Controlled Release Polymeric Inhaled Microspheres for Treatment of Pulmonary Hypertension
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Purpose
Pulmonary hypertension (PAH) is a condition of the lungs characterised by an elevated arterial pressure and increased vascular resistance. Current treatment options are not patient compliant due to their administration techniques or frequent dosing regimens. To overcome this problem, polymeric controlled release inhalation microspheres, which provide a targeted route of delivery, were developed, thus leading to a decrease in the dosing frequency and improved patient compliance.

Methods
Microspheres were formulated by spray drying and then characterised in terms of particle size, morphology, crystalline nature, in vitro release profile and in vitro aerosolisation profile. The interaction between PVA and nifedipine was determined using Fourier transformed infra-red spectroscopy (FTIR) and thermal analysis (differential scanning calorimetry) of the microsphere samples. As the microspheres are expected to reside within the lungs over a prolonged duration of time, it was imperative to test the toxicity of PVA on lung epithelial cells. For this, human alveolar basal epithelium, A549 cell line, was used and cell viability after 48h of exposure to PVA was determined using the MTT assay.

Results
The microspheres were within the inhalable range (1-10 µm) with spherical morphology. X-ray diffraction study showed that nifedipine encapsulated within the microspheres was amorphous in nature. The in vitro release profile showed an initial burst release followed by extended release. The in vitro aerosolisation study showed that the FPF of the microspheres is greater than 20%, which is in good agreement with the current marketed formulations. PVA was found to have insignificant effect on cell viability after 48h of exposure to the A549 cell line. Upon statistical analysis, it was shown that there was no significant difference in the percentage cell viability between 24h and 48h of MTT assay.

Conclusion
In conclusion, microspheres of nifedipine and PVA, prepared by spray drying were found to exhibit suitable properties to achieve controlled release by inhalation.