Development of Inhalable Powder Formulation of Broad-Spectrum Antiviral Agent for Respiratory Viral Infections

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In response to emerging and re-emerging respiratory viral infections with high morbidity and mortality such as Coronavirus Disease 2019 (COVID-19), Middle East respiratory syndrome coronavirus (MERS-CoV), and influenza, early administration of broad-spectrum antivirals can facilitate pandemic control and improve patient outcomes. This provides empiric therapeutic options during the time-lag for developing specific drug/vaccine. AM80 (tamibarotene), an orally active retinoid, was demonstrated with broad-spectrum antiviral efficacy in a recent study. To maximise antiviral efficacy in respiratory tract, an inhalable powder formulation of AM80 was developed by spray freeze drying (SFD) technology with hydroxypropyl-β-cyclodextrin (HPβCD) as solubiliser. The formulation showed good aerosol performance, as evaluated by Next Generation Impactor, with a fine particle fraction of 65.1 ± 7.9% and an emitted fraction of 95.1 ± 1.7%. The sublimation of solvent crystal led to the formation of porous particles, which was visualised by scanning electron microscopy. In contrast to the slow-dissolving unformulated AM80, the SFD AM80 powder displayed a burst-release dissolution, which is postulated to be a combined result of enhanced solubility by HPβCD and increased surface area of porous structure. The *in vivo* pharmacokinetics of the SFD AM80 powder after intratracheal administration was investigated in mice. With the same dose given, inhaled AM80 powder resulted in higher bioavailability in both lungs and plasma than intraperitoneally injected unformulated AM80 in 0.1% DMSO solution. This study demonstrated a strategy to develop an inhaled formulation for a broad-spectrum antiviral agent, which could be a strong candidate in clinical applications for various respiratory viral infections.