STUDIES OF LIVER DEVELOPMENT IN CHICK EMBRYO AND ULTRASTRUCTURAL CHANGES AFTER APPLICATION OF TOXINS AND PROTECTORS

A THESIS

Submitted for the Partial Fulfilment of The M.D. Degree (Anatomy)

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

﴿ نَرْفَعُ دَرَجَاتٍ مَّن نَّشَاءُ
وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ ﴾

صَدَقَ اللَّهُ الْعَظِيمْ
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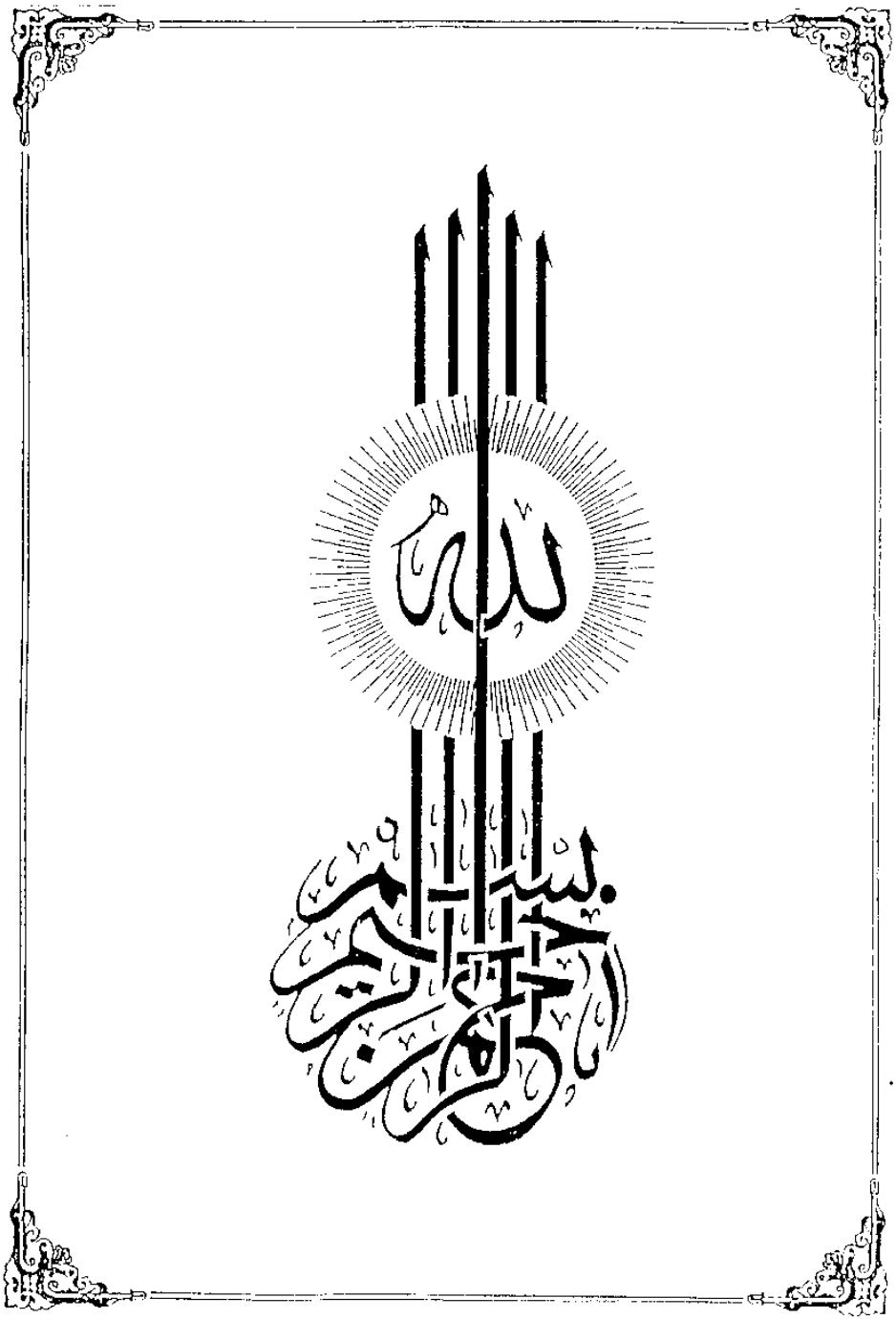

To the soul of my father

&

To my husband,

who suffered a lot during the

preparation of this work

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INTRODUCTION
AND AIM OF THE WORK

The increasing variety and number of chemicals and drugs introduced onto the market and also into the environment each year, and the resulting requirements for protection of human health and human environment, necessitated the monitoring of environmental materials as well as the development of rapid and reliable methods for toxicity evaluation and risk assessment. Furthermore, both ethical and legal obligations, e.g. animal protection laws, must be taken into consideration ***(Kemper and Leupke, 1986; and Leupke, 1986).***

The developing chick embryo was among the earliest and still remains one of the most extensively used living system for biological research. The availability of fertile eggs, the rapid growth of the embryo, and the ease of manipulating it and altering its environment, had made the chick embryo an ideal model system which is recommended as screening investigations in testing embryonic development and embryotoxicity ***(Karnofesky, 1955).***

