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HEPATIC DRUG DELIVERY: PHYSIOLOGICAL STATUS AND DYSFUNCTION

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ABSTRACT

Even though the liver has many receptors, hepatic disorders are becoming one of the rare conditions that cannot be successfully healed for several reasons. Nowadays, a lot of passive targeted delivery methods are used to deliver drugs or genes to treat disorders of interior organs. More importantly, by interacting with target receptors and orienting ligands, entirely different actions would be taken in tandem with the desired cell that was damaged or dysfunctioned. This would improve the accumulation of medication within the target cell and reduce nonspecific toxicity towards other cells or organs. Millions of people worldwide suffer from severe liver illnesses that are incurable despite numerous attempts, necessitating the search for novel therapeutic approaches. Strong medications may not work well enough in vivo or may have negative side effects; this could be significantly improved by increasing distribution into the target cells. Our goal is to provide an overview of the available options for medication administration to the different intrahepatic cell types.

Key Words: *Liver drug delivery, Hepatic dysfunction, Hepatic disease*

INTRODUCTION

Liver

The **liver** is a vital organ present in vertebrates and some other animals. It has a wide range of functions, including detoxification, protein synthesis, and production of biochemical's necessary for digestion. The liver is necessary for survival; there is currently no way to compensate for the absence of liver function. This organ plays a major role in metabolism and has a number of functions in the body, including glycogen storage, decomposition of red blood cells, plasma protein synthesis, hormone production, and detoxification. It lies below the diaphragm in the thoracic region of the abdomen. It produces bile, an alkaline compound which aids in digestion, via the emulsification of lipids. It also performs and regulates a wide variety of high-volume biochemical reactions requiring highly specialized tissues, including the synthesis and breakdown of small and complex molecules, many of which are necessary for normal vital functions.[1]

Anatomy

The liver is a reddish brown organ with four lobes of unequal size and shape. A human liver normally weighs between 1.4–1.6 kg (3.1–3.5 lb), and is a soft, pinkish-brown, triangular organ. It is both the largest internal organ (the skin being the largest organ overall) and the largest gland in the human body. It is located in the right upper quadrant of the abdominal cavity, resting just below the diaphragm. The liver lies to the right of the stomach and overlies the gallbladder. It is connected to two large blood vessels, one called the hepatic artery and one called the portal vein. The hepatic artery carries blood from the aorta whereas the portal vein carries blood containing digested nutrients from the small intestine and the descending colon. These blood vessels subdivide into capillaries which then lead to a lobule. Each lobule is made up of millions of hepatic cells which are the basic metabolic cells.

