent connection. The MPI was oxidized with sodium periodate and functionalized with amine linker. The amine modified MPI was then attached to PCA using EDC/NHS coupling chemistry. The novel MPI-drug conjugate was confirmed by characterization using ¹H NMR spectroscopy, Fourier-Transformed Infrared Spectroscopy (FTIR), Scanning Electron Microscopy (SEM) and Dynamic light scattering (DLS) techniques. The drug loading and release were evaluated using HPLC. The cellular uptake of the MPI-drug conjugate was analysed using flow cytometry and fluorescence microscopy. SEM of the modified MPI-drug conjugates shows spherulite-like discoid morphology with a diameter of ~2μm. A positive zeta-potential of 22 mV should assist the efficient uptake of MPI-drug conjugates by phagocytes. The drug loading was ~ 3% and MPI -drug conjugate showed a pH-dependent release, with ~40% released over 6 days at pH 4.5 compared with 8% at pH 7.4. A cellular uptake study confirmed the targeting ability of the MPI-drug conjugate for monocytes and support future testing to see whether MPI-drug conjugates are uptaken by infected human monocytes and exhibit enhanced anti-TB activity.

References