INTRODUCTION AND REVIEW OF LITERATURE

LIVER

Liver is the largest organ in the body and is a mixed gland with both an endocrine and exocrine function, releasing several substances directly into blood stream and secreting bile into a duct system *(William and Harry, 1994).*

The liver primordium arises from the endodermal lining of the foregut during the middle of the third week of gestation. The hepatic diverticulum is situated at the ventral part of the foregut, cranial to its opening into yolk sac *(Hamilton et al., 1962).*

Liver is situated in right upper quadrant of the abdominal cavity with its rounded upper surface conforming to the dome of diaphragm *(Fawcett, 1994).*

The liver is anchored to the anterior body wall by falciform ligament and to the diaphragm by the coronary ligament. Blood vessels enter the liver while bile duct and lymphatic vessels leave it through a deep transverse fissure called the porta hepatis *(Schiff and Schiff, 1987).*

The liver consists of stroma of connective tissue and parenchyma of liver cells. The stroma contains fixed histiocytes, monocytes, plasma cells and lymphocytes. It forms the Glisson's capsule which contains regularly arranged collagenic fibers and scattered fibroblasts. It is covered mostly by peritoneum. At the porta hepatis, the connective tissue of the capsule extends like the trunk of a tree into the substance of the liver.

Within the liver this tree of connective tissue branches extensively dividing the liver parenchyma into lobes and lobules ***(Kelly et al., 1984; Snell, 1984 and Leeson et al., 1988).***

There is a mesh of reticular fibers suspended among the bundles of connective tissue fibers around the portal and hepatic venous tree. This reticulum runs between the parenchyma from the periphery of the lobule toward the center where it is condensed around the central vein. The argentaffin reticulum framework is formed of reticular cells and reticular fibers. It sustains the liver cords and plates ***(Freeman and Bracegirdle, 1976; Snell, 1984 and Cormack, 1987).***

The liver is completely divided on its anterior surface into large right lobe and smaller left lobe by the attachment of peritoneal falciform ligament on the inferior and posterior surfaces. There are two additional lobes, the quadrate and the caudate lobe delineated by the presence of inferior vena cava, attachment of the lesser omentum, ligamentum teres and the gall bladder ***(Snell, 1984).***

The classical lobule is the basic anatomical and functional unit of the liver. It is hexagonal or pentagonal in cross section, each lobule is seen to consist of mass of liver cells called hepatocytes that drain into central vein. There are connective tissue septa surrounding the lobules and separate them from one another. At the periphery of each lobule are small branches of hepatic artery and portal vein and a tributary of the bile duct and lymphatic vessels. These structures are components of the portal triad or tract, they are supported by connective tissue ***(Snell, 1984; Cormack, 1987 and Leeson et al., 1988).***

The portal lobule is a mass of liver cells that drain its secretion into a common bile duct. It is a triangular area of hepatocytes which is delineated by drawing imaginary lines connecting three central veins of three adjacent classical lobules and at the center of the triangle is a portal tract ***(Han and Holmsted, 1981; Snell, 1984; Leeson et al., 1988 and Junqueira et al., 1989).***

The liver acinus is a small functional unit of the liver which is rhomboidal in shape. It is made up of parts of two adjacent classical lobules and is formed of a central vein at each end and portal canal in the middle of each side. The liver acinus is defined as hepatic tissue supplied by a terminal branch of the portal vein and a terminal branch of the hepatic artery and drained by a terminal branch of the bile duct, these branches run towards the periphery of lobule ***(Kurt, 1992).***

The liver cells are arranged in cords or columns radiating from the central vein to the periphery of the lobule. These cords are always perpendicular to the central vein and may branch at the periphery of the lobules. The cords are formed of two adjacent rows of cells which enclose between them a tiny bile canaliculus. The cords are separated from each other by blood sinusoids ***(Freeman and Bracegirdle, 1976; Kelly et al., 1984 and Leeson et al., 1988).***

Hepatocytes appear hexagonal in cross section and have three distinct types of surfaces. One faces the sinusoid and its surface is greatly increased by extension of numerous microvilli. This surface represents the membrane across which blood liver exchange occurs. The second surface faces the adjacent hepatocytes. The third surface lies between adjacent hepatocytes near the center of the liver cell plates forming the

boundary of the bile canaliculus. This surface also forms microvilli that project into the bile canaliculi *(Burkel and Low, 1966 and Fawcett, 1994).*

The cytoplasm of a hepatocyte contains numerous organelles and inclusions. The most discrete organelle is the mitochondria, which are rounded or elongated in shape. The longest being near the portal tracts. In the matrix of mitochondria, the enzymes and cofactors of the Krebs cycle are located *(Loud, 1967; Snell, 1984; Fawcett, 1986 and Cormack, 1987).*

The cytoplasm of hepatocyte has abundance of the endoplasmic reticulum both in its smooth and granular varieties *(Junqueira et al., 1989).*

The cytoplasm of a hepatocyte contains a Golgi apparatus and its close proximity to the bile canaliculi is concerned with bile secretion *(Claude, 1970 and Whaley, 1972).*

Lysosomes present in hepatic cell vary in appearance. They contain lipofuscin and ferritin like substance which may be stored in large amount in iron storage disease. There are about 25 microbodies per liver cell *(DeDuve and Baudhuin, 1966).*

The centriole is found near Golgi apparatus in the hepatic cells which are recently divided, also the cytoplasm of hepatocytes contains two prominent cell inclusions. First one is glycogen found in the form of granules and secound is fat *(Greep and Weiss, 1973 and Anderson and Scotl, 1976).*

There is a central rounded nucleus in the hepatocyte. Approximately 25% of hepatocytes are binucleated. The nuclei of the parenchymal cells stain less intensively than the smaller nuclei of other cells in the liver. In the interior of the nucleus one or more nucleoli are embedded. These nucleoli are the site of synthesis of three forms of RNA ***(Fawcett, 1986).***