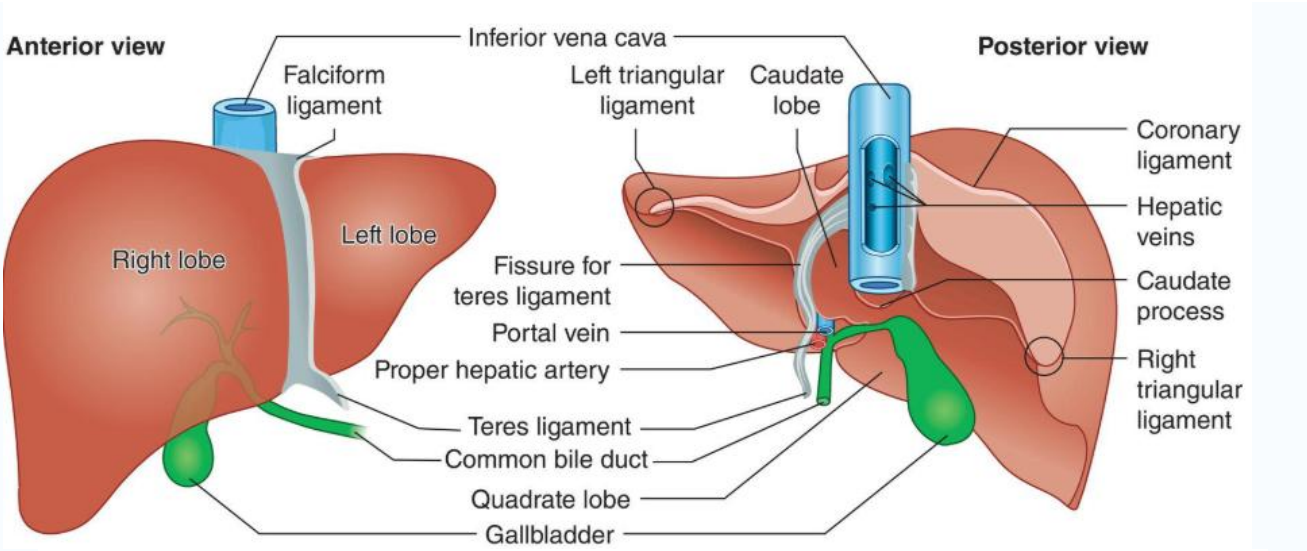

Figure.1; The liver has a smooth, dome-shaped diaphragmatic surface and a mildly irregular visceral one, which is moulded by the adjacent organs and indented by the interlobar fissures.

Blood flow

The liver receives a dual blood supply from the hepatic portal vein and hepatic arteries. Supplying approximately 75% of the liver's blood supply, the hepatic portal vein carries venous blood drained from the spleen, gastrointestinal tract, and its associated organs. The hepatic arteries supply arterial blood to the liver, accounting for the remainder of its blood flow. Oxygen is provided from both sources; approximately half of the liver's oxygen demand is met by the hepatic portal vein, and half is met by the hepatic arteries.
Blood flows through the sinusoids and empties into the central vein of each lobule. The central veins coalesce into hepatic veins, which leave the liver and empty into the inferior vena cava.

Biliary flow

The term *biliary tree* is derived from the arboreal branches of the bile ducts. The bile produced in the liver is collected in bile canaliculi, which merge to form bile ducts. Within the liver, these ducts are called *intrahepatic* (within the liver) bile ducts, and once they exit the liver they are considered *extrahepatic* (outside the liver). The intrahepatic ducts eventually drain into the right and left hepatic ducts, which merge to form the common hepatic duct. The cystic duct from the gallbladder joins with the common hepatic duct to form the common bile duct. Bile can either drain directly into the duodenum via the common bile duct or be temporarily stored in the gallbladder via the cystic duct. The common bile duct and the pancreatic duct enter the second part of the duodenum together at the ampulla of Vater.

Surface anatomy:

Peritoneal ligaments

Apart from a patch where it connects to the diaphragm (the so-called "bare area"), the liver is covered entirely by visceral peritoneum, a thin, double-layered membrane that reduces friction against other organs. The peritoneum folds back on itself to form the falciform ligament and the right and left triangular ligaments. These "lits" are in no way related to the true anatomic ligaments in joints, and have essentially no functional importance, but they are easily recognizable surface landmarks. An exception to this is the falciform ligament, which attaches the liver to the posterior portion of the anterior body wall.

Lobes

Traditional gross anatomy divided the liver into four lobes based on surface features. The falciform ligament is visible on the front (anterior side) of the liver. This divides the liver into a left anatomical lobe, and a right anatomical lobe. If the liver is flipped over, to look at it from behind (the visceral surface), there are two additional lobes between the right and left. These are the caudate lobe (the more superior), and below this the quadrate lobe. From behind, the lobes are divided up by the ligamentum venosum and ligamentum teres (anything left of these is the left lobe), the transverse fissure (or *porta hepatis*) divides the caudate from the quadrate lobe, and the right sagittal fossa, which the inferior vena cava runs over, separates these two lobes from the right lobe. Each of the lobes is made up of lobules; a vein goes from the centre of each lobule which then joins to the hepatic vein to carry blood out from the liver. On the surface of the lobules there are ducts, veins and arteries that carry fluids to and from them.

