Characterization of the Plasma Lipoproteins and Apoproteins of the *Erythrocebus patas* Monkey†

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ABSTRACT: Patas monkey lipoproteins were fractionated into four distinct classes by a combination of ultracentrifugation and Geon-Pevikon block electrophoresis and characterized with respect to their chemical and physical properties. Very low density lipoproteins (VLDL) were isolated at $d < 1.006$, were triglyceride rich, and were in the size range 300–850 Å. They were similar in apoprotein content to the VLDL of man, dog, and swine. The Patas monkey low density lipoprotein referred to as LDL-I had β mobility and a size which ranged from 190 to 240 Å in diameter. Their chemical composition and apoprotein content were similar to those of human LDL. A second low density lipoprotein referred to as LDL-II occurred at a density of 1.05–1.085, ranged in size from 190 to 300 Å, and contained the B, arginine-rich, and A-I apoproteins. Differences between LDL-I and LDL-II included a higher sialic acid content for LDL-II and lipid to protein ratios of 3.7 and 3.0 for LDL-I and LDL-II, respectively. In addition, the LDL-II, but not LDL-I, reacted immunochemically with antisera prepared to human Lp(a). The physical, chemical, and immunochemical properties indicated that monkey LDL-II were equivalent to the human Lp(a). Patas monkey HDL, equivalent to human HDL, were protein and phospholipid rich and ranged in size from 70 to 100 Å in diameter. The two major HDL apoproteins, A-I and A-II, were isolated from apo-HDL by column chromatography. The amino-terminal sequence of Patas A-I showed striking homology to that reported for human, dog, and swine A-I. The amino acid composition of monkey A-II was very similar to that of human A-II; however, unlike human A-II, the monkey apoprotein was shown to exist as a monomer similar to that reported for Rhesus monkey A-II. The similarities between the plasma lipoproteins of the monkey and of man suggest that the Patas monkey would serve as a suitable model for metabolic studies.

In the search for models of atherosclerosis, the nonhuman primates represent a group of animals with considerable promise. However, detailed biochemical studies on only a few species are available (Paula and Rudel, 1974; Illingworth et al., 1974; Scanu et al., 1973). It is the purpose of this study to present a detailed analysis of the plasma lipoproteins of a species of monkey which has not been investigated and which appears potentially to be an excellent model for studies of lipoprotein metabolism and atherosclerosis. The *Erythrocebus patas* monkey is an old world monkey which ranges widely in Ethiopia and the Sudan (Napier and Napier, 1967). It is readily available, relatively easy to handle, and large enough (6–12 kg at maturity) for various metabolic studies. The similarities between the plasma lipoproteins and their apoproteins of the Patas monkey and those of man are presented.

Experimental Procedure

The Patas monkeys were approximately 4 years of age and had been in quarantine for 3 months, during which time they were fed commercial monkey chow (Ralston Purina). Plasma was obtained after an overnight fast.

Preparation of Plasma Lipoproteins. The plasma was fractionated into various density classes in a 60 Ti (Beckman) rotor by ultracentrifugation (Havel et al., 1955) and the lipoproteins were purified by the Geon-Pevikon electrophoretic method (Mahley and Weisgraber, 1974a). The $d < 1.006$ fraction was washed by a second ultracentrifugation in saline ($d = 1.006$). The $d = 1.10$–1.21 or $d = 1.09$–1.21 was obtained by an initial ultracentrifugation for 48 h and was recentrifuged for 24 or 36 h. The purity of these lipoproteins was determined by paper and agarose electrophoresis and negative staining electron microscopy as previously described (Mahley and Weisgraber, 1974a,b)

Characterization of the Lipoproteins. Chemical analysis of the plasma and purified lipoproteins included total (Abell et al., 1952) and esterified cholesterol (Sperry and Webb, 1950), triglyceride (Fletcher, 1968), phospholipid (Zilversmit and Davis, 1950), and protein (Lowry et al., 1951). Sialic acid was measured on the native lipoproteins, and values were corrected for interference from unsaturated lipids (Warren, 1959). Purified lipoproteins were analyzed for their apoprotein content by polyacrylamide gel electrophoresis on 10% gels in a Tris buffer system (pH 8.9) in 8 M urea (Reisfeld and Small, 1966) and on 10% gels in 0.1% sodium dodecyl sulfate at pH 8.2 (Weber and Osborn, 1969). The lipoproteins were delipidated and apoproteins solubilized as previously reported (Mahley and Weisgraber, 1974b). Polyacrylamide gels were stained for carbohydrate with the periodic acid–Schiff reagent (Zacharius et al., 1969). Antisera were prepared and gel diffusion was performed as described (Mahley and Weisgraber, 1974b).

