قسم الكيمياء الحيوية
Biochemistry Department

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1957
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BLOOD

Plasma

Blood plasma an aqueous straw-colored liquid of electrolytes, nutrients, metabolites, proteins, vitamins ,trace elements, and signaling substances. The fluid phase of coagulated blood is known as blood serum. It differs from the plasma in that it lacks fibrin and other coagulation proteins.

Water > 90%

Small molecule 2 %, it is electrolytes, nutriment, metabolic products, hormone, enzyme, etc.

Protein 60-80 g/L, plasma protein include albumin (40-50 g/L), globulin (20-30 g/L, α_1-, α_2-, β-, γ-) and fibrinogen. Most of albumin and globulin made in liver. A/G had clinical importance.

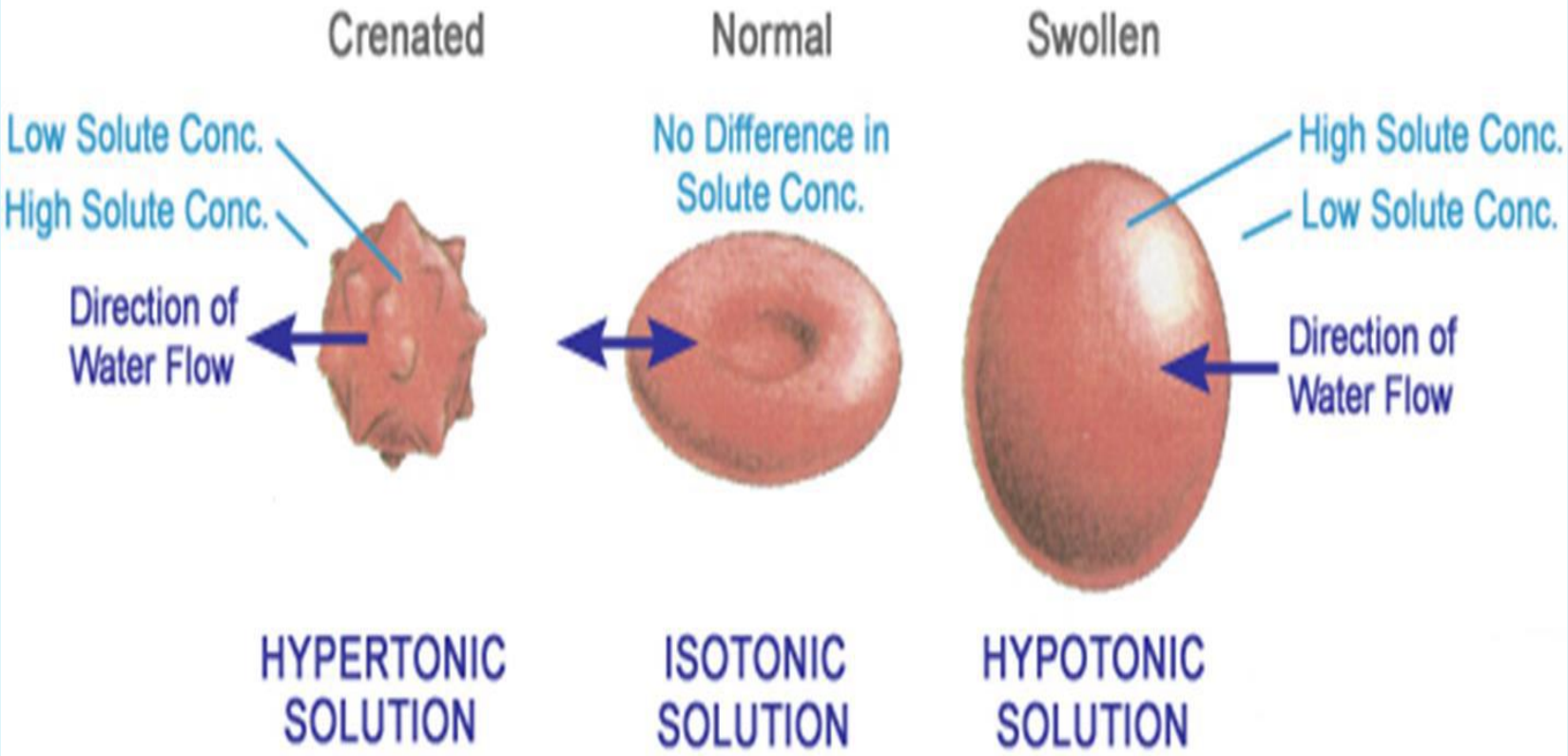
Function of plasma protein

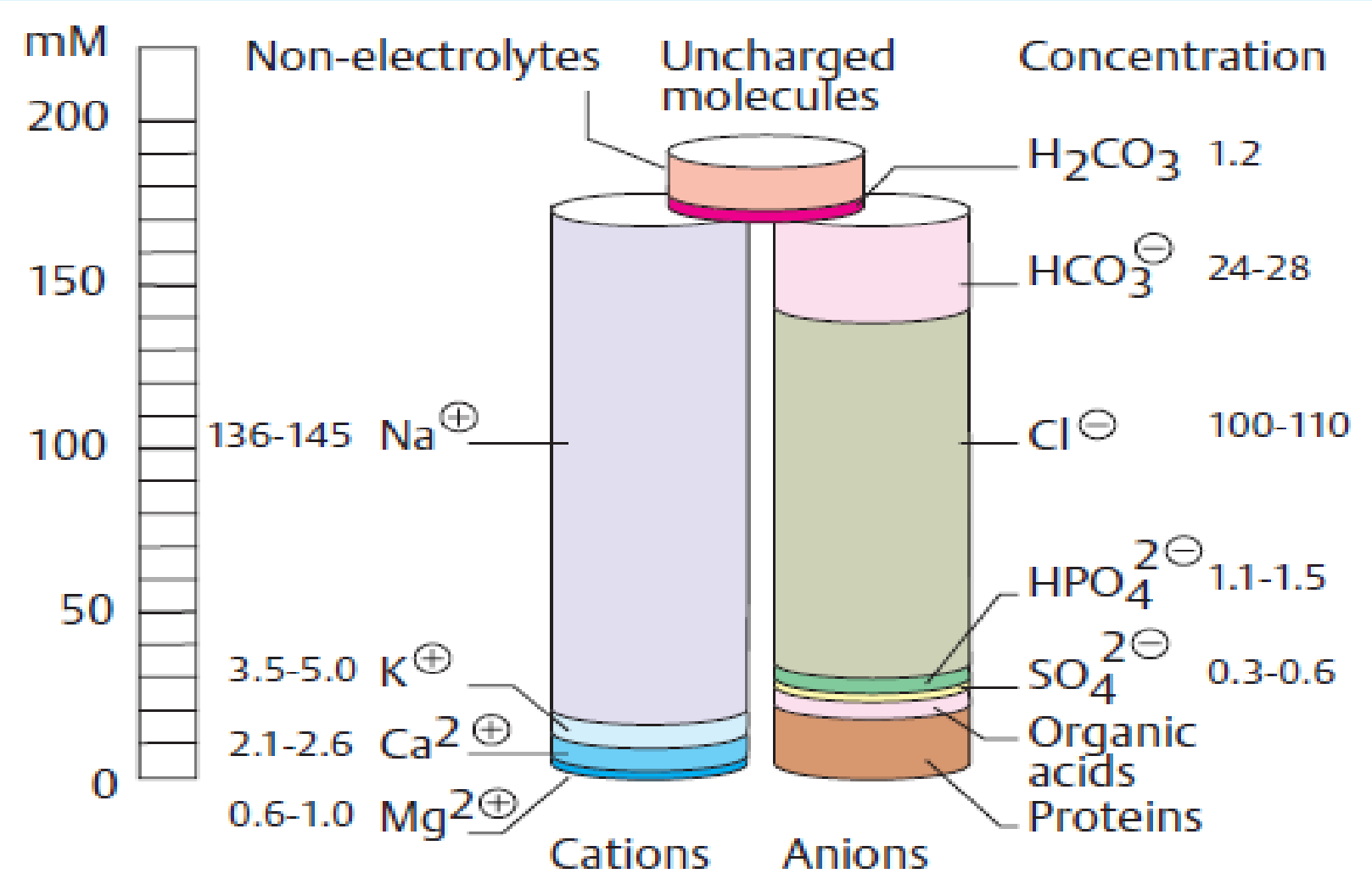
(1) transportation, (2) nutrition, (3) forming colloid osmotic pressure, (4) coagulation and anticoagulation, (5) pH value buffer, (6) immunity (globulin).

