9787 JK

THE BIOCHEMICAL EFFECTS OF PYROGENIC SUBSTANCES ON METABOLISM IN EXPERIMENTAL ANIMALS

By

Abd El Rahman Abbas El Garawany

B. Sc. (Agric. Biochemistry) Ain Shams Univ. (1968)

M. Sc. (Agric. Biochemistry) Ain Shams Univ. (1975)

THESIS

Submitted in Partial Fulfilment of the Requirements for the Degree of

DOCTOR OF PHILOSOPHY

in

Agricultural Biochemistry

19018

Faculty of Agriculture Ain Shams University Cairo — A. R. K.

ر مانع

1984

619

APPROVAL SHEET

Name: Abd El Rahman Abbas El Garawany

Title of Thesis:

THE BIOCHEMICAL EFFECTS OF PYROGENIC

SUBSTANCES ON METABOLISM IN

EXPERIMENTAL ANIMALS

Ph. D. Thesis approved by

Committee in charge

- Ca.M. Khaled.

Date: 6 /(2/1984



ACKNOWLEDGEMENT

and the control of the

The author wishes to express his highest appreciation and gratitude to Professor Dr. Gamal Morsi Khaled, Prof. of Biochemistry, Faculty of Agriculture, Ain Shams University for his kind supervision, valuable guidance and encouragement.

The sincere help and continuous interest offered by Dr. A. El-Assar, Assistant Prof. of Biochemistry, Faculty of Agriculture, Ain Shams University, and Dr. H.A. Samaan, Head of Toxicology Department, National Organisation for Drug Control and Research (NODCAR).

The kind help and continuous cooperation offered by Dr. E.A. Shereef, Lecturer of Chemistry, Faculty of Agriculture, Ain Shams University was greatly appreciated.

Our thanks are due to Dr. T. Rashad, Head of Pyrogen department (NODCAR) for his kind help and encouragment, Dr. A. El-Zawahry, Head of Histopathology Department (NODCAR) for his help during the histopathological study.

CONTENTS

	Page
INTRODUCTION	1
I- REVIEW OF LITERATURE	4
. Pyrogen	4
. Metabolic responses to hyperthermia	7
. The chemical induction of hepatotoxicity	12
. Metabolic responses to hepatotoxic state	14
. Biological function of nucleic acids	20
II- MATERIALS AND METHODS	24
. The pyrogen source	24
. The experimental animals	24
. Treatments of rabbits	25
. Body temperature response	27
. Blood biochemical analysis	28
1- Determination of serum proteins	29
2- Determination of serum albumins	31
3- Determination of serum transaminases content	32
4- Estimation of serum alkaline phosphatase activity	3 4
5- Determination of serum triglycerides	3 6
6- Determination of serum bilirubin	38
7- Determination of serum creatinine	39
<pre>8- Determination of liver nucleic acids (DNA & RNA) and total proteins</pre>	41
. Histological changes in the liver \dots	45
. Statistical analysis of the data	45
III- RESULTS AND DISCUSSION	46
 Rectal temperature responses of normal rabbits to TAB vaccine 	46
 Rectal temperature responses of hepato- toxic rabbits to TAR vaccine 	48

- ii -

Pag	е
. Metabolic responses to hyperthermia: 54	
1- Serum proteins 54	
2- Serum alkaline phosphatase 61	
3- Serum transaminases 65	
4- Serum triglycerides 68	
5- Serum total bilirubin 68	
6- Serum Creatinine 72	
. Serum biochemical changes in response	
of induced hepatotoxicity 76	
. Serum biochemical changes of hepatotoxic	
rabbits in response to TAB vaccine 79	
1- Serum proteins 79	
2- Serum alkaline phosphatase 86	
3- Serum transaminases 90	
4- Serum triglycerides 96	
3- Serum bilirubin 96	
6- Serum creatinine	
. Liver nucleic acids in response to TAB	
vaccine	
. Liver nucleic acids in response to	
induced hepatotoxicity 102	
. Liver nucleic acids of hepatotoxic rabbits in response to TAB vaccine	
Liver histological findings	
110	
IV- SUMMARY	
REFERENCES	
ARABIC SUMMARY	