Isolation and Characterization of Apoproteins. HDL[1] apoproteins were solubilized in column buffer, 0.2 M Tris-Cl (pH 8.2), containing 4 M guanidine-HCl. Gel chromatography was performed with G-200 Sephadex (Pharmacia) equilibrated with column buffer on 200 × 2.5 cm columns at room temperature. Column fractions were dialyzed against 5 mM NH_4HCO_3 (pH 8.2) and lyophilized. DEAE-cellulose chro-

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[1] Abbreviations used are: HDL, high density lipoproteins; VLDL, very low density lipoproteins; LDL, low density lipoproteins.

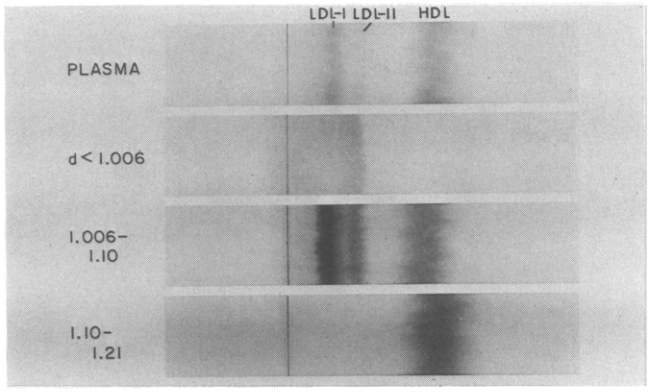

FIGURE 1: Paper electrophoretograms of plasma lipoproteins and ultracentrifugal density fractions.

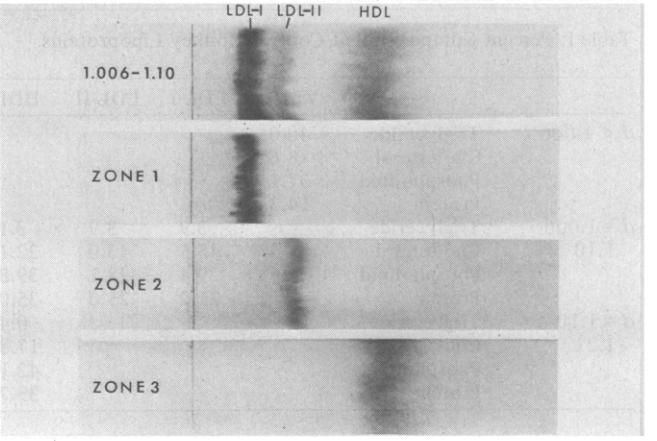

FIGURE 2: Paper electrophoretograms of the monkey lipoproteins isolated by Geon-Pevikon block electrophoresis from the 1.006 to 1.10 density fraction. Zone 1 obtained from the Geon-Pevikon is the LDL-I, zone 2 is LDL-II, and zone 3 is the HDL.

matography (DE 52 Whatman, W. and R. Balston Ltd.) was performed on the low molecular weight monkey HDL apoproteins obtained by gel chromatography. The low molecular weight proteins were solubilized in the starting buffer, 0.025 M Tris-Cl (pH 8.0) containing 6 M urea, and chromatographed on 25 × 0.9 cm columns (Kontes Glass) at 4 °C. An 800-ml linear gradient was used to elute the columns with 0.125 M Tris-Cl (pH 8.0) containing 6 M urea as the limiting buffer. Column fractions were dialyzed against 5 mM NH_4HCO_3 (pH 8.2) and lyophilized.

