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Thermo-Optical Protein Characterization for Straightforward Preformulation Development

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Abstract

The determination of protein unfolding and aggregation characteristics during preformulation is of major significance for the development of biopharmaceuticals. The aim of this study was to investigate the feasibility of a new immobilization- and label-free thermo-optical approach as an orthogonal method for material and time saving early formulation and drugability screenings. In the experimental setup used, changes in the intrinsic tryptophan fluorescence of the protein were measured during IR-laser induced heating of the samples. This temperature increase leads to characteristic fluorescence changes over time, which can be attributed to separable effects of protein unfolding, aggregation, and precipitation, depending on the stability of the respective formulation. The obtained signals were compared with data from forced degradation- and thermal stability measurements, and correlated well both with the aggregation propensity, as well as with the reversibility of unfolding in different formulations. These results, gathered with only 4 μ L sample volume and 150 s measurement time per formulation, demonstrate potential for general applicability in rapid candidate and formulation selections.

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