Functional anatomy

The central area where the common bile duct, hepatic portal vein, and hepatic artery proper enter is the hilum or "porta hepatis". The duct, vein, and artery divide into left and right branches, and the portions of the liver supplied by these branches constitute the functional left and right lobes. The functional lobes are separated by an imaginary plane joining the gallbladder fossa to the inferior vena cava. The plane separates the liver into the true right and left lobes. The middle hepatic vein also demarcates the true right and left lobes. The right lobe is further divided into an anterior and posterior segment by the right hepatic vein. The left lobe is divided into the medial and lateral segments by the left hepatic vein. The fissure for the ligamentum teres also separates the medial and lateral segments. The medial segment is also called the quadrate lobe. In the widely used Couinaud (or "French") system, the functional lobes are further divided into a total of eight subsegments based on a transverse plane through the bifurcation of the main portal vein. The caudate lobe is a separate structure which receives blood flow from both the right- and left-sided vascular branches. [2,3,4,5]

Physiology

The various functions of the liver are carried out by the liver cells or hepatocytes. Currently, there is no artificial organ or device capable of emulating all the functions of the liver. Some functions can be emulated by liver dialysis, an experimental treatment for liver failure.

Synthesis

Further information: Proteins produced and secreted by the liver

- A large part of amino acid synthesis
- The liver performs several roles in carbohydrate metabolism:
    - Gluconeogenesis (the synthesis of glucose from certain amino acids, lactate or glycerol). Note that humans and some other mammals cannot synthesize glucose from glycerol.
    - Glycogenolysis (the breakdown of glycogen into glucose)
    - Glycogenesis (the formation of glycogen from glucose)(muscle tissues can also do this)
- The liver is responsible for the mainstay of protein metabolism, synthesis as well as degradation
- The liver also performs several roles in lipid metabolism:
    - Cholesterol synthesis
    - Lipogenesis, the production of triglycerides (fats).
- The liver produces coagulation factors I (fibrinogen), II (prothrombin), V, VII, IX, X and XI, as well as protein C, protein S and antithrombin.
- In the first trimester fetus, the liver is the main site of red blood cell production. By the 32nd week of gestation, the bone marrow has almost completely taken over that task.
- The liver produces and excretes bile (a greenish liquid) required for emulsifying fats. Some of the bile drains directly into the duodenum, and some is stored in the gallbladder.
- The liver also produces insulin-like growth factor 1 (IGF-1), a polypeptide protein hormone that plays an important role in childhood growth and continues to have anabolic effects in adults.
- The liver is a major site of thrombopoietin production. Thrombopoietin is a glycoprotein hormone that regulates the production of platelets by the bone marrow.

Breakdown

- The breakdown of insulin and other hormones
- The liver breaks down hemoglobin, creating metabolites that are added to bile as pigment (bilirubin and biliverdin).
- The liver breaks down or modifies toxic substances (e.g., methylation) and most medicinal products in a process called drug metabolism. This sometimes results in toxication, when the metabolite is more toxic than its precursor. Preferably, the toxins are conjugated to avail excretion in bile or urine.
- The liver converts ammonia to urea.

Other functions

- The liver stores a multitude of substances, including glucose (in the form of glycogen), vitamin A (1–2 years' supply), vitamin D (1–4 months' supply), vitamin B12, iron, and copper.
- The liver is responsible for immunological effects- the reticuloendothelial system of the liver contains many immunologically active cells, acting as a 'sieve' for antigens carried to it via the portal system.
- The liver produces albumin, the major osmolar component of blood serum.
- The liver synthesizes angiotensinogen, a hormone that is responsible for raising the blood pressure when activated by renin, an enzyme that is released when the kidney senses low blood pressure.[6]

Liver disease:

The liver supports almost every organ in the body and is vital for survival. Because of its strategic location and multidimensional functions, the liver is also prone to many diseases. [7]

The most common include: Infections such as hepatitis A, B, C, E, alcohol damage, fatty liver, cirrhosis, cancer, drug damage (especially acetaminophen, cancer drugs). Many diseases of the liver are accompanied by jaundice caused by increased levels of bilirubin in the system. The bilirubin results from the breakup of the haemoglobin of dead red blood cells; normally, the liver removes bilirubin from the blood and excretes it through bile.There are also many pediatric liver diseases including biliary atresia, alpha-1 antitrypsin deficiency, alagille syndrome, progressive familial intrahepatic cholestasis, and Langerhans cell histiocytosis, to name but a few. Diseases that interfere with liver function will lead to derangement of these processes. However, the liver has a great capacity to regenerate and has a large reserve capacity. In most cases, the liver only produces symptoms after extensive damage. [8]

