

Study of the cytotoxic effects of insecticides on hepatocytes by light and electron microscope

Thesis

Submitted for Fulfillment of Master Degree
in Histology

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(2007)

Abstract

This Study Was Made On 48 Female Albino Rats , 24 Non Pregnant , 24 Pregnant , The Offsprings Of Pregnant Rats Were Included. The Results Were: Shrunken Hepatocytes , Pyknotic Nuclei And Areas Of Degeneration (By Light Microscope).

Small Mitochondria , Fragmented Rough Endoplasmic Reticulum & Appearance Of Lysosomes (By Electron Microscope)

These Were For Malathion

Rats Given Cypermethrin Showed Hypertrophied Hepatocytes, Pyknotic Nuclei And Congested Central Veins (By Light Microscope).

Key Words :

Adenosine Triphosphate – Caudate Lobe – Lysosomes .

ACKNOWLEDGMENT

First and foremost thanks are due to God the most kind and the most merciful.

I would like to express my deep appreciation and profound gratitude to **Prof. Dr. Mohamed Abd EL** Hafez, Professor of Histology, Faculty of Medicine, Cairo University, who was very kind saving no time or effort in helping me, and for his constant support and his guidance through the conduction of this work.

I will always be grateful to **Dr. Dina Mohamed Radwan**, Assistant Professor of Histology Department, Faculty of Medicine, Cairo University, for her supervision, and valuable advice throughout this work.

Also, I would like to express my sincere thanks to **Dr. Sameh Fawzi Gad EL-Sonbaty**, Lecturer of Histology Department, Faculty of Medicine, October 6 University, for his great efforts and valuable supervision.

To My Parents
My Husband
Dr. Mazin EL
Sergany
and
My lovely Daughter
Noura

List of abbreviation

ADI	ACCEPTABLE DAILY INTAKE
ATP	Adenosine triphosphate
CBD	Common bile duct
CL	Caudate lobe
Cy puso	Cytochrome P450
CYP	Cypermthrin
DDT	Dichloro-Diphenyl-Trichloroethane
EPA	Environmental protection agency
FDA	Food and drug administration
Hx&E	Hematoxylin and Eosin
ILL	Inferior lateral lobe
L	Lysosomes
LC	Lethal concentration
LD ₅₀	Lethal dose to 50% of subjected population
LLL	Left lateral lobe
LM	Light microscopy
LML	Left medial lobe
M	Mitochondria
MFO	Mixed-function oxidases
Mg/kg	Milligrams per kilogram
ML	Median lobe
NOEL	No-Observable-Effect-Level
O.M	Original magnification

OP	Organophosphate
PCC	Poison control center.
Ppm	Part per million
RBCs	Red blood corpusdes
rER	Rough endoplasmic reticulum
RfD	Reference Dose
RL	Right lobe
RLL	Right liver lobe
RML	Right medial lobe
ROS	Reactive oxygen species
RUP	Restricted use pesticides
sER	Smooth endoplasmic reticulum
SRL	Superior right lobe
TEM	Transmission electron microscope
USEPA	United states environmental protection agency

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Embryology of the liver

The liver develops from the foregut as follows:

- In the middle of the 3rd week, a liver bud (also called hepatic diverticulum) appears as an outgrowth of the endoderm at the lower end of the foregut. As the liver bud enlarges, the connection between it and the foregut (duodenum) becomes narrow and forms the "common" bile duct (**Duncan, 2003**).

The liver bud then divides into 2 parts :

1-Pars hepatica : a large part which will form the liver itself.

2-Pars cystica : a small part which will form (a) the cystic duct and (b) the gall bladder.

- The pars hepatica divides into two branches (right and left): each branch will give rise to columns of hepatic cells and thus will form one lobe of the liver.
- As the pars hepatica (which consists of rapidly dividing and branching cell columns) enlarges, it penetrates the septum transversum: and as the cords of liver cells extend into the septum transversum, they meet the vitelline veins and convert them into the sinusoids of the liver (**Duncan, 2003**).

Formation of the "falciform ligament" and the "lesser omentum"

As the liver enlarges, it begins to leave the septum transversum and gradually protrudes into the abdominal cavity :

(a) The mesoderm of the septum transversum between the liver and the anterior abdominal wall becomes stretched and forms a thin membrane called the falciform ligament.

The umbilical vein (which lies originally in the mesoderm of the septum transversum) lies now in the free lower margin of the falciform ligament.

(b) The mesoderm of the septum transversum between the liver and the foregut (stomach and duodenum) becomes stretched and forms the lesser omentum (also called gastrohepatic ligament) (**LeDouarin, 1995**).

