The Molecular Properties of ApoA-I from Human High Density Lipoprotein

JOHN GWYNNE, BRYAN BREWER, JR., AND HAROLD EDELHOCH

From the Clinical Endocrinology Branch, National Institute of Arthritis, Metabolism, and Digestive Diseases, and Molecular Disease Branch, National Heart and Lung Institute, National Institutes of Health, Bethesda, Maryland 20014

SUMMARY

The molecular properties of the principal protein component of human high density lipoprotein have been evaluated in aqueous solution at pH 2.0, 7.4, and 12.0 and in guanidine hydrochloride at pH 7.4. The high helical content observed at neutral pH by circular dichroism is partly eliminated in hydrochloride at pH 7.4. The high helical content observed in aqueous solution at pH 2.0, 7.4, and 12.0 and in guanidine hydrochloride. The fluorescence properties of the tryptophanyl residues also indicate greater loss of structure in 1.7 M guanidine hydrochloride than in aqueous solutions at any pH.

ApoA-I contains both secondary and tertiary structure in water at neutral pH comparable to that found in native globular proteins and undergoes molecular transitions below pH ~7, above pH ~11, and in guanidine hydrochloride solutions between 0.8 to 1.4 M.

The properties of succinylated apoA-I at neutral pH resemble those of apoA-I at pH 12.0.

The elucidation of the physical chemical properties of the plasma lipoproteins and their apoproteins should facilitate our understanding of lipid metabolism and afford insight into the problems of hyperlipoproteinemia and atherosclerosis. The nature of the interactions between the lipid moieties and apoprotein constituents is of interest in itself and could also shed light on the nature of lipid-protein interactions in membranes. The present study was initiated to compare the properties of the major apoprotein of human HDL when free of lipid and when combined with lipid in the native state.

Each density class of lipoproteins has been shown to contain several different polypeptide chains (1). Human HDL contains two major (apoA-I and apoA-II) and at least three minor (apoC-I, apoC-II, and apoC-III) apoproteins.1 The structural interrelations between the lipid and apoprotein constituents are not yet understood. In previous work on the properties of the apoproteins, an unfractinated mixture of apoproteins was generally used. It is clearly necessary to characterize the individual apoproteins before one can understand their structure in the native lipoprotein.

Recent studies have shown that apoA-I comprises approximately 65 to 70% by weight of the total protein of HDL (7, 13, 14). It has a molecular weight of 25,000 to 28,000 (6, 12) with NH2-terminal aspartic acid and COOH-terminal glutamine (2, 4). The sequence of the initial 39 residues (15) and the separation of the cyanogen bromide peptides (16) have been reported. In this report we have evaluated some of the molecular and structural properties of highly purified apoA-I.

MATERIALS AND METHODS

Plasma for the isolation of HDL was collected from a single normal male (C. Z.) by plasmapheresis in EDTA. HDL was prepared by ultracentrifugal flotation in KBr between densities 1.063 and 1.210 g per ml. The product was delipidated with chloroform-methanol (2:1 v/v) as previously described (8). Less than 1% phospholipid remained after delipidation. ApoA-I was isolated from the mixture of apoproteins by chromatography of delipidated HDL on Sephadex G-200 in 0.1 M Tris-HCl, 6 M urea, pH 8.5, according to the method of Scanu et al. (13). The eluates were monitored by disc gel electrophoresis and amino acid analysis. In these studies the leading edge of the apoA-I peak was consistently homogeneous by disc gel electrophoresis, whereas the descending edge was frequently contaminated by apoA-II. The purified apoA-I was dialyzed free of urea and lyophilized. The degree of purity was evaluated by polyacrylamide disc gel electrophoresis and NH2-terminal amino acid analysis. A single band seen on electrophoresis and a single residue, aspartic acid, was found for the NH2-terminal residue. Polyacrylamide gel electrophoresis was performed in 10% gels containing 8 M urea at pH 9.4 (17). NH2-terminal residues were determined by the three-stage phenylisothiocyanate procedure of Edman (18) and the phenylthiohydantoins were identified by gas-liquid chromatography (19).

