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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Abstract

This Study Was Made On 48 Female Ulbino Rats, 24 Non Pregnant,

24 Pregnant, The Offsprings Of Pregnant Rats Were Included.

The Renults Were: Shrunken Hebato Cytes , Pyknotic Nuclie

And Areas Of Degeneration (By Light Microscope).

Small Mitochondria, Pragmented Rough Endoplanmic Raticulum

& Appearance Of Lysosomes (By Electron Microscope)

These Were For Malathio

Rats Given Cypermethrin Showd Hypertrophied Hepatocyten,

Pyknotic Nuclei And Congested Centrel Veins (By Light Microscope).

Key Words:

Adenosine Triphosphate - Caudate Lope - Lysosomes .

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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
М	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

List of tables

No	Title	Page
1	Physical Properties Of Malathion	29
2	Doses Of Malathion Put By Toxicity Categorg of U. S. EP. A	40

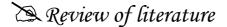
List of figures

No	Title	Page
1	Induction of hepatogenesis by FGFs and BMPs	5
2	Rat proximal digestive tract	8
3	Different surfaces of rat liver.	12
4	Rat liver in situ	13
5	Rat liver ex situ	14
6	Most common anatomy of the hepatic veins	17
7	General chemical structure of malathion	47
8	Space-filling model of malathion, showing van der Waals radii for each atom	47
9	Proposed metabolic pathway for Malathion in rats	49
10	Photo from adult female albino rat 250 gm with 50 mg malathion showing hepatocytes	70
	with dark pyknotic nuclei	
11	Photo from adult female albino rat 250 gm with 1500mg malathion showing;	70
	hepatocytes with intracytoplasmic accumulation	
12	Photo from foetus of female albino rat with 1500mg malathion showing loss of liver	71
	architecture	
13	Photo from foetus of female albino with 500mg malathion showing loss of liver	71
	architecture with lymphocytes infiltration	
14	Photo of adult female albino rat 100 gm with 600mg malathion showing hyaline	72
	degeneration and sinusoidal congestion	
15	Photo of adult albino rat 100gm with 200mg Malathion showing hyaline degeneration	72
16	Photo from adult female albino rat 250gm with 50mg cypermethrin showing normal	73
	hepatocytes normal liver architectural	
17	Photo from adult female albino rat 250 gm with 110 mg cypermethrin showing hyaline	73
	degeneration with fatty infiltration	
18	Photo from control group showing normal nucleus, normal desomsomes, normal	74
	mitochondria and normal rough endoplamic reticulum.	
19	Photo from female albino rat 100 gm with 4 gm malathion showing mononuclear	75
	cellular infiltration and indented nuclei.	
20	From female albino rat 250gm with 50mg malathion showing hepatocytes with dark	76
	nucleus swelling mitochondria.	
21	Photo from female albino rat 250 gm with 50 mg cypermethrin showing hepatocytes	77

	with normal nuclei, mitorchondria and normal rough endoplasmic reticulum with slight	
	vacuolation.	
22	From female albino rat 250 gm with 50 mg cypermethrin showing hepatocytes with	78
	normal nuclei, mitorchondria and normal rough endoplasmic reticulum with slight	
	vacuolation.	
23	Photo from female albino rat 250 gm with 50 mg cypermethrin showing hepatocytes	79
	with normal nuclei, mitorchondria and normal rough endoplasmic reticulum with slight	
	vacuolation.	
24	Photo from for female albino 250 gm with 6 mg cypermethrin showing vacuolar	80
	degeneration of hepatocytes, Slight swelling of rough endoplasmic reticulum and	
	mitochondria and appearance of vankupher cells	
25	Photo from for female albino 250 gm with 6 mg cypermethrin showing vacuolar	81
	degeneration of hepatocytes, Slight swelling of rough endoplasmic reticulum and	
	mitochondria and appearance of vonkupffer cells	
26	Photo from foetus of adult albino rat with 110 mg cypermethrin showing vacuolar	82
	degeneration	
27	Photo from adult female rat 100 g with 20 mg cypermethrin Showing slight vacuolar	83
	degeneration.	

CONTENTS

Contents	Page
Introduction and Aim of work	1
Review of Literature	
- Embryology of the liver	3
- Anatomy of the liver	6
-Histology of the liver	10
- Pesticides	19
-Toxicity of pesticides	21
-Malathion	27
-Cypermethrin	35
Materials and Methods	
Results	43
Discussion	66
Summary and Recommendations	
References	
Arabic Summary	_



Embryology of the liver

The liver developes 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 (doudenum) 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.

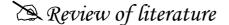
(b) The mesoderm of the septum transversum between the liver and the foregut (stomach and duodenum) becomes stretched and forms the lesser omentum (also called gastrohepatic ligament) (LeDouarin, 1995).

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).