Laboratory assessment of the composition of the blood plasma is often carried out in clinical biochemistry.

Among the electrolytes, there is a relatively high concentration of Na^+, Ca^{2+}, and Cl^-ions in the blood in comparison with the cytoplasm. By contrast, the concentrations of K^+, Mg^{2+}, and phosphate ions are higher in the cells. Proteins also have a higher intracellular concentration. The electrolyte composition of blood plasma is similar to that of sea water, due to the evolution of early forms of life in the sea. The solution known as "physiological saline" (NaCl at a concentration of 0.15 mol/L) is almost isotonic with blood plasma.

Tonicity Effects on the Red Blood Cell





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Metabolite	Concentration (mM)
Glucose	3.6 – 6.1
Lactate	0.4 – 1.8
Pyruvate	0.07 – 0.11
Urea	3.5 – 9.0
Uric acid	0.18 – 0.54
Creatinin	0.06 – 0.13
Amino acids	2.3 – 4.0
Ammonia	0.02 – 0.06
Lipids (total)	5.5 – 6.0 $g \cdot l^{-1}$
Triacylglycerols	1.0 – 1.3 $g \cdot l^{-1}$
Cholesterol	1.7 – 2.1 $g \cdot l^{-1}$

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Plasma proteins

Proteins are the most important part of the soluble components of the blood plasma. With concentrations of between 60 and 80 g/L, they constitute approximately 4% of the body's total protein. Their tasks include transport, regulation of the water balance, hemostasis, and defense against pathogens. Some 100 different proteins occur in human blood plasma. Based on their behavior during electrophoresis, they are broadly divided into five fractions: albumins and α_1–, α_2–, β– and γ-globulins.

The distinction between the albumins and globulins was based on differences in the proteins' solubility – albumins are soluble in pure water, where as globulins only dissolve in the presence of salts. The most frequent protein in the plasma, at around 45 g/L, is albumin. Due to its high concentration, it plays a crucial role in maintaining the blood's colloid osmotic pressure and represents an important amino acid reserve for the body. Albumin has binding sites for a polar substances and there fore functions as a transport protein for long –chain fatty acids, bilirubin, drugs, and some steroid hormones and vitamins.

In addition, serum albumin binds Ca2+ and Mg2+ ions. It is the only important plasma protein that is not glycosylated. The albumin fraction also includes transthyretin (prealbumin), which together with other proteins transports the thyroxine hormone and its metabolites.

Group	Protein	M_r in kDa	Function
Albumins:	Transthyretin Albumin: 45 g · l^{-1}	50-66 67	Transport of thyroxin and triiodothyronin Maintenance of osmotic pressure; transport of fatty acids, bilirubin, bile acids, steroid hormones, pharmaceuticals and inorganic ions.

The α- and β- globulins are involved in the transport of lipids, hormones, vitamins, and metal ions. In addition, they provide coagulation factors, protease inhibitors, and the proteins of the complement system. Soluble antibodies make up the γ – globulin fraction.