The purity of the column fractions was judged by sodium dodecyl sulfate or Tris-urea–polyacrylamide gel electrophoresis. Pure apoproteins were hydrolyzed in 6 N HCl at 150 °C for 2 h in a nitrogen atmosphere and subjected to amino acid analysis on a Phoenix amino acid analyzer. The amino-terminal sequences of A-I were determined by the automated Edman technique. The amino acid phenylthiohydantoins were identified by mass spectrometry (Fales et al., 1971; Fairwell and Brewer, 1973) and gas chromatography (Pisano et al., 1972). Tryptophan was determined spectroscopically (Edelhoch, 1967) and cysteic acid was determined after performic acid oxidation (Moore, 1963).

Results

Plasma lipid levels (mean ± standard deviation) in Patas monkeys fed commercial monkey chow (Ralston Purina) and fasted overnight prior to sampling were as follows: triglyceride, 27 ± 12; total cholesterol, 122 ± 25; esterified cholesterol, 108 ± 22; and phospholipid, 213 ± 31 mg/100 ml. The monkeys had been in quarantine for 3 months prior to any studies and during that time had been fed commercial chow. The control values represent the mean obtained from 24 males and 24 females at 1 and 2 months after quarantine.

Lipoprotein electrophoresis on paper revealed three bands which have been referred to as LDL-I (β), LDL-II (α_2), and HDL (α_1) (Figure 1). It will be shown that LDL-I and HDL correspond to human LDL and HDL, respectively. The LDL-II band in the α_2 position which will be suggested as equivalent to the human Lp(a) was usually seen on routine plasma electrophoresis (sample applied equal to 0.02 ml) and was present in the plasma of the eight control animals which underwent detailed lipoprotein analysis. VLDL which also have α_2 mobility were present in low concentration and not seen on routine lipoprotein electrophoresis.

Lipoprotein Distribution in Ultracentrifugal Fractions. The flotation densities of the monkey lipoproteins were determined by sequentially raising the plasma to higher densities, from d = 1.006 to 1.21, by the addition of potassium bromide. Based on analysis of the various ultracentrifugal fractions by paper or agarose electrophoresis, it was found that VLDL with pre-β mobility, present in small amounts, floated at $d < 1.006$. LDL-I with β mobility floated between densities 1.02 and 1.06, whereas LDL-II with α_2 mobility floated between d = 1.05 and 1.085. The HDL with α_1 mobility were present in the density range between 1.07 and 1.21. The intermediate density fraction between 1.006 and 1.02, referred to as ILDL, was a lipoprotein with β mobility which represented only about 1% of the total lipoprotein protein.

The combination of ultracentrifugation and preparative Geon-Pevikon block electrophoresis was required to isolate LDL-I, LDL-II, and HDL because of the overlapping densities (Figure 1). VLDL were obtained by ultracentrifugation of plasma at d = 1.006. The ultracentrifugal density fraction between 1.006 and 1.10 which contained all the LDL-I and LDL-II plus a variable amount of HDL was subjected to the block electrophoretic procedure. The zones corresponding to the LDL-I, LDL-II, and HDL were eluted from the support media for subsequent analysis (Figure 2). An intermediate zone (0.5 to 1 cm wide) between the LDL-I and LDL-II which accounted for 10 to 20% of the protein applied to the block contained a variable mixture of LDL-I and LDL-II. Recovery of lipoprotein cholesterol and protein from the electrophoretic block in all the fractions was greater than 85%. HDL, in addition to being isolated by Geon-Pevikon electrophoresis from the d = 1.006 to 1.10 fraction, were obtained by ultracentrifugation at d = 1.10–1.21. Approximately 80–90% of the total plasma triglyceride and cholesterol was recovered by these isolation procedures.

