The effect of chemical chaperones on test systems with different kinetic regime of aggregation

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The kinetic regime of the protein aggregation process, which includes the stages of the protein molecule unfolding, nucleation and growth of aggregates, is determined by the rate-limiting stage of this process. In the presence of chemical chaperones, the kinetics of target protein aggregation can change significantly. In this work, we propose a method for analyzing aggregation curves obtained by dynamic light scattering, which allows us to quantitatively characterize the effect of chaperones on individual stages of the model protein aggregation process. The test systems characterized by the order of aggregation with respect to the protein (n) equal to 0.5, 1 or 2 and based on thermal aggregation of muscle glycogen phosphorylase *b* (Ph*b*) at 48 °C (n = 0.5), UV-irradiated Ph*b* (UV-Ph*b*) at 37 °C (n = 1) and apo-form of Ph*b* (apo-Ph*b*) at 37 °C (n = 2) were used. It has been shown that the effects of the chemical chaperones betaine and lysine are not the same for test systems with different aggregation kinetics, while arginine stimulates the formation of aggregates for all proteins under study. Betaine protects Ph*b* and apo-Ph*b* from aggregation, but accelerates aggregation of UV-Ph*b*. Lysine increases the rate of Ph*b* aggregates formation, but slows down the process of UV-Ph*b* and apo-Ph*b* aggregation. The protective effect of chaperones is accompanied by a slowdown of the stages of nucleation and aggregates growth, while accelerating the target protein aggregation results in a decrease in the duration of the nucleation stage and an increase in the rate of protein aggregates growth. The mechanisms of chaperones action on the aggregation kinetics of various test systems have been discussed. This work was supported by the Russian Science Foundation (grant 16-14-10055) and the Ministry of Science and Higher Education of the Russian Federation.