Three structures : the hepatic artery, the portal vein and the bile duct now lie in the free margin of the lesser omentum. The mesoderm on the surface of the liver differentiates into peritoneum except on its cranial surface (in the region in which the liver remains in contact with the part of the septum transversum which will form an important part of the diaphragm).

This area of the liver will never be covered by peritoneum and is called the "*bare area*" of the liver.

The size and weight of the liver:

- The size and weight of the liver are large in fetal life (in the 10th week the liver is about 10% of the total body weight); the large size and weight of the liver is due to 2 factors : (a) partly due to large numbers of sinusoids from the vitelline and umbilical veins and (b) partly due to the fact that the liver in fetal life is a haematopoietic organ producing red and white blood cells.
- The weight of the liver is only about 5% of the total body weight at birth (**Medlock and Haar, 1993**).

Development of the hepatic ducts and the "common" bile duct:

- (a) The right and left hepatic ducts develop as the stems of the right and left branches of the pars hepatica become canalised.
- (b) The original stalk of the liver bud elongates to form the common bile duct.

At first, the common bile duct opens into the anterior wall of the duodenum; later as a result of rotation of the duodenum the opening of the common bile duct becomes posterior and the common bile duct is found passing behind the duodenum (**Duncan, 2003**).

ANATOMY OF RAT LIVER

The rat liver is multilobulated as in other mammals. In rats, the liver mass represents approximately 5% of the total body weight, while in adult humans it represents 2.5%. In rats weighing between 250 and 300 g, the liver mean weight is 13.6 g and the liver transverse diameter measures from 7.5 to 8.0 cm. The superior–inferior diameter measures from 3.8 to 4.2 cm, while the anterior–posterior diameter ranges from 2.2 to 2.5 cm (**Zanchet and Monteiro, 2002**)

Surfaces

The rat liver, when the rat is in the decubitus position, has basically three surfaces: superior, inferior and posterior. A sharp, well-defined margin divides the inferior from the superior surface. Different from the human liver, the other margins are also sharp. Although the rat liver is lobated, it has rather uniform surfaces as lobes lie flat against each other. The only exception to this is the posterior caudate lobe (CL), which is separated from the remainder of the liver by the stomach (**Kongure et al., 1999**).

The superior (parietal) surface comprises a part of the left lateral and medial lobes, and, as a whole, is convex, and fits under the vault of the diaphragm. It is completely covered by the peritoneum, except along the line of attachment of the falciform ligament. The line of attachment of the falciform ligament divides the liver into two parts, termed the right and left lobes. Different from human livers, in which the right lobe is much larger than the left one, the rat left and right liver have approximately the same volume (**Martins and Peter, 2007**)

The inferior (visceral) surface is uneven, concave and is in relation to the stomach, duodenum, right colic flexure, the superior part of the pancreas, the right kidney and suprarenal gland. The rat liver inferior surface does not have the

fossae in the shape of the letter H as in humans. This surface is almost completely invested by the peritoneum. Through the porta (transverse fissure) goes the portal vein, the hepatic artery and nerves, the hepatic duct and lymphatics. Liver impressions (colic, renal, duodenal and suprarenal) are not as evident as in human livers (**Kent, 2001**).

The posterior surface is not covered by the peritoneum over some part of its extent, and is in direct contact with the diaphragm. It extends obliquely between the CL and the bare area of the liver. The inferior vena cava is completely intrahepatic (**Martins and Peter, 2007**)

Ligaments

Similar to the human liver, the rat liver is connected to the undersurface of the diaphragm and to the anterior wall of the abdomen by five ligaments: the falciform, the coronary, and the two laterals are peritoneal folds; the fifth, the round ligament, is a fibrous cord, the obliterated umbilical vein. The liver is also attached to the lesser curvature of the stomach by the hepatogastric ligament, and to the duodenum by the hepatoduodenal ligament (**Martins and Peter, 2007**)

Liver lobes

- The middle or median lobe (ML) is the largest, accounting for approximately 38% of the liver weight. It has a trapezoidal shape and is fixed in the diaphragm and abdominal wall by the falciform ligament. It is in continuity with the left lateral lobe (LLL) and is subdivided by a vertical fissure (main fissure or umbilical fissure) into a large right medial lobe (RML) (2/3 of the volume of the medial lobe) and a smaller left medial lobe (LML; 1/3 of the volume). The RML has both left and right hepatic vascular components (**Kongure et al., 1999**).