Characterization of Plasma Lipoproteins. The chemical composition of the lipoprotein classes isolated as described for a representative experiment is presented in Table I. The VLDL were typically triglyceride rich but contained more phospholipid and less cholesterol than described for human VLDL. The LDL-I and LDL-II were similar in composition and composed of approximately 45% cholesterol of which approximately 65–70% was esterified. The principal constituents of the HDL were phospholipid and protein; the HDL composition was similar to that of human HDL. The total plasma HDL accounted for approximately 75% of the total lipoprotein protein (mean HDL protein from 5 animals was 92 mg/100 ml with a range of 83 to 104). Approximately 20% of the total lipoprotein protein was in the LDL-I (24 mg/100 ml), 5% in the LDL-II (6 mg/100 ml), and 1% in the VLDL. Values for the

Table I: Percent Composition of Control Monkey Lipoproteins.

		VLDL	LDL-I	LDL-II	HDL
$d < 1.006$	Triglyceride	40.0			
	Cholesterol	8.6			
	Phospholipid	37.1			
	Protein	14.3			
$d = 1.006–1.10$	Triglyceride		3.9	3.9	3.1
	Cholesterol		45.5	43.0	22.1
	Phospholipid		29.4	28.1	39.8
	Protein		21.2	25.0	35.0
$d = 1.10–1.21$	Triglyceride				0.4
	Cholesterol				17.8
	Phospholipid				42.1
	Protein				39.7

Table II: Particle Size (A) by Negative Staining.[a]

	VLDL	LDL-I	LDL-II	HDL
$d < 1.006$	300–850			
1.006–1.02		250–400		
1.02–1.06		190–240	190–300	
1.06–1.09			190–240	100–150
1.09–1.21				70–100

[a] The diameters of approximately 200 particles for each lipoprotein class were measured. Each range represents more than 95% of the particles measured excluding the occasional particles at either end of the spectrum of sizes.

LDL-I and LDL-II are estimated because of the variable mixture of LDL-I and LDL-II in the intermediate fraction obtained by the electrophoretic separation. The size distribution of the lipoprotein classes was determined by negative staining electron microscopy (Table II).

The apoproteins of the purified monkey lipoproteins on polyacrylamide gel electrophoresis resembled the patterns of human, canine, and swine lipoproteins (Fredrickson, 1974; Mahley and Weisgraber, 1974a,b). A major apoprotein of VLDL which did not enter the 10% gel in the sodium dodecyl sulfate system appeared to be equivalent to the B apoprotein as described in other species (Figure 3). Another main VLDL apoprotein (labeled b in Figure 3) appeared to be the arginine-rich apoprotein. This band co-electrophoresed with the arginine-rich apoprotein of the swine VLDL and human type III B-VLDL, as well as with the arginine-rich apoprotein isolated from the $d < 1.006$ lipoproteins of cholesterol-fed monkeys (Mahley et al., 1975). The purified arginine-rich apoprotein from cholesterol-fed monkeys with an apparent molecular weight of 34 000 is shown for comparison (Figure 3). The arginine-rich apoprotein was isolated on a G-200 Sephadex column in 4 M guanidine and complete characterization of this apoprotein will be presented elsewhere (Mahley et al., 1976). A minor apoprotein component of VLDL (labeled c) co-electrophoresed with the major apoprotein of HDL which has been identified as the A-I apoprotein (characterization to follow). Proteins with a molecular weight less than 20 000 were also present in the VLDL and presumably represent the C-apoprotein equivalents.

The LDL-I and LDL-II contained the B apoprotein (Figure 3). In addition, the LDL-II revealed two minor bands (labeled b and c) which appeared to be equivalent to the arginine-rich and A-I apoproteins based on electrophoretic migration. The major apoprotein of monkey HDL was the A-I apoprotein.

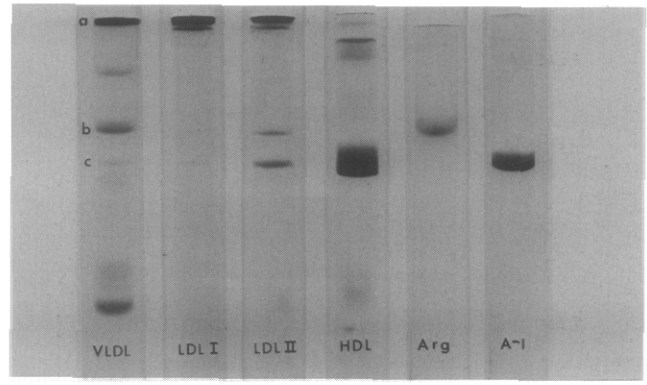

FIGURE 3: Sodium dodecyl sulfate–polyacrylamide gel electrophoresis of the monkey apolipoproteins and the purified arginine-rich and A-I apoproteins. The bands labeled a–c correspond to the B apoprotein, arginine-rich apoprotein, and A-I apoprotein, respectively.

