

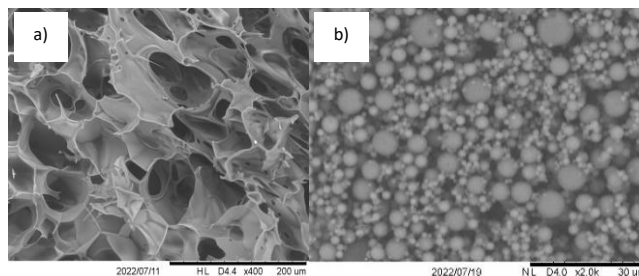
# Influence of drying technique on the enzymatic activity of lactate dehydrogenase before and after tableting

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**ABSTRACT:** The objective of our work is to investigate the effect of the drying process (freeze-drying or spray-drying) followed by compaction, on the residual enzymatic activity of the lactate dehydrogenase (LDH), a model protein used in this study. Freeze and spray-drying were the drying techniques used for preparing the dried biopharmaceuticals formulations. Since biomolecules are subjected to stresses such as temperature and pressure during the drying processes, trehalose, a non-reducing sugar, was added in the formulation as a biomolecule cryo and lyoprotectant. Freeze-dried (FD) and spray-dried (SD) powders containing LDH were tableted using a Styl'One Evolution tableting press and different compaction pressures were applied (in the range of 50 –250 MPa). Internal structure images of the FD and SD powders as well as tablets were assessed by scanning electron microscopy (SEM). DSC measurements were done on the FD and SD powders. The water content of FD and SD were measured by a Karl-fisher titrator. Those physico-chemical characterizations show that FD and SD trehalose powders present distinctive properties. Firstly, the texture of these two powders is different with honeycombed structure after the freeze-drying process, vs spherical particles after spray-drying (Figure 1). Secondly, the residual moisture RM content was higher for SD trehalose (5.8%) than FD samples (1.3%). Thirdly, DSC thermograms show a significantly higher glass transition temperature ( $T_g$ ) for FD samples ( $T_g = 95^\circ\text{C}$ ) compared to the SD powder ( $T_g = 50^\circ\text{C}$ ). Finally, the enzymatic activity of LDH was measured before and after each process (freeze-drying, spray-drying and tableting). The results of LDH activity measurements, immediately after freeze and spray-drying, show no loss of activity compared to the native protein. Concerning compaction, an exhaustive study has been carried out first to evaluate the mechanical properties under/after compression of these two powders. The study showed a specific and different behavior in terms of compressibility and compatibility. This is probably due to the differences seen in their texture. Then, the LDH activity was measured after compaction of both, FD and SD powders. Results showed the preservation of a 100% of its activity for FD powder regardless of the pressure applied but a loss of enzymatic activity for SD powder was observed when a high compaction pressure was applied (250 MPa)



**Figure 1: SEM of (a) freeze-dried trehalose powder and (b) spray-dried trehalose powder.**