α_1-Globulins:	Antitrypsin	51	Inhibition of trypsin and other proteases
	Antichymotrypsin	58-68	Inhibition of chymotrypsin
	Lipoprotein (HDL)	200-400	Transport of lipids
	Prothrombin	72	Coagulation factor II, thrombin precursor (*3.4.21.5*)
	Transcortin	51	Transport of cortisol, corticosterone and progesterone
	Acid glycoprotein	44	Transport of progesterone
	Thyroxin-binding globulin	54	Transport of iodothyronins
α_2-Globulins:	Ceruloplasmin	135	Transport of copper ions
	Antithrombin III	58	Inhibition of blood clotting
	Haptoglobin	100	Binding of hemoglobin
	Cholinesterase (3.1.1.8)	ca. 350	Cleavage of choline esters
	Plasminogen	90	Precursor of plasmin (*3.4.21.7*), breakdown of blood clots
	Macroglobulin	725	Binding of proteases, transport of zinc ions
	Retinol-binding protein	21	Transport of vitamin A
	Vitamin D-binding protein	52	Transport of calciols
β-Globulins:	Lipoprotein (LDL)	2.000-4.500	Transport of lipids
	Transferrin	80	Transport of iron ions
	Fibrinogen	340	Coagulation factor I
	Sex hormone-binding globulin	65	Transport of testosterone and estradiol
	Transcobalamin	38	Transport of vitamin B_{12}
	C-reactive protein	110	Complement activation

γ-Globulins:	IgG	150	Late antibodies
	IgA	162	Mucosa-protecting antibodies
	IgM	900	Early antibodies
	IgD	172	B-lymphocyte receptors
	IgE	196	Reagins

Synthesis and degradation of proteins

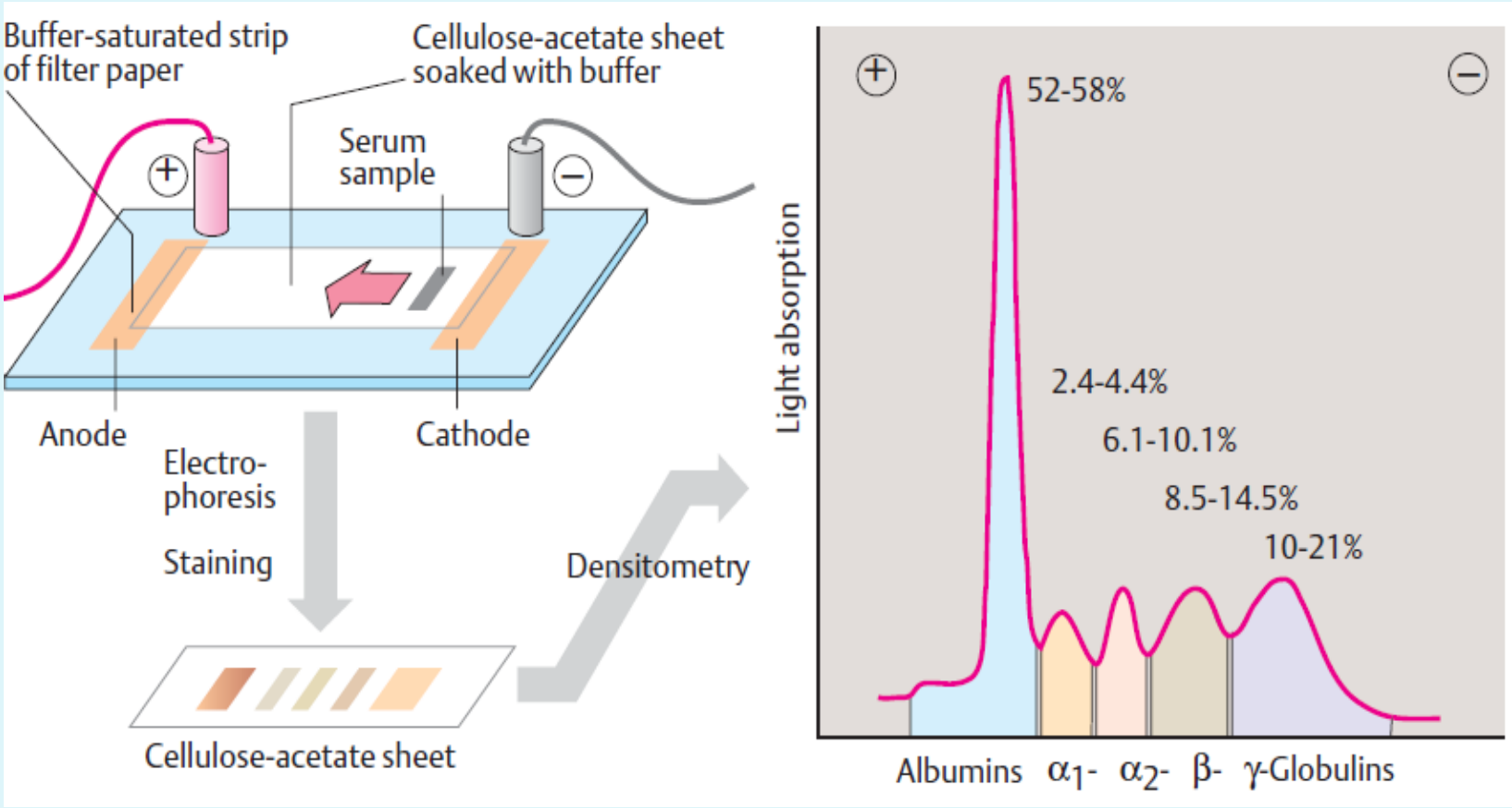
Most plasma proteins are synthesized by the liver. Exceptions to this include the immunoglobulins, which are secreted by B lymphocytes known as plasma cells and peptide hormones, which derive from endocrine gland cells. With the exception of albumin, almost all plasma proteins are glycoproteins. They carry oligosaccharides in N-and O-glycosidic bonds. N-acetyl neuraminic acid often occurs as a terminal carbohydrate among sugar residues. Neuraminidases (sialidases) on the surface of the vascular endothelia gradually cleave the sialic acid residues and there by release galactose units on the surfaces of the proteins.