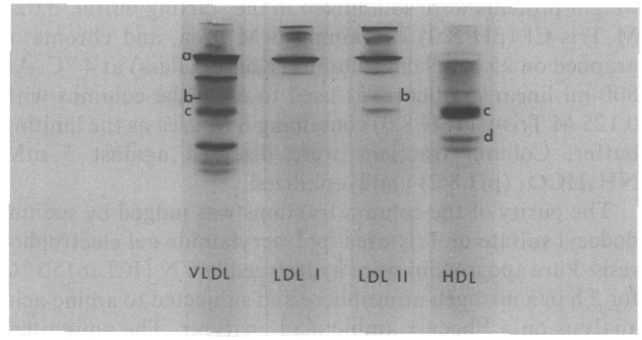

FIGURE 4: Polyacrylamide gel electrophoresis of the monkey apolipoproteins on 10% acrylamide gels in 6 M urea (pH 8.9). The sample applied contained 50 μg of lipoprotein apoprotein. The bands labeled a–d correspond to the B apoprotein, arginine-rich apoprotein, A-I apoprotein, and A-II apoprotein, respectively.

The above observations were confirmed and extended by use of polyacrylamide gel electrophoresis in the Tris-urea system (Figure 4). VLDL, in addition to the B and arginine-rich apoproteins, had two poorly separated bands in the region of the A-I apoprotein. The VLDL contained a small amount of the A-I apoprotein as shown in the sodium dodecyl sulfate gel (Figure 3). However, the major protein in this band on the Tris-urea gels eluted from G-200 Sephadex with the C apoproteins and was found to elute from DEAE-cellulose with the starting buffer, unlike A-I. Further characterization of this apoprotein, which can be confused with A-I based on migration in the Tris-urea system, has not been completed. The HDL, in addition to the A-I apoprotein (labeled c in Figure 4), contained a band which will be shown to be equivalent to the A-II apoprotein (labeled d).

Identification of the arginine-rich and A-I apoproteins based on electrophoretic mobility in the two polyacrylamide gel systems was confirmed by immunochemistry on gel diffusion. Antiserum prepared to the purified monkey A-I apoprotein reacted with identity with the monkey VLDL, LDL-II, and HDL. Antiserum to the human arginine-rich apoprotein isolated and prepared from the B-VLDL of type III hyperlipoproteinemic patients cross-reacted with the arginine-rich apoprotein obtained from the $d < 1.006$ fraction of the cholesterol-fed monkey. In addition, the arginine-rich apoprotein antiserum reacted with identity with the monkey VLDL and LDL-II.

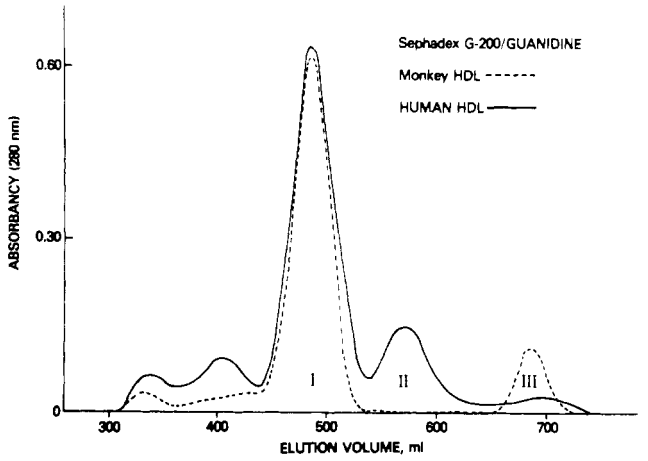

FIGURE 5: The elution profiles obtained by gel chromatography of monkey and human HDL on G-200 Sephadex in 4 M guanidine. The fractions labeled I–III on the human HDL profile correspond to the A-I apoprotein, A-II apoprotein, and low molecular weight C apoproteins, respectively. On the monkey profile fraction I contains the A-I apoprotein and fraction III represents a mixture of the A-II apoprotein and the low molecular weight C apoproteins.