Succinylation of apoA-I was performed in 0.1 M NaHCO3, pH 8.0, at 4°C using a 50-fold excess of succinic anhydride over free amino groups (20). After 1 hour, apoA-I was resolved from the reaction mixture by gel filtration on Sephadex G-10 in 0.05 M NH4HCO3 and lyophilized. The extent of modification of the lysine residues was determined by total enzymatic digestion of succinylated apoA-I (8), followed by amino acid analysis. Amino acid analyses were performed on a Beckman model 122C or 120 Fraction V D4 (12); apoC-III to: apoLp-Ala (10), R-Ala (5), D4 (11), and Fraction V D2, D4 (12).
amino acid analyzer equipped for high sensitivity (21) and accelerated elution schedule (22).

Concentrated solutions of apoA-I were kept frozen in 0.002 M PO4 at neutral pH. ApoA-I stored at 4° in 0.002 M PO4 for extended periods exhibited some loss in structure, as manifested by a pH 7.4 showed a 3% decrease in absorption at 280 nm. Consequently the molar extinction coefficient is expected to be 32,350 in aqueous solution. Absorption difference spectra were obtained on a Cary model 14 recording spectrophotometer. The molar extinction coefficient (ε) of apoA-I at 280 nm was calculated to be 31,720 in 6 M Gu-HCl from the aromatic amino acid composition reported by Lux and John (4), a molecular weight of 26,600, and molar extinction values of 1280 and 5690 for tyrosine and tryptophan, respectively (23).

Difference spectra of apoA-I in 6 M Gu-HCl relative to water at pH 7.4 showed a 3% decrease in absorption at 280 nm. Consequently the molar extinction coefficient is expected to be 32,350 in aqueous solution. Total sample weight as determined by amino acid analysis indicated a value 1% higher for e. Small corrections for any residues destroyed by the 24-hour acid hydrolysis would reduce the experimental value of e slightly. We have used the mean residue weight of apoA-I calculated from its amino acid analysis (4). Molecular weights determined from the amino acid composition (4) are in accord with those found by physical measurements in dispersing solvents.

Structure at Neutral pH

The secondary structure of proteins can be estimated by CD measurements in the far ultraviolet wavelength region (27, 28). The CD spectrum of apoA-I at pH 7.4 (Fig. 2) (in 0.002 M phosphate) is in good agreement with that previously published by Scanu et al. (13) and Lux et al. (29). The characteristic minima at 220 and 208 nm and the large negative ellipticities indicate a high helical content. Lux et al. (29) have estimated that about 55% of the peptide groups are in helical segments. The maximum amount of helix formation was estimated by measuring the CD spectrum of apoA-I in 2-chloroethanol-H2O (85:15, v/v), a solvent known to favor strongly helix formation (30) (Fig. 3). There is an increase in mean residue ellipticity at 220 nm from 18,000 to 24,600. This latter value suggests a helical content of about 70% in 2-chloroethanol if there are few peptide residues determined. Solutions containing 2.1 μM apoA-I (in 0.01 phosphate, 0.01 M acetate) were incubated for 18 hours at 25°, and then centrifuged at 30,000 × g for 1 hour at 4°. The absorbance of the supernatant was measured at 280 nm. Solutions examined between pH 2 and 7 were found to be incompletely soluble in the pH region 3.8 to 5.8 (Fig. 1).

The molecular weight of apoA-I in 8 M urea and 0.1% sodium dodecyl sulfate has been found by Scanu et al. (6, 13) to be 26,000 to 28,000. Similar values have been obtained by diseg electrophoresis in sodium dodecyl sulfate by Lux and John (4). Molecular weights determined from the amino acid composition (4) are in accord with those found by physical measurements in dispersing solvents.

The state of association of apoA-I in water was evaluated by equilibrium centrifugation at pH 7.36 (in 0.01 M Tris, 0.01 M acetate). A plot of c versus r² was found to be linear throughout the cell. A molecular weight of 26,600 was calculated (r = 0.738) indicating that apoA-I is monomeric at neutral pH to concentrations at least as great as 20 μM. Small corrections for dilution were made where necessary. All chemicals used were reagent grade except guanidine hydrochloride which was Heico "Synthesized Extreme Purity."

