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Deposition of amyloids occurs in a number of diseases known generally as amyloidoses. However, proteins, such as myoglobin, which are not involved in any known disease, are also able to form amyloid fibrils. Apomyoglobin is well known by its ability to populate an intermediate in its folding binding and we asked whether the stability of the intermediate could control amyloid formation. For that, we examined the rates of amyloid formation of wild-type apomyoglobin and three of its mutants (W7F/W14F, H24V/H119F and H36Q). Kinetics were measured by following the time dependence of ThT binding upon incubation of proteins at pH 9.0, 65°C in 50mM sodium borate. Mutants W7F/W14F and H36Q showed a rate of amyloid formation significantly greater than wild-type, while H24V/H119F mutant showed a lower rate of amyloid formation. The stability of the intermediate forms was investigated by urea-induced unfolding at pH 4.2, and our results showed that, when compared to the wild-type, W7F/W14F is less stable, H24V/H119F is more stable, and H36Q has parallel stability. In conclusion, our results suggested that the ability to form amyloid may be related to partially unfolded structures like those presented in the intermediates. More likely, by the exposition of hydrophobic patches which become available to unspecific contacts like those present in the pre-aggregated forms.

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