Table III: Amino Acid Analysis of the A-I and A-II Apoproteins.[a]

Amino Acid	Patas A-I[b]	Human A-I[c]	Patas A-II[d]	Rhesus A-II[e]	Human A-II[f]
Lys	6.8	8.6	10.2	10.3	11.7
His	3.0	2.0	0	0	0
Arg	5.3	6.5	1.1	1.3	0
Asp	8.7	8.6	5.5	5.1	4.1
Thr	3.8	4.9	7.2	7.7	7.8
Ser	7.2	5.7	7.3	7.7	7.7
Glu	19.7	19.2	21.0	21.8	20.5
Pro	3.9	4.1	5.3	5.1	5.2
Gly	4.6	4.1	3.7	2.6	4.1
Ala	8.1	7.8	7.6	7.7	6.4
Val	6.6	5.3	9.6	8.8	7.6
Met	0.9	1.2	1.2	1.3	1.2
Ile	0	0	0	0	1.4
Leu	16.1	15.9	10.3	10.3	10.7
Tyr	3.0	2.0	4.8	5.1	5.2
Phe	2.3	2.4	5.3	5.1	5.4
Trp		1.6	0	0	0
Cys		0	0	0	1.2

[a] Expressed as mole percent. [b] Single determination. [c] Calculated from Baker et al. (1975). [d] Values are the average from two independent samples. [e] Calculated from Edelstein et al. (1973). [f] Lux et al. (1972).

Further Characterization of LDL-I and LDL-II. Apoprotein content, composition, and size suggested that LDL-I were equivalent to the LDL in other species. On the other hand, consideration was given to the possibility that LDL-II were equivalent to HDL_1 (HDL_c) described in dogs and swine (Mahley and Weisgraber, 1974b; Mahley et al., 1975). However, the dog and swine lipoproteins lack detectable B apoprotein. Studies were undertaken to determine whether the presence of the B apoprotein was secondary to LDL contamination.

The LDL-II class, purified from plasma as described above, was subjected a second time to the Geon-Pevikon electrophoretic procedure. The LDL-II band was divided into several zones which were eluted and analyzed separately. Apoprotein analysis by sodium dodecyl sulfate–polyacrylamide gel electrophoresis revealed that all the zones contained the bands interpreted as the B, arginine-rich, and A-I apoproteins. It was not possible to isolate a lipoprotein from this class which lacked the B apoprotein. In addition, the isolated LDL-II class of lipoproteins was subjected to A-50m and A-15m agarose column chromatography based on the method described by Rudel et al. (1974). Across the entire elution profile the apoprotein content remained qualitatively the same.

Consideration was given to the possibility that LDL-II were equivalent to the Lp(a) lipoproteins described in man (Albers and Hazzard, 1974; Dahlén et al., 1974; Harvie and Schultz, 1970; Berg, 1963; Ehnholm et al., 1972). One of the characteristics which distinguishes human LDL and Lp(a) is the sialic acid content. The sialic acid contents (micrograms/milligram of protein) of the Patas LDL-I and LDL-II isolated from the $d = 1.006$ to 1.10 fraction were 11.7 ± 0.4 and 33.4 ± 1.4, respectively. These results were obtained on two independent analyses performed in duplicate. Polyacrylamide gels (100 μg of protein/gel) stained with the periodic acid–Schiff reagent indicated that the increased sialic acid content was associated with the B apoprotein (no detectable carbohydrate-positive bands entered the gels). Another characteristic of the human Lp(a) is the occurrence of a specific "Lp(a) protein" which can be detected immunochemically. The Patas monkey serum and LDL-II were found to react on gel diffusion with the human Lp(a) specific antiserum. The monkey VLDL, LDL-I, and HDL did not react (immunochemical screening was kindly performed by Dr. John J. Albers, Seattle, Wash.). The serum was pooled from three animals, and the protein concentration of the lipoprotein fractions was 1–2 mg/ml.

