Abstract

In the lungs of cystic fibrosis (CF) patients, *Pseudomonas aeruginosa* commonly causes chronic infections. It has been shown that the *P. aeruginosa* quorum sensing (QS) system controls the expression of virulence factors during invasion and infection to host cells. PvdQ is an acyl–homoserine lactone (AHL) acylase able to degrade the signal molecule of *P. aeruginosa* QS. The role of PvdQ in inhibiting the QS and its successive virulence determinants has been established in *in vitro* as well as in *in vivo*, the latter in a *Caenorabdhitis elegans* model. For the treatment of pulmonary *P. aeruginosa* infections, we propose that PvdQ can be best administered directly to the lungs of the patients as a dry powder because this is expected to give specific advantages in delivery as compared to nebulizing. Therefore in this study we investigated the production of a PvdQ powder by spray-freeze drying using mannitol, trehalose and inulin as excipient. The activity of PvdQ in the powder was determined immediately after production and after subsequent storage during 4 weeks at 20 °C and 55 °C. We found that the enzymatic activity of PvdQ is fully maintained during spray-freeze drying using mannitol, trehalose or inulin as excipient. However, mannitol was not able to stabilize the protein during storage, while PvdQ incorporated in trehalose or inulin was fully stabilized even during storage at 55 °C for at least 4 weeks. The poor stabilizing capacities of mannitol during storage could be related to its crystalline nature while the excellent stabilizing capacities of trehalose and inulin during storage could be related to their amorphous nature. The trehalose and inulin-based particles consisted of porous spheres with a volume average aerodynamical diameter of ~1.8 μm implying that they are suitable for pulmonary delivery. This is the first study in which an AHL-degrading enzyme is processed into spray-freeze-dried powder suitable for inhalation.