SOCIETY FOR CRYOBIOLOGY

CRYO 2025

HANNOVER

»ABSTRACTS

CRYO2025 HANNOVER JULY 22-25

Funding: The IGF project 22205 N of the FEI was supported within the programme for promotion the industrial Collective Research (IGF) for the German Ministry of Economics and Climate Action (BMWK) based on a resolution of the German Parliament. The AiF project KK5022306BS0 was supported by the AiF as part of the central innovation program for medium-sized business (ZIM) based on a resolution of the German Parliament.
Conflict of Interest: None to disclose
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S37 SPRAY FREEZE-DRYING OF INHALABLE MONOCLONAL ANTIBODIES: ENHANCING STABILITY AND FLOWABILITY

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Spray freeze-drying (SFD) is an advanced technique for producing dry powders, particularly suited for pulmonary drug delivery via dry powder inhalers (DPIs), due to its ability to generate porous microparticles with low density and excellent aerodynamic properties. The SFD process, which involves atomization, freezing, and drying, is especially advantageous for formulating biologics such as monoclonal antibodies (mAbs), as it operates under low-temperature conditions. However, this method presents challenges, including the risk of mAb denaturation caused by shear forces, freezing, and dehydration stresses during processing. This study assessed the physical stability of spray freeze-dried powders and the stress-induced aggregation of an mAb under these conditions. The protective effects of sugars (trehalose and mannitol), amino acids (leucine), cyclodextrins (2-hydroxypropyl-β-cyclodextrin), and surfactants (Tween 80) were systematically investigated using a Design of Experiments approach. mAb chemical stability was analyzed via size exclusion chromatography following the SFD process to evaluate the effectiveness of each formulation at different times. The stability of the spray freeze-dried mAb powders was examined under storage conditions of 5 °C, 25 °C, and 40 °C. The resulting inhalable mAb powders demonstrated excellent aerodynamic properties, rapid dissolution within the lung, and remarkable stability across various storage conditions. Notably, trehalose, when combined with either leucine or 2-hydroxypropyl-β-cyclodextrin, effectively preserved mAb stability throughout the SFD process, ensuring high fine particle fractions (50–60%) and superior physical stability. By contrast, formulations containing mannitol as the sole sugar exhibited increased mAb aggregation, while 2-hydroxypropyl-β-cyclodextrin proved to be a more effective stabilizer than leucine. These findings highlight the potential of SFD for developing stable, high-performance biologic formulations for pulmonary drug delivery.

Funding: This publication is part of the project PNRR-NGEU, which has received funding from the MUR—DM352/2022. This research was funded by Chiesi Farmaceutici S.p.A.
Conflict of Interest: Lorena Pasero holds a Doctorate Studentship and collaborates with

Chiesi Farmaceutici S.p.A as part of her PhD training. Adamo Sulpizi and Tomaso Guidi are employees of Chiesi Farmaceutici S.p.A. All authors declare no conflicts of interest.
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S38 UNDERSTANDING BACTERIAL STRESS SENSITIVITY AND ENVIRONMENTAL IMPACT TO PROPOSE ECO-FRIENDLY PRESERVATION STRATEGIES

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Lactic acid bacteria (LAB) are widely used to produce fermented foods and probiotics. Freezing and drying are applied to preserve their functionalities. However, stabilization processes can damage cells, causing loss of viability and activity, and are highly energy-consuming. This work aimed to integrate the mechanisms underlying bacteria damage, product quality, and environmental performance to deliver practical recommendations for improving LAB preservation protocols.

The experimental approach involved two LABs of interest to the food industry that exhibit different sensitivity to manufacturing processes. Samples were characterized following freezing, freeze-drying, spray-drying, and storage by measuring the acidifying activity, the membrane integrity by flow cytometry, and the biochemical composition by infrared micro-spectroscopy to identify cell damage. Freeze-drying induced osmotic and mechanical stresses, which damaged the cell membrane and wall, while the thermal stress applied during spray drying altered nucleic acids and proteins. It was also evidenced that the glass transition temperature of the dried bacterial concentrates must be at least 40°C higher than the storage temperature for long-term preservation.

Life Cycle Assessment was applied to evaluate the environmental performance of different scenarios. Pilot-scale data were used to calculate the environmental impacts. Fermentation, freeze-drying, spray-drying, and frozen storage were the hotspots of the process. The choice of the stabilization alternative exhibiting the lowest environmental impacts depended on the storage time and the LAB sensitivity (loss of acidifying activity). When considering storage time lower than 4 months, freezing and frozen storage displayed the best environmental performance. For the most sensitive LAB and long-term storage, since similar losses of functionality were observed for both drying processes, spray-drying appeared as a less energy-consuming and more environmentally friendly alternative than freeze-drying. The role of the protective solution’s composition, as well as the fermentation conditions, deserve further studies. Improving the biomass yield after fermentation could significantly reduce the environmental impact.