Isolation and Characterization of the A-I and A-II Apoproteins. The apoproteins of monkey HDL were fractionated by gel filtration on Sephadex G-200 in 4 M guanidine (Figure 5). The elution profile of human HDL is superimposed on the monkey profile for comparison. The major fraction (I) contained the A-I apoprotein which was free of contamination by other proteins. Patas monkey A-I co-electrophoresed with human A-I and had an apparent molecular weight of 28 000 as determined by sodium dodecyl sulfate–polyacrylamide gel electrophoresis. A comparison of the amino acid analysis of human and monkey A-I is presented in Table III. The amino-terminal portion of the A-I apoprotein from the monkey as determined by the automated Edman procedure is compared to the terminal portions of human A-I (Baker et al., 1975), swine A-I (Mahley et al., 1975), and dog A-I (unpublished observation) (Table IV). These data suggest homology of A-I among the species.

The profile of monkey HDL revealed the absence of a distinct A-II fraction eluting immediately after the A-I as occurred with human HDL (Figure 5, fraction II). It was found that the Patas monkey A-II eluted with column fraction III which contained the C apoproteins. Monkey A-II was purified by DEAE-cellulose chromatography and eluted at a conductivity of 1.35 mmho/cm. Amino acid analysis of Patas monkey A-II revealed striking similarities to reported values for Rhesus monkey (Edelstein et al., 1973) and human A-II (Lux et al., 1972) (Table III). On sodium dodecyl sulfate–polyacrylamide gel electrophoresis (Figure 6), monkey A-II migrated faster than human A-II, as has been described for Rhesus A-II (Edelstein et al., 1973). Reduction of the purified apoproteins with β-mercaptoethanol did not change the mobility of the monkey A-II but converted the human A-II to its monomeric form. The migration of this form was identical with that of monkey A-II (Figure 6). Patas monkey A-II has an apparent molecular weight of 8500.

Table IV: Amino-Terminal Sequences of the A-I Apoproteins.

Monkey	NH_2-Asp-Glu-Pro-Pro-Gln-Thr-Pro-Trp-Asp-Arg-Val-Lys-Asp-Leu-Val-Thr-Val-Tyr-Val-Glu
Human	NH_2-Asp-Glu-Pro-Pro-Gln-Ser-Pro-Trp-Asp-Arg-Val-Lys-Asp-Leu-Ala-Thr-Val-Tyr-Val-Asp
Swine	NH_2-Asp-Asp-Pro-Gln-Ser-Pro-Trp-Asp-Arg-Val
Dog	NH_2-Asp-Glu-Pro-Gln-Ser-Pro-Trp-Asp-Arg-Val
	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20

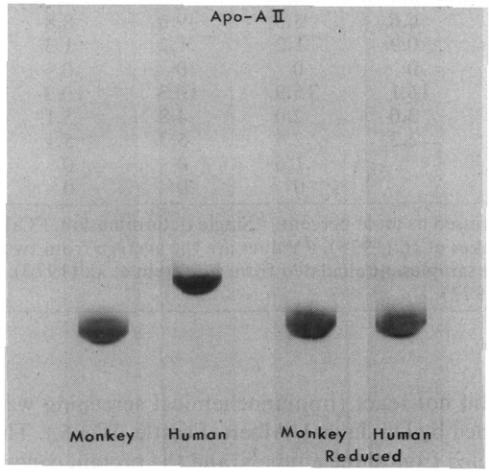

FIGURE 6: Sodium dodecyl sulfate–polyacrylamide gel electrophoresis of the purified monkey and human A-II apoproteins before and after reduction with β-mercaptoethanol.

Discussion

The *Erythrocebus patas* monkey has plasma lipoproteins which closely resemble those of man. The VLDL are triglyceride-rich particles which range in size from 300 to 850 Å in diameter. The major protein constituents of the VLDL appear to be the B, arginine-rich, and C apoproteins, similar to those described for man. The class referred to as LDL-I closely resembles human LDL with respect to density, size by electron microscopy (~200 Å), and chemical composition. The major protein component is the B apoprotein. Monkey HDL are similar to the corresponding human class with respect to physical and chemical properties. The A-I, A-II, and C apoproteins are the major protein moieties of this class.