RESULTS

Solubility and Molecular Weight

Since the mixture of apoproteins of HDL is only slightly soluble in dilute acid solutions (26), the solubility of apoA-I was

FIG. 1. The pH dependence of the solubility of apoA-I in acid solutions. The solutions contained 56 μg per ml (2.1 μM) of apoA-I in 0.01 M phosphate and 0.01 M acetate. The concentrations of the supernatant solutions were obtained by absorbance measurements at 280 nm.
in $\beta$-structures (31). ApoA-I was found to be insoluble in 100% 2-chloroethanol.

The sedimentation behavior was measured to assess the tertiary organization of apoA-I. The sedimentation coefficient of an 11 $\mu$M solution of apoA-I at pH 7.36 (0.1 M KCl, 0.01 M phosphate), corrected to water at 20°C, was 2.23. This value can be assumed to be the sedimentation constant since the concentration of apoA-I was very low in this experiment. A frictional coefficient of 1.39 was calculated from this sedimentation constant and a molecular weight of 26,600.

The emission peak of apoA-I at 333 nm (Fig. 4) is in accord

with that observed with many native proteins and is considerably blue-shifted with respect to simple tryptophanyl peptides in aqueous solution (32). A value of 0.130 was measured for the polarization at 25°.

Conformational Changes

It is evident that apoA-I contains organized elements similar to those found in most proteins. The extent of this organized structure was investigated by examining the stability of apoA-I to various conditions and reagents which are known to unfold and denature native proteins.

Effects of Acid—The properties of apoA-I in acid were evaluated by the fluorescence behavior of the tryptophanyl residues. When the pH is reduced from 7.4 to 2.3, the wavelength of the emission peak of apoA-I shifts from 333 nm to 338 nm (Fig. 4).

The pH dependence of the acid transition could not be ascertained since unusual time effects indicating a complex reaction were observed. Some of these effects are shown in Fig. 5. The unusual kinetics may result from several overlapping molecular transitions which could affect the fluorescence of each of the four tryptophanyl residues in apoA-I differently. The situation is even more complicated than indicated in Fig. 5 since data obtained at pH 5.0 and 4.0 (not shown in Fig. 5) had final fluorescence values which were between those observed at pH 3.0 and 2.5. The unusual behavior may be due to the formation of soluble complexes of unfolded forms of apoA-I as the minimum solubility for this protein is near pH 4.5 to 5.0 (Fig. 1).

A fall in polarization and red shift in fluorescence usually represent unfolding of the polypeptide chain to a more open, flexible form. This point of view was confirmed by sedimentation velocity and circular dichroic measurements. The sedimentation rate of a dilute solution of apoA-I (11 $\mu$M) at pH 2.2
tein investigated (35, 36). Many proteins are unfolded but a due to succinylation depends very much on the particular protein investigated (35, 36). Many proteins are unfolded but a few appear to remain native with extensive succinylation. A structural change produced by the increase in negative charge occurs in apoA-I between neutrality and pH 11. Significant changes in structural parameters were observed, however, between pH 11 and 12, and indicate that apoA-I is more extensively disorganized at pH 12 than at pH 2.0. The emission peak is shifted from 333 nm at pH 11.0 to 348 nm at pH 12 (Fig. 4). The peak value at 348 nm is close to that found in simple tryptophanyl peptides in water (33) (Fig. 4) and indicates that the tryptophanyl residues in apoA-I are now highly exposed to the solvent. The fluorescence intensity of the tryptophanyl residues, however, is continuously quenched beginning at pH 9. The quenching below pH 11 is almost certainly due to energy transfer to the phenolic groups which ionize in this pH region (34). The shift in emission peak, however, results from a change in the environment of the tryptophanyl residues. The pH dependence of tryptophanyl polarization of apoA-I supports the above analysis of the fluorescence data in that there is no change until pH ~11 and a large decrease by pH 12 (Fig. 6).

The structural disorganization observed by polarization was confirmed by sedimentation and circular dichroism. The sedimentation coefficient of apoA-I declines to a value of 1.82 (s_{20,w}) at pH 11.5. The optical activity of the peptide chromophore is also strongly reduced between pH 11 and 12. The pH dependence of the mean residue ellipticity at 220 nm agrees with that of the polarization data (Fig. 6). There is evidently a distinct molecular transition above pH 11.