Disease signs

The classic signs of liver damage include the following:

- **Pale stools** occur when stercobilin, a brown pigment, is absent from the stool. Stercobilin is derived from bilirubin metabolites produced in the liver.
- **Dark urine** occurs when bilirubin mixes with urine
- **Bilirubin** when it deposits in skin, causes an intense itch. Itching is the most common complaint by people who have liver failure. Often this itch cannot be relieved by drugs.
- **Swelling** of the abdomen, ankles and feet occurs because the liver fails to make albumin.
- **Excessive fatigue** occurs from a generalized loss of nutrients, minerals and vitamins.
- **Bruising** and easy bleeding are other features of liver disease. The liver makes substances which help prevent bleeding. When liver damage occurs, these substances are no longer present and severe bleeding can occur.[9]

1.2 Type of liver dysfunction

Hepatitis: inflammation of the liver, caused mainly by various viruses but also by some poisons (e.g. alcohol), autoimmunity (autoimmune hepatitis) or hereditary conditions.

Ascites is pathologic fluid accumulation within the abdominal cavity. In liver disease ascites represents a state of excess total-body sodium and water.

Non alcohlic fatty liver disease: a spectrum in disease, associated with obesity and characterized as an abundance of fat in the liver; may lead to a hepatitis, i.e. steatohepatitis and/or cirrhosis.

Cirrhosis is the formation of fibrous tissue in the liver, replacing dead liver cells. The death of the liver cells can for example be caused by viral hepatitis, alcoholism or contact with other liver-toxic chemicals.

- **Haemochromatosis,** a hereditary disease causing the accumulation of iron in the body, eventually leading to liver damage.
- **Cancer** of the liver (primary hepatocellular carcinoma or cholangiocarcinoma and metastatic cancers, usually from other parts of the gastrointestinal tract)**.**
- **Wilson's disease**, a hereditary disease which causes the body to retain copper.
- **Primary sclerosing cholangitis**, an inflammatory disease of the bile duct, likely autoimmune in nature.
- **Primary biliary cirrhosis**, autoimmune disease of small bile ducts.
- **Budd-Chiari syndrome**, obstruction of the hepatic vein.
- **Gilbert's syndrome**, a genetic disorder of bilirubin metabolism, found in about 5% of the population.
- Glycogen storage disease type II, the build-up of glycogen causes progressive muscle weakness (myopathy) throughout the body and affects various body tissues, particularly in the heart, skeletal muscles, liver and nervous system.
- **Jaundice:** Jaundice is a yellowish coloring of the skin. It is a temporary condition and is not dangerous to most infants. Jaundice usually becomes visible on the second or third day of life and begins to decrease between the fifth and seventh days. Most infants have some mild jaundice. For a few babies jaundice can be the sign of a very serious problem, and it can be treated. So, all babies must be watched closely.[10]
- **Hepatomegaly:** Hepatomegaly an enlarged liver, indicates potentially reversible primary or secondary liver disease This sign may stem from diverse pathophysiologic mechanisms, including dilated hepatic sinusoids (in heart failure), persistently high venous pressure leading to liver congestion (in chronic constrictive pericarditis), dysfunction and engorgement of hepatocytes (in hepatitis), fatty infiltration of parenchymal cells causing fibrous tissue (in cirrhosis), distention of liver cells with glycogen (in diabetes), and infiltration of amyloid (in amyloidosis).Hepatomegaly may be confirmed by palpation, percussion, or radiologic tests It may be mistaken for displacement of the liver by the diaphragm, in a respiratory disorder; by an abdominal tumor; by a spinal deformity, such as kyphosis; by the gallbladder; or by fecal material or a tumor in the colon.[11]

