PFDA binding-induced secondary structure changes in alpha-lactalbumin

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Per- and polyfluoroalkyl substances (PFAS) are linked to negative health effects in living organisms. Human exposure to PFAS can occur through environmental presence, contaminated water, household products, or food ingestion. In this study, we investigate the impact of perfluorodecanoic acid (PFDA), one of the PFAS substances, on alpha-lactalbumin (ALAC), a protein that is essential for lactose biosynthesis in lactating mammary glands. Since lactose provides 40% of an infant's nutritional needs during development, and PFAS was found in both human and cow milk, understanding ALAC's interactions with PFDA is critical. Circular dichroism (CD) experiments show a significant reduction in ALAC helicity upon PFDA exposure. To determine the interactions driving these structural changes, we performed docking calculations and classical molecular dynamics (MD) simulations. Our results identify two primary PFDA binding sites on the ALAC surface, with multiple PFDA molecules binding to those sites at higher concentrations, revealed by the MD trajectory analysis codes that we developed. Steered MD simulations further reveal which helices are most susceptible to unwinding in the presence of PFDA. This combined computational and experimental approach provides new insights into how PFDA compromises the structural integrity and function of ALAC, advancing our understanding of protein interactions with perfluorinated compounds.