Succinylated ApoA-I—Succinylation of the ε-amino groups of a protein is used frequently to increase solubility. The extent of structural change produced by the increase in negative charge due to succinylation depends very much on the particular protein investigated (35, 36). Many proteins are unfolded but a few appear to remain native with extensive succinylation. In the case of apoA-I the parameters characterizing the helical structure and the molecular dimensions of the nonsuccinylated molecule have been significantly affected. Judging from the CD activity (Fig. 3), polarization, and sedimentation coefficient (Table I), succinylation of apoA-I at pH 7.4 results in about the same degree of disorganization as when apoA-I is brought from neutrality to pH 12.

Effects of Guanidine Hydrochloride—Solutions of 6 M Gu-HCl convert most globular proteins to random-coil polypeptides (37, 38). The relative stability of a protein can be evaluated from the concentration of Gu-HCl needed for 50% denaturation. The effect of Gu-HCl on the fluorescence intensity and polarization is seen in Fig. 7. It is clear that a molecular transition occurs between 0.8 and 1.4 M Gu-HCl with a midpoint near 1.1 M.

The normalization of the tryptophanyl emission peak and the small final polarization value indicate extensive loss of structure. This result was confirmed by the effect of Gu-HCl on the absorption spectrum of apoA-I. A blue-shifted difference absorption spectrum was found in 1.6 M Gu-HCl at pH 7.0 with two peaks at 292 and 285 nm (Fig. 8) which are characteristic of tryptophanyl and tyrosyl groups, respectively (39). There was a 7% decrease in absorption at the 292-nm peak, i.e. ΔA_{292}/A_{292}.

The helical content of apoA-I is also largely eliminated in 1.7 M Gu-HCl. The negative ellipticity at 220 nm is reduced by 70% in 1.7 M Gu-HCl (Fig. 3) and 85% in 6.0 M Gu-HCl.

**Table I**

| pH        | \(\bar{v}_{w}^{a}\) | \(s/s_{0}\) | \(P_{220}\) | \(\|\mu_{m}\) |
|-----------|-----------------|-------------|-------------|-------------|
| 7.4       | 2.35            | 1.39        | 0.130       | 18,000      |
| 2.2       | 1.96            | 1.58        | 0.072       | 10,000      |
| 11.5      | 1.82            | 1.70        | 0.053       | 5,000       |
| 7.4 (succ) | 1.92            | 1.61        | 0.061       | 5,000       |
| 7.4 (1.7 M Gu-HCl) | 0.052b  |       |            | 4,000       |

\(\bar{v}_{w}^{a}\) Approximately equivalent to \(s_{20,w}\) as determinations were made using photoelectric scanner at very low protein concentrations.

\(s/s_{0}\) Polarization is uncorrected for greater solvent viscosity compared to the measurements in water.

**Discussion**

There are considerable data on the properties of the apoproteins of HDL and on the reconstituted forms of HDL obtained...
apoA-I is less than 0.055 mg per ml (2.2 formed gels and quite soluble above pH 8.0. The solubility of proteins were the least soluble between pH 4.0 and 6.0 where they protein. Scanu (26) has measured the solubility of the apos at pH 7.4 in 0.002 M phosphate at 25°C.

The CD data indicate that many of the helical residues become random by pH 2.0. The unfolding of the polypeptide chain is evident from the increase in frictional ratio \(f/f_0\) which changes from 1.39 to 1.58 between pH 7.4 and pH 2.2. The rather large fall in polarization is in harmony with chain unfolding, since an increase in polarization would be expected if the change in frictional ratio represented an increase in axial ratio of a rigid ellipsoid (41). The unfolding is also revealed by the red shift in the tryptophanyl emission maximum which represents the exposure of indole groups to the aqueous solvent. The molecular disorganization that occurs by pH 2.2, however, does not result in a structureless polymer, since more extensive changes occur in alkali and in guanidine hydrochloride.

In contrast to the instability of apoA-I below pH 7 there is no evidence of a conformational change between pH 7 and 11. There are, however, important structural changes between pH 11 and 12. The molecular parameters indicate that less structure remains at pH 12.0 than at pH 2.0. The smaller values of the polarization, the mean residue ellipticities (at 220 and 206 nm), and sedimentation coefficient indicate greater flexibility of the polypeptide chain at pH 11.5 (Table I).