1.2.1 Epidemiology of liver dysfunction:

Epidemiology:

ALF affects approximately 2000 people per year in the United States . Early studies were based on small case series; for example, in 1969 an analysis of 31 patients found that 74% of cases were secondary to viral hepatitis and 23% to drugs. More recent studies have analyzed data from the multicenter Acute Liver Failure Study Group, formed in 1997. Their first prospective series, of 308 cases between 1998 and 2001, reported that 39% of ALF cases were caused by acetaminophen (paracetamol) poisoning, and only a minority were caused by viral hepatitis . Most cases involved women; the median age was 38 years (range, 15–78 years).

There were significant differences in survival rates and percentage of patients receiving transplantation depending on the cause of ALF. In the acetaminophen group there was 68% rate of spontaneous survival, and 6% received a liver transplant; in patients who had ALF secondary to idiosyncratic drug reactions, there was a 25% survival rate, and 53% of patients received transplantation. Acetaminophen poisoning leading to ALF was virtually unknown in the United States before 1980 but has now become the commonest cause of ALF. A recent analysis from the ALF Study Group reviewed 275 cases of acetaminophen-induced ALF over a 6-year period from 22 tertiary centers in the United States. The percentage of ALF cases secondary to acetaminophen rose during the study from 28% in 1998 to 51% in 2003. Unintentional overdoses accounted for 48% of cases, intentional overdoses accounted for 44%, and in 8% the intent was unknown. Overall, 178 (65%) survived, 74 (27%) died without liver transplantation, and 23 (8%) underwent transplantation. The transplant-free survival rates and rates of transplantation were similar in the intentional- and unintentional-overdose groups. Although accounting for only 13% of the 308 cases in the original ALF Study Group review and having a slower clinical evolution, idiosyncratic drug reactions were associated with a worse prognosis and higher rate of liver transplantation. Examples of causative drugs include bromfenac and troglitazone, both of which were withdrawn from the market in the United States. Other reported causes included trimethoprim, propylthiouracil, phenytoin, disulfiram, and herbal medications In the same study, 8% of ALF cases were secondary to hepatitis B (HBV) and 4% to hepatitis A. No patients had acute hepatitis C (HCV). Eight of the 308 cases were caused byWilson's disease, 17 were related to cardiogenic causes, 6 were pregnancy-related, and cancer was the underlying cause in 4. Autoimmune disease and Budd-Chiari syndrome were responsible in a few patients. Seventeen percent of cases were of indeterminate cause. [(12)]

1.2.2 Cause of liver dysfunction:

Liver dysfunction and subsequent damage can cause by:

Metabolic disorders such as obesity, diabetes, and high triglycerides – When the body's metabolism is not running properly, fat can accumulate around the liver.

Alcoholism – Excessive and chronic alcohol consumption is the leading cause of cirrhosis. Alcohol Converts To acetaldehyde, a carcinogenic toxin.

Illness – Certain illnesses, such as tuberculosis and malabsorption syndrome, can cause liver damage.

Pharmaceuticals – Certain prescription medications and over-the-counter drugs list liver damage as a side effect and a risk. Some of these include psychotropic medications (such as antidepressants, antipsychotics, and mood stabilizers), corticosteroids, non-steroidal anti-inflammatory medications (NSAIDs), and others. It's always important to review side effects and risks of pharmaceuticals with your healthcare professional and pharmacist.

Chemotherapy –chemotherapy drug can damage the liver is a side effect.

Pregnancy –In rare case, fatty liver can problem in pregnancy.

.**Poor diet** – A diet high in Tran's fats and heavily refined simple carbohydrates can cause metabolic disturbance that cause fatty liver.

Pesticides and heavy metals – These can be stored in body fat over a lifetime and have the potential to produce fatty liver.

Excess vitamin A – mega dosing of vitamin a can cause liver damage.

Candida – Candida yeast ferments sugars into acetaldehyde, which is the same carcinogen that causes alcohol hangovers. Candida also appears to increase gut and urinary levels of ammonia, which is another liver toxin.

Viral Hepatitis – Hepatitis A to E can liver infection.

