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Aerosol characterisation of nebulised liposomes co-loaded with erlotinib and genistein using an abbreviated cascade impactor method

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Abstract: Erlotinib and genistein co-loaded liposomes were prepared by the thin-film hydration method. The effect of probe sonication as a size reduction method on drug incorporation and the properties of aerosols generated using air-jet and vibrating-mesh nebulisers was studied. The use of the Next Generation Impactor (NGI) to characterise inhaler formulations is limited by the need accurately to quantify drug deposited across 8 stages and is labour intensive to use. The Fast Screening Impactor (FSI) comprising two impaction stages was compared with the NGI to evaluate its applicability as a simple screening and labour-saving tool to characterise nebulised systems. For the developed liposomal formulations, an air-jet nebuliser generated a two-fold higher fine particle fraction (FPF) than a vibrating-mesh nebuliser. The findings demonstrated that the cooled FSI (5°C) operated at 15 L/min was effective in differentiating the aerosol properties of the nebulised liposome formulations investigated. Overall, the optimised co-loaded liposomes were more effectively delivered by an air-jet nebuliser, than from a vibrating-mesh nebuliser over a 10 minute period as determined using the abbreviated impactor.

Keywords: erlotinib; genistein; probe-sonication; impactor; nebuliser

1. Introduction

Genistein and erlotinib, hydrophobic drugs of BCS class II, are characterised by low aqueous solubility and high permeability. Combination treatment with these drugs has shown synergistic activity with epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKIs) in three separate non-small cell lung cancer (NSCLC) cell lines; H3255, H1650 and H1781(Gadgeel et al., 2009). Genistein and erlotinib represent a rational and challenging combination for co-delivery directly to the airways in an appropriate delivery system for local