CONFORMATIONAL PROPERTIES OF POLYPEPTIDE MODELS OF COLLAGEN

Rajendra S. Bhatnagar and Rao S. Rapaka
University of California, San Francisco
San Francisco, California 94143 and
V.S. Ananthanarayanan
Indian Institute of Science
Bangalore, India

ABSTRACT

Individual collagen chains exist as Polypro II helices because of their large imino content and their super-coiling into the collagen triple helix is facilitated by Gly in every third position. Because of this, collagen may be considered as being made up of Gly-led triplets. One fourth of such triplets in collagen have the sequence Gly-Pro-X and another one fifth, Gly-X-Hyp, where X is an α-amino residue. The stereochemical properties of the imino peptide bond, the position of the imino residue in the sequence and its interactions with neighboring residues, determine the conformation. Synthetic polytripeptides of sequence (Gly-Pro-X)$_n$ generate collagen-like conformations in aqueous solutions whereas (Gly-X-Pro)$_n$ sequences usually do not. This difference has been attributed to different H-bonding properties of X-NH in the two sequences. Stabilizing interactions are said to occur between the side chain of X and Pro ring atoms in X-Pro but not in Pro-X. We investigated this question using (Gly-Pro-Sar)$_n$ (I) and (Gly-Sar-Pro)$_n$ (II). (I) generated collagen-like conformations in aqueous solutions but (II) did not although some order was elicited in helix promoting solvents. Since NH-H bonds are not possible at Sar residues, they may not play a final role in stabilizing the collagen helix. It appears likely that non-bonding interactions of the imino residue with the residue on its C-terminal may play a significant role in stabilizing collagen-like conformations.
INTRODUCTION

Collagen, the principal skeletal protein in the body is eminently well-equipped for its various structural and mechanical functions by virtue of a unique, highly ordered triple helical conformation, aggregation properties, and an unusual amino acid composition expressed in a polymer-like sequence. While covalent cross-links play a significant role in defining the ultimate properties of large polymeric aggregates of collagen, the individual triple-helices derive their stability from the unusual features of the amino acid composition and sequence. Interactions between neighboring residues in the sequence play a major role in defining the conformational features of collagen. Our discussion concerns some of these interactions.

SIGNIFICANT FEATURES OF THE COLLAGEN SEQUENCE

Collagen has a very high content of glycine, which accounts for one-third of the total amino acid residues and appears in every third position in the helical region extending over 10 percent of the length of the molecule. Each chain in the triple helix can thus be regarded as being made up of glycine-led triplets and may therefore be considered to be a polymer \((\text{Gly-2-3})_n\). Another major difference between the composition of collagen and most other proteins is the unusually high content of the imino acid residues proline and hydroxyproline. These account for one-fourth of the total residues in collagen and appear in over half of the glycine-led triplets. Proline occurs in the second position, with an \(\alpha\)-amino acid (A) as the third position, as \(-(\text{Gly-Pro-A})-\) in over one-fourth of the triplets. Another one fifth of the triplets contain an \(\alpha\)-amino acid residue in the second position followed by an imino residue, usually hydroxyproline, as \(-(\text{Gly-A-Hyp})-\). Nearly one-tenth of the triplets contain two imino residues, \(-(\text{Gly-Pro-Hyp})-\). The placement of the imino residue in relation to the \(\alpha\)-amino residue in a triplet, profoundly affects the conformational features of the sequence.

STABILIZATION OF THE COLLAGEN HELIX AND ITS RELATION TO THE SEQUENCE

Homopolymers of glycine, \((\text{Gly})_n\) and proline, \((\text{Pro})_n\) form helical structures which share many similarities. Because of the preponderance of these residues in collagen, collagen helices may be expected to be similar to \((\text{Gly})_n\) and \((\text{Pro})_n\) helices. In fact the individual helices of collagen bear strong conformational resemblance to these helices but differ in the fact that unlike the homopolymers, they exist in a triple helical "coiled-coil" conformation. Super-coiling of three peptide chains into the