Relatively low concentrations of Gu-HCl at neutral pH are sufficient to eliminate most of the nonequivalent interactions responsible for the globular form of apoA-I. The polarization and circular dichroic activity in 1.7 M Gu-HCl are reduced to values smaller than those observed in either acid or alkali. The molecular transition in 1.7 M Gu-HCl is also revealed by an enhanced exposure of tyrosyl and tryptophanyl residues to the solvent, as seen by the denaturation blue shift in the difference absorption measurements.

Succinylation unfolds many proteins by increasing their negative charge (35). The properties of apoA-I are more drastically altered by succinylation than by decreasing the pH to 2.0. The effect of succinylation is, however, less disruptive on the structure of apoA-I than that of 1.7 M Gu-HCl or the effects of pH greater than 11.5 (Table I).

ApoA-I is isolated from the other apoproteins found in HDL by chromatography in 8 M urea (13). In this solvent,apoA-I should have very little, if any, organized structure. In fact, the optical rotatory and viscosity behavior of the apoproteins of HDL are almost the same in 8 M urea as in 8 M Gu-HCl (42). The extensive secondary and tertiary structure that is observed at neutral pH in water indicates that apoA-I refolds when urea is eliminated. It appears to be quite stable to pH between pH ~7 and 11 and to guanidine at concentrations below 1 M. It is less stable to guanidine denaturation than other well characterized proteins, such as ribonuclease or lysozyme (43, 44).

The molecular structure of apoA-I at neutral pH resembles that of many native globular proteins in that it has a large percentage of helical residues and a relaxation time large enough to indicate extensive folding of the polypeptide chain. The magnitude of the difference absorption data in 1.7 M Gu-HCl and the rather low wavelength maximum of tryptophanyl emission also reflect significant tertiary structure. The molecule is either not quite as symmetric or not quite as rigid as other proteins of similar size, since the frictional ratio of apoA-I at neutral pH, i.e. 1.39, is somewhat larger than found for many globular proteins, i.e. 1.1 to 1.3 (40). If the higher frictional ratio is due to backbone flexibility and solvent penetration, the interaction of apoA-I with lipid constituents could result in a more rigid and structured molecule.

Important elements of both the secondary and tertiary structure of apoA-I are lost in acid (Table I). The CD data indicate that many of the helical residues become random by pH 2.0. The unfolding of the polypeptide chain is evident from the increase in frictional ratio \(f/f_0\) which changes from 1.39 to 1.58 between pH 7.4 and pH 2.2. The rather large fall in polarization is in harmony with chain unfolding, since an increase in polarization would be expected if the change in frictional ratio represented an increase in axial ratio of a rigid ellipsoid (41). The unfolding is also revealed by the red shift in the tryptophanyl emission maximum which represents the exposure of indole groups to the aqueous solvent. The molecular disorganization that occurs by pH 2.2, however, does not result in a structureless polymer, since more extensive changes occur in alkali and in guanidine hydrochloride.

