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Application of QbD Principles in Hydrophobic-Ion Pairing Complexation of Proteins

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Delivery of biopharmaceuticals such as peptides and proteins has been faced with several difficulties including low encapsulation efficacy in hydrophobic micro/nanocarriers. To overcome this, hydrophobic ion pairing (HIP) complexation was proposed, by which the hydrophobicity of hydrophilic macromolecules could be significantly increased via a reversible electrostatic complexation with an oppositely charged amphipathic molecule in a suitable pH environment. The HIP complex of lysozyme (LYZ), as model protein in nonparenteral formulations, with ion pairing agents (IPA) such as sodium dodecyl sulphate (SDS) was reported in several studies using variable settings and conditions leading to discrepancies in the yield in terms of complexation efficiency. This work aimed to investigate different variables affecting the preparation of the HIP complex of LYZ and SDS with the aid of the quality by design (QbD) approach. Risk assessment (RA), as one of the QbD tools, was applied to identify and rank of different factors influencing the preparation of such a complex. This assessment shows that the molar ratio of the SDS:LYZ, pH and the drying conditions are the most highly ranked influential factors and the experimental investigations were focused on them. The smart electrostatic titration approach was helpful in the determination of the optimum molar ratios for this complexation at selected pH values. These ratios were confirmed by a series of complexation experiments that revealed a high yield of the hydrophobic complex. Moreover, our optimized ventilated oven-drying was superior to the commonly used freeze-drying method in terms of time and energy and resulted in a dry complex of comparable quality to that obtained by the latter.

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Reference:

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