Synthesis and characterization of theophylline and budesonide co-encapsulated PLA nanoparticles

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Two asthma drugs were successfully encapsulated by a biodegradable polymer with an modified emulsion polymer process as nanoparticles with high active loadings.

The resultant products showed controlled release over time in simulated tests, and show potential for the controlled release of asthma drugs in the lungs from powder inhalation as well as other applications.

A novel co-encapsulated nanoparticle (NP) system using the anti-asthmatic drugs theophylline and budesonide and the biodegradable polymer poly (lactic acid) (PLA) was synthesised using a modified double emulsification solvent diffusion (DESD) method. This method was developed to allow increased loading efficiency of both the drugs into the PLA nanoparticles. By use of nanoparticles, the aim was to modify and sustain the release of the two drugs in the lungs. Synthesized NPs were lyophilized and characterized for particle size and zeta potential analysis, SEM, FT-IR and drug loading efficiency by means of high performance liquid chromatography (HPLC). Drug release was determined by HPLC using Franz diffusion cells. NPs suspended in simulated lung fluid (SLF) were added to the donor chamber of Franz cell and aliquots were withdrawn at regular time points from the receiver chamber. Drug release from NPs was compared with equivalent concentration of drug controls.

Co-encapsulation was successfully achieved with particles formulated in the submicron range (200-400 nm). No drug was adsorbed on the surface of the NPs confirmed by FT-IR, SEM and electronegative charge obtained on zeta potential analysis. Higher drug loading was obtained for budesonide (39.1%) than theophylline (18.6%). A sustained release of both theophylline and budesonide from the nanoparticles was achieved; after a period of 24 hours 21.55% theophylline and 0.79% budesonide were released from the nanoparticles. Study of the drug control solution showed a higher concentration of drugs at the equivalent time points, compared to nanoparticles. The NPs are further developed for pulmonary drug delivery; dry powder inhalation (DPI) formulations and delivery by nebulization will be compared using various lung models (MSLI and TSI) and assessment of particle size and drug concentration at the different stages delivered in the lungs.