Using Electrophoresis to Quantify the Kinetic Stability of Transthyretin

by

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ABSTRACT

In this study, an attempt was made to create a simple assay which could identify and quantify the denaturation of the protein Transthyretin (TTR) using gel electrophoresis to identify the denaturation of other proteins. Currently, more sophisticated techniques of identifying protein denaturation are used, including fluorescence spectroscopy. However, this is costly and not available in many laboratories. The misfolding and aggregation of TTR has been associated with cardiomyopathy (familial amyloid cardiomyopathy), familial amyloid polyneuropathy (FAP) (systemic neuropathies), and central nervous system amyloidoses (CNSA). In general, TTR amyloidogenesis occurs via dissociation of the tetramer, then partial monomer unfolding, which in turn leads to amyloid formation. Time courses were performed by incubating samples of wild type TTR and variants of TTR in sodium dodecyl sulphate (SDS) over several days, in an attempt to show the gradual denaturation of TTR from its native tetrameric form into its constituent monomers. Although the results showed that the assay worked and was able to monitor the denaturation of TTR, the gel quality was in much need of improvement, and quantification of the gels in the future will be a requirement