The liver, because of its central anatomic location and pivotal role in drug metabolism, is especially susceptible to injury from foreign compounds ***(Tolman, 1990).***

Paracetamol (N-acetyl-P-aminophenol) or (acetaminophen) is a widely used analgesic. Although safe in therapeutic doses, an overdose

resulted in marked hepatic damage and in severe cases, death in both laboratory animals and man ***(Boyed and Bereczky, 1966).***

Acute overdosage with paracetamol is becoming increasingly common and is of particular clinical importance, because a significant proportion of such patients develop acute hepatic necrosis with occasional death from liver failure ***(Dixon, Dixon, Aparicio and Loney, 1975).***

The effect of paracetamol on the liver and kidney of the four-day chicken embryo was studied by light microscope ***(Walton and Osborne, 1988).***

The present work was done as an attempt to clarify the ultrastructural changes in the liver cells after application of paracetamol using the chick embryo as an experimental model, with a trial to protect the liver from the toxic effect of paracetamol.

Therefore, the aim of the present work was to study :

I- The normal development of the liver in the chick embryo.

II- The effect of paracetamol on the developing liver.

III- Protection of the liver against paracetamol using N-acetyl-L-cysteine.

Review Of Literature

REVIEW OF LITERATURE

I- DEVELOPMENT OF THE LIVER

Shore and Jones (1889) stated that, the vertebrate liver was originally a solid mass of cells which became penetrated by blood vessels, and thus divided into a network of anastomosing cylinders. They described the liver of the birds as dense tissue with obscuring cellular outlines. They added that, in young chicken, the hepatocytes were arranged into tubules having a diameter of 30-40 μm. Those tubules were convoluted and anastomosed frequently so as to form a close network, and the lumina were distinct. The cytoplasm of the hepatocytes was completely honeycombed by a number of clear spaces filled with oil globules. The blood capillaries were small and there was a uniform distribution of larger blood vessels, around which there was a tendency to a radiating arrangement, but no distinction into interlobular and intralobular veins could be seen.

Hans (1912) said that, as the liver of the developing chick embryo increased in size, it assumed gradually more and more the colour of the yolk. Material derived from the yolk was gradually stored in the liver, and that material was largely of a fatty nature. He added that, accumulation of fatty globules started in the liver cells of the six-day chick embryo. That condition persisted, and fat accumulation increased until hatching occurred. The author observed also that, the liver of nineteen days chick embryo was brilliant yellow in colour due to high fat content.

Lynch (1921) stated that, in culture, the chicken embryo liver cells were thick, polygonal, and opaque having a greenish grey colour due to the dense packing of their cytoplasm with mitochondria. The nucleus was spherical and clear with a very distinct boundary which made it conspicuous under all magnifications. The nucleolus was usually single with variable location and sometimes two or more nucleoli were present. As regards the mitochondria, they were not constant in shape, size, position or number. In some cells, most of the larger mitochondria were present near the periphery of the cytoplasm. However, they were often found in contact with the nucleus or scattered in the cytoplasm. They varied in length from 1.5-4 μm and in width from 0.5-1.5 μm. In shape, they were also variable. They were spherical, oblong, triangular, pear-shaped or entirely irregular.

He observed that, there was a correlation between the age of the embryo from which the explants were taken and the amount of free fat globules accumulating in the media. Explants taken from five days embryos gave very little amount of fat, while those from sixteen days embryos gave an enormous amount of fat. However, there was no correlation between the amount of fat and the age of the culture. The number or size of the fat globules in the cells did not change as the culture advanced in age.

Sharpey-Schafer (1929) said that, blood channels in the liver lobules were interstitial spaces which were distinguished from capillaries by the term sinusoids and there was no endothelium between the blood and the hepatocytes : the cells were directly bathed by the blood. He added that,

Kupffer cells represented endothelial remnants which were included in the reticuloendothelial system.

Arey (1932) stated that, the liver parenchyma of the seal was characterized by being arranged into lobules with a central vein as an axis. There was also a striking tendency towards a radial arrangement of the liver cords about the portal canals. He added that, coarse connective tissue was scarce in the seal's liver and was chiefly limited to the vicinity of portal canals.

Calhoun (1933) stated that, the liver of the chicken differed a little from that of the mammal. He observed that the liver epithelium was arranged in a tubule of four to six cells about an intralobular bile capillary. The liver cell was pyramidal in shape with its apex bordering the lumen of the tubule. A large spheroidal nucleus was present in the distal half of the cell. He observed also that, the blood sinusoids were lined by endothelial cells and Kupffer cells.

Dalton (1934) stated that, in the liver of the three days chick embryo, the majority of the mitochondria were filamentous in nature. There was no marked changes in the mitochondrial pattern from the third to the eleventh day. On the fourth day of incubation, those filaments were somewhat thicker and a little shorter. On the sixth day, the filaments had changed into definite rods of varying lengths, sometimes curved but usually straight or nearly so. The curved rods were usually located near the nucleus. From the sixth to the eleventh day, there was a very slight increase in the length of the