Inappropriate use of herbal remedies – Plants of the Senecio, Crotalaria and Heliotopium families, plus chaparral, germander, comfrey, mistletoe, skullcap, margosa oil, mate tea, Gordolobo yerba tea, pennyroyal, and Jin Blu Huan are all toxic to the liver. [(13)]

1.2.3 Symptoms associated with liver dysfunction

Abnormal metabolism of fats

- Abnormalities in the level of fats in the blood stream. For example; elevated LDL cholesterol and reduced HDL cholesterol and elevated triglycerides.
- Arteries blocked with fat, leading to high blood pressure, heart attacks and strokes.

- Build up of fat in other body organs (fatty degeneration of organs).
- Lumps of fat in the skin (lipomas and other fatty tumors).
- Excessive weight gain, which may lead to obesity.
- Inability to lose weight even while dieting.
- Sluggish metabolism.
- Protuberant abdomen (pot belly).
- Cellulite.
- Fatty liver.
- Roll of fat around the upper abdomen - (liver roll).

Blood sugar problems

- Craving for sugar.
- Hypoglycaemia and unstable blood sugar levels.
- Mature onset diabetes (Type 2) is common in those with a fatty liver.

Digestive problems

- Indigestion.
- Reflux.
- Haemorrhoids.
- Gall stones and gall bladder disease.
- Intolerance to fatty foods.
- Intolerance to alcohol.
- Nausea and vomiting attacks.
- Abdominal bloating.
- Constipation.
- Irritable bowel syndrome.
- Pain over the liver - (upper right corner of abdomen & lower right rib cage).

Nervous system

- Depression.
- Mood changes such as anger and irritability.
- Metaphysically the liver is known as the "seat of anger".
- Poor concentration and "foggy brain".
- Overheating of the body, especially the face and torso.
- Recurrent headaches (including migraine) associated with nausea.

Immune dysfunction

- Allergies - sinusitis, hay fever, asthma, dermatitis, hives, etc.
- Multiple food and chemical sensitivities.
- Skin rashes and inflammations.
- Increased risk of autoimmune diseases.
- Chronic Fatigue Syndrome.
- Fibromyalgia.
- Increase in recurrent viral, bacterial and parasitic infections.

Hormonal Imbalance

- Intolerance to hormone replacement therapy or the contraceptive pill (eg. side effects)
- Menopausal symptoms such as hot flushes may be more severe.
- Premenstrual syndrome may be more severe.

1.2.4 External signs associated with liver dysfunction

- Coated tongue.
- Bad breath.
- Skin rashes.
- Itchy skin (pruritus).
- Excessive sweating.
- Offensive body odour.

- Dark circles under the eyes.
- Yellow discoloration of the eyes.
- Red, swollen, itchy eyes (allergic eyes).
- Acne rosacea - (red pimples around the nose, cheeks and chin).
- Brownish spots and blemishes on the skin (liver spots).
- Red palms and soles which may also be itchy and inflamed.
- Flushed facial appearance or excessive facial blood vessels (capillaries/ veins).[14]

1.2.5 Examination and Test:

1. Physical examination:

Age & Sex of patients , Duration of the liver dysfunction ,Sign & Symptoms of liver dysfunction: pallor, jaundice, dark urine, Liver enlargement , anorexia , Symptoms of liver affection: tender hepatomegaly , bleeding & clotting tendency , Duration of liver affection ,Frequency of blood transfusion ,History of previous surgical procedure or any risk of viral infection ,History of cholecystectomy , weight, height, skin colour, jaundice and hepatomegaly.

I1. Liver function tests:

Liver function tests (LFTs or LFs), which include **liver enzymes**, are groups of clinical biochemistry laboratory blood assays designed to give information about the state of a patient's liver. Most liver diseases cause only mild symptoms initially, but it is vital that these diseases be detected early. Hepatic (liver) involvement in some diseases can be of crucial importance. This testing is performed by biomedical scientists on a patient's serum or plasma sample obtained by phlebotomy. Some tests are associated with functionality (eg. albumin); some with cellular integrity (eg. transaminase) and some with conditions linked to the biliary tract (gamma-glut amyl transferase and alkaline phosphates). Several biochemical tests are useful in the evaluation and management of patients with hepatic dysfunction. These tests can be used to (1) detect the presence of liver disease, (2) distinguish among different types of liver disorders, (3) gauge the extent of known liver damage, and (4) follow the response to treatment.