Bile canaliculi are present between layers of liver cellc of each plate which have no lining and bile enters canaliculus then go toward the periphery of lobule ***(Fawcett, 1994).***

The liver blood sinusoids are wider than capillaries and their wall conform to the surface of the plates of hepatocyte on either side but are seperated from them by a narrow space, and are lined by two types of cells. Endothelial cells: are greater in number and form a discontinuous lining for the wall of sinusoids. They have large fenestrations and the absence of basment membrane allow to percolate unformed blood elements and plasma through sinusoidal wall into the space of Disse ***(Fawcett, 1992).***

Kupffer cells: are phagocytic cells that are derived from monocyte, that lie within the sinusoid and are fixed to its endothelium. They can be easily demonstrated in animals by intravascular injection of vital dyes as trypan Blue ***(Leslie, et al., 1992 and Fawcett, 1994).***

Space of Disse, is a subendothelial space between the liver cells and the lining cells of the sinusoids which can be visualized by electron microscopy. It contains stellate shaped fat storing cells, reticular fibers,

non myelinated nerve fibers and short blunt microvilli of hepatocytes *(Leslie et al., 1992).*

The liver receives approximately 25% of the entire cardiac output, which enters at porta hepatis. About 75% of the liver's blood is supplied by the portal vein, which drains the gastro intestinal tract and therefore, carries nutrient rich blood. The branches of portal vein follow connective tissue bundles into the lobes and then into lobules, where they branch further in the portal canals. Then smallest branches of portal vein enter the sinusoids. The remaining 25% of the liver's blood is supplied by the hepatic artery. The branches of hepatic artery follow the trabeculae, suppling the connective tissue with blood. Small branches enter the portal canals carrying blood to capillary beds and to the cells of the portal canal. Few small branches of the hepatic artery drain directly into sinusoids however, most capillary beds derived from the hepatic artery drain into the venules carrying blood to portal vein which carry the drainage to sinusoids. Most of the blood that flows through the liver passes through sinusoids, then blood flow from sinusoids into central veins and then into hepatic vein which merge with the inferior vena cava *(Kurt, 1992).*

The liver produces a large volume of lymph. From one quarter to one half of the lymph of thoracic duct come from the liver which contains a large amount of plasma protein. The network of lymphatics parallels to the branches of the portal vein from interlobular portal areas to porta hepatis. Lymphatics have not been demonstrated within hepatic lobules *(Cormack, 1987).*

Liver is innervated mainly by efferent autonomic nerves found in portal triads and also adrenergic endings in space of Disse *(Cormack, 1987).*

The liver is a complex gland and has a wide variety of functions. It has an exocrine function which is production and secretion of bile which is passed into intestinal tract. Bile is composed of bilirubin, bile salts, cholestrol, phospholipids, electrolytes and water *(Snell, 1984)*. Liver cell produces various plasma proteins as albumin, prothrombin, fibrinogen and lipoprotein. These proteins are synthesized on polyribosomes attached to the rough endoplasmic reticulum. The hepatocyte does not store proteins in its cytoplasm as secretory granules but continuously releases them into blood stream, thus functioning as endocrine gland *(Junqueira, et al., 1992).*

In the liver carbohydrates are stored in the form of glycogen and lipids are stored in the form of triglycerides. This metabolite storage function is important because it supplies body with energy between meals *(Leslie, et al., 1992).*

Hepatocytes are responsible for converting lipids and aminoacids into glucose by means of a complex enzymatic process called gluconeogensis *(Junqueira, et al., 1992).*

Hepatocytes are responsible for detoxification of certain endogenous and exogenous compounds that are deleterious to body such as amonia, toxins and various drugs *(Fawcett, 1994).*

Hepatocytes have an important accessory function in the immune system of the intestine, immunoglobin A is present in bile four times its concentration in the blood *(Cormack, 1987).*

Glycogen is normally formed in most tissues of the body. The major sites for its formation are the liver and muscle *(Becker, 1974).* It is abundantly present in the cytoplasm of liver cells and it appears as coarse granules or clumps by light microscope *(Anderson and Scotl, 1976).*

Fat droplets appear as inclusions in the cytoplasm of hepatocytes particularly after fasting or ingestion of excess fat. The amount of fat which may be demonstrated in the hepatic cells varies inversely with the amount of glycogen *(Kelly et al., 1984).* Fat droplets occur transiently after meals and accumulate when fat metabolism is disturbed *(Greep and Wess, 1973).*

Alkaline phosphatase enzyme is found to some extent in liver bile canaliculi. An increase in alkaline phosphatase enzyme activity is detected in liver diseases *(Colowick and Kaplan, 1955). Jacopy and Martin (1951)* compared the biochemistry of bile with histochemical distribution of alkaline phosphatase in the liver. There is a rough correlation between the bile alkaline phosphatase and histochemical distribution of alkaline phosphatase in the liver.

Acid phosphatase enzyme is widely distributed in animal tissues, spleen, prostate and liver are the richest sites *(Pearse, 1968).* Acid phosphatase present in hepatic cells *(Roche, 1950 and Goodlad and Mills, 1957).* Kupffer cells contain large lysosomes which were rich in acid phosphatase *(Rutenburg and Seligman, 1955).*

Succinic dehydrogenase is one of the enzymes of citric acid cycle ***(Troyer, 1980).*** The activity of respiratory enzymes such as succinic dehydrogenase and cytochrome oxidase in the liver is concentrated in peripheral cells of hepatic lobules. It is associated with mitochondrial inner membrane ***(Chinquoine, 1953 and Estrabrook and Pullman, 1962).***