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In vivo/in vitro pharmacokinetic and pharmacodynamic study of spray-dried poly-(dl-lactic-co-glycolic) acid nanoparticles encapsulating rifampicin and isoniazid

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Abstract

Poly-(DL-lactic-*co*-glycolic) acid (PLGA) nanoparticles were prepared by a double emulsion solvent evaporation spray-drying technique and coated with polyethylene glycol (PEG 1% v/v). The PLGA nanoparticles had a small size (229 ± 7.6 to 382 ± 23.9 nm), uniform size distribution and positive zeta potential (+12.45 ± 4.53 mV). *In vitro*/*in vivo* assays were performed to evaluate the pharmacokinetic (PK) and pharmacodynamic (PD) performance of these nanoparticles following nanoencapsulation of the anti-tuberculosis drugs rifampicin (RIF) and isoniazid (INH). The results demonstrated the potential for the reduction in protein binding of these drugs by protection in the polymer core. Furthermore, *in vitro* efficacy was demonstrated using *Mycobacterium tuberculosis* (*M. tb.*) (strain H_{37}Rv). Sustained drug release over seven days were observed for these drugs following once-off oral administration in mice with subsequent drug distribution of up to 10 days in the liver and lungs for RIF and INH, respectively. It was concluded by these studies combined with our previous reports that spray-dried PLGA nanoparticles demonstrate potential for the improvement of tuberculosis chemotherapy by nanoencapsulation of anti-tuberculosis drugs.