LAMELLASOME Technology: Off the bench and into production

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Background: LAMELLASOME™ technology is being engineered to deliver active payloads in the treatment of pulmonary conditions including idiopathic pulmonary fibrosis and cystic fibrosis. Two key challenges exist in relation to the production of LAMELLASOME vesicles: 1) The use of scalable downsizing procedures and 2) the commercial compatibility of production methods. The implementation of a simple, solvent-free method produced LAMELLASOME vesicles with desirable characteristics while eliminating hazardous waste and reducing energy requirements.

Methods: LAMELLASOME vesicles were prepared at an optimised concentration using a solvent free process whereby, components were combined and homogenised with pre-warmed Tris buffer (70 °C; pH 7.4) for 1 h at 8750 rpm (Silverson Homogeniser). The Microfluidizer (M110P; 25k psi) was used as a scalable method to downsize lipid vesicles to express desirable characteristics as determined using Dynamic Light Scattering (DLS; Malvern Panalytical). Lipid recovery was monitored over time using ELSD-HPLC. With an ultimate goal of formulating a pulmonary delivery system, the impact of nebulisation on physicochemical characteristics was further investigated.

Results: Downsized LAMELLASOME vesicles produced using scalable methods expressed similar characteristics to those produced at the lab-scale. As expected, LAMELLASOME vesicles were formulated to express an anionic surface charge, low PDI (< 0.3) and average vesicle size between 50 and 60 d.nm. Depending on the nebulisation method, the average aerosol size was found to be between 4 and 6 µm and was not significantly altered based on total lipid concentration. Further physicochemical characterisation supports the generation of stable formulations which may successfully deliver cargo to the lung.

Conclusions: The implementation of a solvent-free method of LAMELLASOME vesicle production generated vesicles with mapped physical properties compared to those prepared using traditional methods, eliminating the use of solvents. In addition, desirable characteristics were achieved using scalable processes. These data support the ability to translate a nebulised pulmonary delivery system from R & D lab-scale production to an industrial-scale manufacturing setting.

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