REMARKABLE THERMAL STABILIZATION OF COLLAGEN-LIKE PEPTIDES VIA 2-AZABICYCLO ALKANE INCORPORATION

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Collagen-like peptides (CLP) provide a controllable reductionist model of the collagen triple helix, serving as a fundamental tool for the rational design of stable, collagen-based biomaterials. In these systems, thermal stability can be tuned by sequence engineering (e.g., conformationally constrained residues) as well as by molecular architecture (e.g., covalent preorganization of three peptide strands on a tripodal scaffold).[1,2]

This study evaluates the impact of introducing a 2-azabicycloalkane residue (azBca) on the apparent melting temperature T_m and examines how concentration (0.5 vs 1.0 mg mL^{-1}) and architecture (linear vs scaffold-preorganized) influence higher-order association. Triple-helix formation and thermal unfolding were monitored by circular dichroism (CD) spectroscopy in PBS (10 mM, pH 7.4) after incubation at 4 °C for $\geq$48 h; thermal ramps (4–70 °C, 1 °C min^{-1}) were followed at 225 nm, with T_m obtained from the extremum of $\mathrm{d}Abs/\mathrm{d}T$ (Fig. 1).

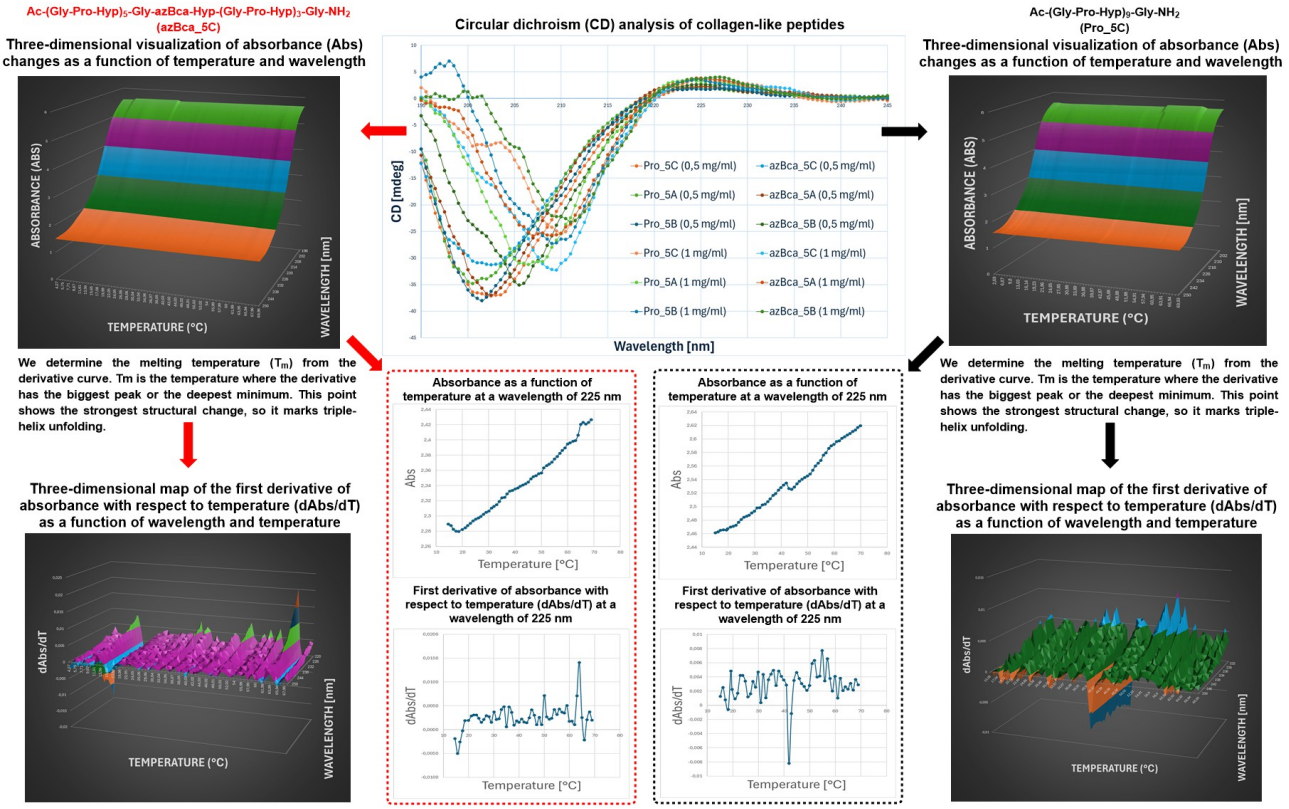

Fig. 1. CD spectra and thermal unfolding of CLP at 0.5 and 1.0 mg mL^{-1} in PBS (10 mM, pH 7.4). T_m was determined from the extremum of $\mathrm{d}Abs/\mathrm{d}T$ at 225 nm. Increasing concentration shifts the CD minimum toward ~205–210 nm, consistent with increased supramolecular ordering.

Results indicate that azBca incorporation strongly increases thermal stability, with T_m rising from 41.89 °C for Pro_5C to 63.95 °C for azBca_5C. With increasing concentration, the CD minimum shifts from approximately 198–205 nm toward approximately 205–210 nm, consistent with increased supramolecular ordering. Similar 204–210 nm features have been reported for type I collagen under fibrillogenesis conditions, although CD alone cannot confirm fiber formation.[3]

These azBca-stabilized CLPs provide a robust platform for introducing bioactive motifs and for integration into hydrogel/ECM-mimetic materials for tissue engineering applications.

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[2] J. Kwak, A. De Capua, E. Locardi, and M. Goodman, "TREN (Tris(2-aminoethyl)amine): An Effective Scaffold for the Assembly of Triple Helical Collagen Mimetic Structures," Journal of the American Chemical Society, vol. 124, no. 47, pp. 14085–14091, Nov. 2002, doi: 10.1021/ja0209621.

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