These asialoglycoproteins (“asialo-” = without sialic acid) are recognized and bound by galactose receptors on hepatocytes. In this way, the liver takes up aged plasma proteins by endocytosis and breaks them down. The oligo saccharides on the protein surfaces thus determine the half-life of plasma proteins, which is a period of days to weeks.

Carrier electrophoresis

Proteins and other electrically charged macromolecules can be separated using electrophoresis. Among the various procedures used, carrier electrophoresis on cellulose acetate foil (CAF) is particularly simple. Using this method, serum proteins — which at slightly alkaline pH values all move towards the anode ,due to their excess of negative charges — can be separated into the five fractions mentioned. After the proteins have been stained with dyes, the resulting bands can be quantitatively assessed using densitometry.

Protein Electrophoresis



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Plasma Lipids

Most lipids are barely soluble in water. Free triacylglycerols would combine into drops that could cause fat embolisms. Lipids deposit in the blood cells membranes and would dissolve them. Long-chain fatty acids are bound to albumin and short-chain ones are dissolved in the plasma, other lipids are transported in lipoprotein complexes, of which there several types in the blood plasma, with different sizes and composition.

Composition of lipoprotein complexes

Lipoproteins are spherical or discoid aggregates of lipids and apoproteins. They consist of a nucleus of non polar lipids (triacylglycerols and cholesterol esters) surrounded by a single-layered shell approximately 2 nm thick of amphipathic lipids (phospholipids and cholesterol; LDL). The shell, in which the apoproteins are also deposited, gives the surfaces of the particles polar properties and there by prevents them from aggregating into large particles.

Classification of lipoproteins

Lipoproteins are classified into five groups. In order of decreasing size and increasing density, these are: chylomicrons, VLDLs (very low density lipoproteins), IDLs (intermediate density lipoproteins), LDLs (low density lipoproteins), and HDLs (high density lipoproteins). The proportions of apoproteins range from 1 % in chylomicrons to over 50 % in HDLs. These proteins serve less for solubility purposes, but rather function as recognition molecules for the membrane receptors and enzymes that are involved in lipid exchange. The classes of lipoproteins differ also in the ways in which they originate and function.