Measurement	Significance	Reference range (Normal Values)
Albumin (Alb)	Albumin is a protein made specifically by the liver, and can be measured cheaply and easily. It is the main constituent of total protein; the remaining fraction is called globulin (including the immunoglobulins). Albumin levels are decreased in chronic liver disease, such as cirrhosis. It is also decreased in nephrotic syndrome, where it is lost through the urine. Poor nutrition or states of protein catabolism may also lead to hypoalbuminaemia. The half-life of albumin is approximately 20 days. Albumin is not considered to be an especially useful marker of liver synthetic function; coagulation factors (see below) are much more sensitive.	3.9 to 5.0 g/dl
Alanine transaminase (ALT)	Alanine transaminase (ALT), also called Serum Glutamic Pyruvate Transaminase (SGPT) or Alanine aminotransferase (ALAT) is an enzyme present in hepatocytes (liver cells). When a cell is damaged, it leaks this enzyme into the blood, where it is measured. ALT rises dramatically in acute liver damage, such as viral hepatitis or paracetamol (acetaminophen) overdose. Elevations are often measured in multiples of the upper limit of normal (ULN).	9 to 60 IU/L OR 6-36 U/ML
Aspartate transaminase (AST)	Aspartate transaminase (AST) also called Serum Glutamic Oxaloacetic Transaminase (SGOT) or aspartate aminotransferase (ASAT) is similar to ALT in that it is another enzyme associated with liver parenchymal cells. It is raised in acute liver damage, but is also present in red blood cells, and cardiac and skeletal muscle and is therefore not specific to the liver. The ratio of AST to ALT is sometimes useful in differentiating between causes of liver damage.[2][3] Elevated AST levels are not specific for liver damage, and AST has also been used as a cardiac marker.	10 to 40 IU/L
Alkaline phosphatase (ALP)	Alkaline phosphatase (ALP) is an enzyme in the cells lining the biliary ducts of the liver. ALP levels in plasma will rise with large bile duct obstruction, intrahepatic cholestasis or infiltrative diseases of the liver. ALP is also present in bone and placental tissue, so it is higher in growing children (as their bones are being remodelled) and elderly patients with Paget's disease.	30 to 120 IU/L

Total bilirubin (TBIL)	Bilirubin is a breakdown product of heme (a part of haemoglobin in red blood cells). The liver is responsible for clearing the blood of bilirubin. It does this by the following mechanism: bilirubin is taken up into hepatocytes, *conjugated* (modified to make it water-soluble), and secreted into the bile, which is excreted into the intestine. Increased total bilirubin causes jaundice, and can signal a number of problems: • 1. **Prehepatic**: Increased bilirubin *production*. This can be due to a number of causes, including hemolytic anemias and internal hemorrhage. • 2. **Hepatic**: Problems with the liver, which are reflected as deficiencies in bilirubin *metabolism* (e.g. reduced hepatocyte uptake, impaired conjugation of bilirubin, and reduced hepatocyte secretion of bilirubin). Some examples would be cirrhosis and viral hepatitis. • 3. **Posthepatic**: Obstruction of the bile ducts, reflected as deficiencies in bilirubin *excretion*. (Obstruction can be located either within the liver or in the bile duct.	0.1–1.2 mg/dl
Direct bilirubin (Conjugated Bilirubin)	The diagnosis is narrowed down further by looking at the levels of direct bilirubin. • If direct (i.e. conjugated) bilirubin is normal, then the problem is an excess of unconjugated bilirubin, and the location of the problem is upstream of bilirubin excretion. Hemolysis, viral hepatitis, or cirrhosis can be suspected. • If direct bilirubin is elevated, then the liver is conjugating bilirubin normally, but is not able to excrete it. Bile duct obstruction by gallstones or cancer should be suspected.	0–0.3 mg/dl
Gamma glutamyl transpeptidase (GGT)	Although reasonably specific to the liver and a more sensitive marker for cholestatic damage than ALP, Gamma glutamyl transpeptidase (GGT) may be elevated with even minor, sub-clinical levels of liver dysfunction. It can also be helpful in identifying the cause of an isolated elevation in ALP. GGT is raised in alcohol toxicity.	0 to 51 IU/L