The data presented suggest that the lipoprotein class referred to as LDL-II may be equivalent to the class of human lipoproteins variously referred to as sinking pre-β_1 (Rider et al., 1970) or, more commonly, Lp(a). The Lp(a) lipoprotein, when originally described, was considered to be a qualitative genetic marker (Berg, 1963), but now appears to be present in most, if not all, persons (Harvie and Schultz, 1970). Lp(a) contains the LDL or apo-B immunologic determinant as well as a specific antigenic determinant which does not react with VLDL, LDL, HDL, or their major apoprotein constituents (Albers and Hazzard, 1974; Ehnholm et al., 1972). The nature of the specificity of the antisera has not been determined. Lp(a) has a similar composition to LDL but has a higher hydrated density (d = 1.05 to 1.09). In addition, Lp(a) has pre-β or α_2 mobility on electrophoresis and has a high carbohydrate content, including a high level of sialic acid (Albers and Hazzard, 1974; Ehnholm et al., 1972).

By comparison, the monkey LDL-II occur at a similar density (1.05 to 1.085), have α_2 mobility, have a high sialic acid content (three times that of LDL), and react with the human "Lp(a) protein" specific antiserum. The lipid to protein ratio of human LDL is higher than that of Lp(a), values being 3.5 and 2.4, respectively (Albers and Hazzard, 1974). This compares with a lipid to protein ratio of 3.7 for monkey LDL-I and 3.0 for LDL-II. By polyacrylamide gel electrophoresis in both the Tris-urea and sodium dodecyl sulfate systems, the LDL-II appear to contain the B apoprotein as the major protein component and the arginine-rich and A-I apoproteins as minor components. Even after fractionation of this lipoprotein class by column chromatography and Geon-Pevikon electrophoresis, the apoprotein constituents were qualitatively the same. The similarity between LDL-II and the class of lipoprotein referred to as HDL_1 (HDL_c) in dogs and swine (Mahley and Weisgraber, 1974b; Mahley et al., 1975) was alluded to earlier. However, unlike LDL-II, HDL_1 (HDL_c) in the lower species lack the B apoprotein. It remains to be determined if functional similarities exist between these classes.

The Patas monkey may serve as an experimental model to gain insight into the origin and fate of Lp(a) in man. Various experimental manipulations, e.g., dietary and hormonal, may suggest a metabolic role for this class of lipoproteins. Cholesterol feeding, for example, results in an alteration in apoprotein content of the monkey LDL-II, with the arginine-rich apoprotein becoming a major protein constituent (unpublished observation).

Characterization of the major proteins of the Patas monkey HDL indicates that the A-I and A-II apoproteins are homologous to corresponding human apoproteins. Examination of the amino-terminal portion of the A-I protein from several species, in addition to suggesting homology, reveals an interesting difference between the higher and lower species. The Patas monkey and human A-I have the amino acid proline at positions 3 and 4 as compared to a single proline at position 3 for the swine and dog. The occurrence of the double proline residues throws the sequence out of phase by one amino acid; thus, for comparison with A-I of the dog and swine the amino acid residues have to be shifted one position as indicated in Table IV. The data for swine and dog A-I are similar to those reported for the bull and chicken (Levy and Martin, 1971; Levy et al., 1972).

The A-II apoprotein of Patas monkey HDL appears to be similar to the monomeric form of human A-II. The contention that Patas monkey A-II occurs as a monomer, but is otherwise similar to human A-II, is supported by similarities in amino acid analyses, with the exception of the absence of cysteine, and by the observation that following conversion of human A-II to its monomeric state by reduction, monkey and human A-II co-electrophorese on polyacrylamide gels. The occurrence of monomeric A-II has previously been described in the HDL of the Rhesus monkey (Edelstein et al., 1973) and in the rat

(Herbert et al., 1974). However, in the chimpanzee the A-II has been reported to be a dimer (Scanu et al., 1974).

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