Chylomicrons **Transport triacylglycerols from the Intestine to the tissues. They are formed in the intestinal mucosa and reach the blood via the lymphatic system. In the peripheral vessels particularly in muscle and adipose tissue lipoprotein lipase on the surface of the vascular endothelia hydrolyzes most of the triacylglycerols. Chylomicron break down is activated by the transfer of apoproteins E and C from HDL. While the fatty acids released and the glycerol are taken up by the cells, the chylomicrons gradually become converted into chylomicron remnants, which are ultimately removed from the blood by the liver.**

VLDLs, IDLs, and LDLs are closely related to one another. VLDLs formed in the liver, transport triacylglycerols, cholesterol, and phospholipids to other tissues. Like chylomicrons, they are gradually converted into IDL and LDL under the influence of lipoprotein lipase. This process is also stimulated by HDL.

HDLs also originate in the liver. They return the excess cholesterol formed in the Tissues to the liver. HDLs promote chylomicron and VLDL turnover by exchanging lipids and apoproteins with them.

Plasma enzymes

Plasma enzymes classified into: Functional plasma enzymes and non functional plasma enzymes.

Functional plasma enzymes

- **Present in plasma in higher concentrations in comparison to tissue and have known functions.**
- **Their substrates are always present in plasma, synthesized in liver and decrease in liver disease.**

Examples: Clotting factors e.g. Prothrombin and Lipoprotein lipase.

Non functional plasma enzymes

- **Present in plasma in very low concentrations in comparison to tissue and no functions known.**
- **Their substrates are absent from plasma, synthesized in different organs e.g. Liver, heart, skeletal muscles and brain and increase in different diseases.**
- **Examples: ALT, AST, CK, LDH, alkaline phosphatase, acid phosphatase and lipase.**

Source

- **Cell damage with the release of its content of enzymes into blood e.g. Myocardial infarction and viral hepatitis.**

- **Obstruction of normal pathways e.g. Obstruction of bile duct increases alkaline phosphatase.**
- **Increase of the enzyme synthesis e.g. bilirubin increases the rate of synthesis of alkaline phosphatase in obstructive liver disease**
- **Increased permeability of cell membrane as in hypoxia.**

Medical Importance:

- **Diagnosis of diseases as disease of different organs cause elevation of different plasma enzymes.**
- **Prognosis of the disease we can follow up of the treatment by measuring plasma enzymes before and after treatment.**

Clinical Disorders & Enzymes

Hepatic disorders:

- **In hepatocellular diseases the plasma levels of ALT, AST, and LDH isoenzyme 5 increased.**
- **In biliary tract diseases the plasma levels of ALP and γGT increased.**

Cardiac disorders:

- **In heart muscle disorders AST and CPK levels increased.**
- **LDH monitor heart diseases.**
- **CPK & LDH1 (Isoenzyme of LDH) indicate amounts of myocardial infarct.**

Skeletal Muscles disorders:

- **The plasma levels of AST & CPK enzymes increase in skeletal muscles diseases.**

Bone disorders:

- **The ALP plasma level used in bone diseases diagnosis.**

Pancreatic disorders:

- **The plasma levels of lipase & β amylase enzymes increase in acute pancreatic diseases.**

Malignancy:

- **Plasma acid phosphatase (ACP) levels increase in prostatic carcinoma & bone metastatic carcinoma.**
- **Plasma levels of Alkaline phosphatase (ALP) increase in pancreatic & biliary carcinoma and in liver tumor metastasis.**
- **Plasma levels of LDH increase in leukemia & lymphomas.**

Example for healthy human weight 70 kg

Density (g/ml)	Class	Diameter (nm)	% protein	% cholesterol	% phospholipid	% triacylglycerol & cholesterol ester
1.063	HDL	5–15	33	30	29	4
1.019–1.063	LDL	18–28	25	50	21	8
1.006–1.019	IDL	25–50	18	29	22	31
0.95–1.006	VLDL	30–80	10	22	18	50
<0.95	Chylomicrons	100-1000	<2	8	7	84