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REFERENCES

1. Fredrickson, D. S., Lux, S. E., and Herbert, P. N. (1972) in Advances in Experimental Medicine and Biology (Holmes, W. T., Paolotti, R., and Kritchevsky, D., eds), p 95, Plenum Press, New York
2. Kostner, G., and Alaupovic, P. (1971) Fed. Eur. Biochem. Soc. Leil., 15, 320
3. McConathy, W. J., Quiroca, C., and Aaloupovic, P. (1972) Fed. Eur. Biochem. Soc. Lett. 19, 323
4. Lux, S. E., and John, K. M. (1972) Biochim. Biophys. Acta 278, 206
5. Shore, B., and Shore, V. (1969) Biochemistry 8, 4510
6. Edelstein, C., Lim, C. T., and Scanu, A. M. (1972) J. Biol. Chem. 247, 5542
7. Rudman, D., Garcia, L. A., and Howard, C. H. (1970) J. Clin. Invest. 49, 365
8. Lux, S. E., John, K. M., and Brewer, H. B., Jr. (1972) J. Biol. Chem. 247, 7510
9. Scanu, A. M., Lim, C. T., and Edelstein, C. (1972) J. Biol. Chem. 247, 5850
10. Herbert, P., Levy, R. I., and Fredrickson, D. S. (1971) J. Biol. Chem. 246, 7068
11. Brown, W. V., Levy, R. I., and Fredrickson, D. S. (1969) J. Biol. Chem. 244, 1238
12. Scanu, A. M. (1972) Biochim. Biophys. Acta 265, 471
13. Scanu, A. M., Toth, J., Edelstein, C., Koga, S., and Stiller, E. (1969) Biochemistry 8, 3309
14. Albers, J. J., and Aladjem, P. (1971) Biochemistry 10, 3436
15. Shore, B., and Shore, V. (1972) Proceedings of the European Society of Atherosclerosis, Masson and Cie, Paris
16. Jackson, R. L., Baker, H. N., David, J. E. K., and Gotto, A. M. (1972) Biochem. Biophys. Res. Commun. 49, 1444
17. Reissfeld, H. A., and Small, P. A., Jr. (1966) Science 152, 1253
18. Edman, P. (1970) Protein Sequence Determination (Needleman, S. B., ed), p. 211, Springer-Verlag, New York
19. Pisano, J. J., Bronzert, T., and Brewer, H. B., Jr. (1972) Anal. Biochem. 45, 43
20. Klote, I. M. (1967) Methods Enzymol. 11, 570
21. Hubbard, R. W., and Keenum, D. M. (1965) Anal. Biochem. 12, 593
22. Huhray, R W (1965) Biochem. Biophys Res Commun 19, 679
23. Edelhoch, H. (1967) Biochemistry 6, 1948
24. Schachman, H. K., and Edelstein, S. J. (1966) Biochemistry 5, 2081
25. Cohn, E. J., and Edsall, J. T. (1943) Proteins, Amino Acids and Peptides, p. 370, Reinhold Publishing Co., New York
26. Scanu, A. (1966) J. Lipid Res. 7, 295
27. Saxena, V. P., and Weisfuss, D. B. (1971) Proc. Nat. Acad. Sci. U. S. A. 68, 969
28. Chen, Y., Yang, J. T., and Martinez, H. M. (1972) Biochemistry 11, 4120
29. Lux, S. E., Hire, R., Shragler, R. I., and Gotto, A. M. (1972) J. Biol. Chem. 247, 2598
30. Dott, P. (1959) Biophysical Science—A Study Program (Oncley, J. L., Schmitt, F. O., Williams, R. C., Rosenberg, M. D., and Bolt, R. H., eds), p. 101, John Wiley and Sons, Inc., New York
31. Greenfield, N., and Fasman, G. D. (1969) Biochemistry 8, 4108
32. Teale, F. W. J. (1960) Biochem. J. 67, 381
33. Bernstein, R. S., Wilchek, M., and Edelhoch, H. (1969) J. Biol. Chem. 244, 4398
34. Edelhoch, H., Brand, L., and Wilchek, M. (1967) Biochemistry 6, 547
35. Habeeb, A. F. S. A., Casiday, H. G., and Singer, S. J. (1958) Biochim. Biophys. Acta 29, 557
36. Gounares, A., and Otteeen, M. (1965) C. R. Lab. Carlsberg 36, 37
37. Tanford, C., Kawahara, K., and Lanfanje, S. (1967) J. Amer. Chem. Soc. 89, 729
38. Tanford, C., Kawahara, K., Lanfanje, S., Hooper, T. M., Jr., Zalongo, M. H., Salahuddin, A., Aune, K. C., and Takagi, T. (1967) J. Amer. Chem. Soc. 89, 5023
39. Donoyan, J. W. (1969) Physical Principles and Techniques of Protein Chemistry (Leach, S. J., ed), Part A, p. 101, Academic Press, New York
40. Tanford, C. (1961) Physical Chemistry of Macromolecules, p. 358, John Wiley and Sons, Inc., New York
41. Weber, G. (1965) Biochem. J. 91, 145
42. Scanu, A. (1965) Proc. Nat. Acad. Sci. U. S. A. 54, 1701
43. Salahuddin, A., and Tanford, C. (1970) Biochemistry 9, 1342
44. Aune, K. C., and Tanford, C. (1969) Biochemistry 8, 4579
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