Other tests:

5' nucleotidase (5'NTD)

5' nucleotidase is another test specific for cholestasis or damage to the intra or extrahepatic biliary system, and in some laboratories, is used as a substitute for GGT for ascertaining whether an elevated ALP is of biliary or extra-biliary origin.

Coagulation test (e.g. INR)

The liver is responsible for the production of coagulation factors. The international normalized ratio (INR) measures the speed of a particular pathway of coagulation, comparing it to normal. If the INR is increased, it means it is taking longer than usual for blood to clot. The INR will only be increased if the liver is so damaged that synthesis of vitamin K-dependent coagulation factors has been impaired: it is not a sensitive measure of liver function.It is very important to normalize the INR before operating on people with liver problems (usually by transfusion with blood plasma containing the deficient factors) as they could bleed excessively.

Serum glucose (BG, Glu)

The liver's ability to produce glucose (gluconeogenesis) is usually the last function to be lost in the setting of fulminant liver failure.

Lactate dehydrogenase (LDH)

Lactate dehydrogenase is an enzyme found in many body tissues, including the liver. Elevated levels of LDH may indicate liver damage. [(15)]

CONCLUSION

With significantly reduced cyanogenic side effects when compared to traditional therapy, targeted medication delivery will be a very intriguing method to improve the therapeutic outcome. In the past, the majority of research was backed by conjugating carriers or medications with targeted ligands, such as sugars and antibodies. Recent techniques employ site-specific drug carriers, such as peptides, antibodies, and natural or modified polymers. In addition to these, prodrugs that are intended to cleave in a highly site-specific manner are being researched. Certain prodrugs acquire cell specificity, whereas others do so by targeting cell-specific surface receptors that help prodrugs enter liver cells, such as the steroid

transporter. The liver-targeted medication delivery system is still marketed as a relatively small number of delivery systems.

REFERENCES

1. Maton, Anthea; Jean Hopkins, Charles William McLaughlin, Susan Johnson, Maryanna Quon Warner, David La Hart, Jill D. Wright (1993). *Human biology and Health*. Englewood Cliffs, New Jersey, USA: Prentice Hall
2. Cotran, Ramzi S; Kumar, Vinay; Fausto, Nelson; Nelso Fausto; Robbins, Stanley L.; Abbas, Abul K. (2005). Robbins and Cotran pathologic basis of disease St. Louis, MO: Elsevier Saunders. pp.878
3. Benjamin L. Shneider; Sherman,Philip M. (2008). *Pediatric Gastrointestinal Disease* Connecticut: PMPH-USA. pp.751
4. Three dimensional anatomy of the couinaud liver segments, Retrieved 2009-02-17
5. Prof. Dr. holger strunk – home page Retrieved 2009-02-17
6. The University of Nottingham- the physiology of liver
7. Cirrhosis overview: National Digestive Diseases Information Clearinghouse. Retrieved on 2010-01-22
8. Liver tissue damage and treatment: Retrieved on 2010-01-22
9 Extraintestinal complication: liver disease Crohn's & Colitis Foundation of America. Retrieved on 2010-01-22
10. Liver disease – Wikipedia, the free encyclopedia
11. www/liver disorder/hepatomegaly.com
12. Shahid A. Khan *et al*, Acute Liver Failure: a Review, Elsevier sunders, *Clin Liver Dis* 2006
13. www/liver disorder/cause of liver disease.com
14. Dr. Sandra cabot's liver doctor- love your liver and live longer.mht
15. Liver function test-Wikipedia, the free encyclopedia