J

LIST OF TABLES

Table	No.	Page
1	The effect of TAB vaccine low dose	
	(0.4%) and high dose (1.0%) on rectal	
	temperature of rabbits	47
		47
2	Means of rectal temperature of rabbits	
	as recorded during induction of hepato-	
	toxicity by isopropanol and carbon tetra-	
	chloride CCl ₄	50
3	Rectal temperature responses of hepato-	
	toxic rabbits to TAB vaccine	52
		32
4	Means of serum total proteins content	
	(g/1) in rabbits after the injection of	
	TAE vaccine low dose (0.4%) and high dose	
	(1.0%)	55
5	Means of serum albumins content (g/l) in	
	rabbits after the injection of TAB vac-	
	cine, low dose (0.4%) and high dose (1.0%)	56
_		
6	Means of serum globulins content (q/l)	
	in rabbits after the injection of TAB	
	vaccine low dose (0.4%) and high dose	
	(1.0%)	59
7	Means of serum albumins/globulins ratio	
	after the injection of TAB vaccine low	
	dose (0.4%) and high dose (1.0%)	60
8		•
O	Means of serum alkaline phosphatase acti-	
	vity $(IU/1)$ in rabbits after the injection of TAB vaccine low dosc (0.4%) and high	
	dose (1.0%)	



- iv -

Table	No.	Page
9	Means of serum GOT content (I.U./dl)	
	in rabbits after the injection of TAB	
	vaccine low dose (0.4%) and high dose	
	(1.0%)	63
10	Means of serum GPT content (I.U./dl) in	
	rabbits after the injection of TAB	
	vaccine, low dose (0.4%) and high dose	
	(1.0 %)	66
11	Means of serum triglycerides content	
	(g/1) in rabbits after the injection of	
	TAB vaccine low dose (0.4%) and high	
	dose (1.0%)	69
12	Means of serum bilirubin content	
	(mg/100 ml) in rabbits after the injec-	
	tion of TAB vaccine low dose (0.4%) and	
	high dose (1.0%)	70
13	Means of serum creatinine content (mg/l)	
	in rabbit after the injection of TAB	
	vaccine low dose (0.4%) and high dose	
	(1.0 %)	74
14	Serum biochemical constituents of rabbits	
	as determined 24 hours after the sequen-	
	tial treatment with isopropanol and ${\rm CCl}_4$.	77
15	Means of serum total proteins content of	
	hepatotoxic rabbits as determined at	
	different time intervals following the	
	injection of TAB vaccine	80

- 37 -

Table No).	Pag
16	Means of serum albumins content of	
	hepatotoxic rabbits as determined at	
	different time intervals following the	
	injection of TAB vaccine	81
17	Means of serum globulins content of	
	hepatotoxic rabbits as determined at	
	different time intervals following the	
	injection of TAB vaccine	84
18	Means of serum albumins/globulins ratio	
	of hepatotoxic rabbits as calculated at	
	different time intervals following the	
	injection of TAB vaccine-85	
19	Means of serum alkaline phosphatase	
	activity of hepatotoxic rabbits as	
	determined at different time intervals	
	following the injection of TAB vaccine.	89
20	Means of serum glutamate ovaloacetate	
	transaminase (GOT) activity of hepato-	
	toxic rabbits as determined at diffe-	
	rent time intervals following the injec-	
	tion of TAB vaccine	21
21	Means of serum glutamate pyruvate transa-	
	minase (GPT) activity of hepatotoxic	
	rabbits as determined at different time	
	intervals following the injection of TAB	
	vaccine	0.3

The second secon

Table No. Page 22 Means of serum triglyceridescontent of hepatotoxic rabbits as determined at different time intervals following the injection of TAB vaccine 94 23 Means of serum bilirubin content of hepatotoxic rabbits as determined at different time intervals following the injection of TAB vaccine 97 Means of serum creatinine content of 24 hepatotoxic rabbits as determined at different time intervals following the injection of TAB vaccine Means of liver total proteins (g/g liver), 25 RNA and DNA (mg/g liver) contents at different time intervals following the injection of TAB vaccine, low dose(0.4%) and high dose (1.0%) 103 26 Means of liver total proteins RNA and DNA, of rabbits as determined 24 hours after the sequential treatment with isopropanol and CCl_A 27 Means of liver total preteins (g/g liver), RNA and DNA (mg/g liver)contents of hepatotoxic rabbits as determined at different time intervals following the injection of TAR vaccine 107

LIST OF FIGURES Fig.No. Page 1 The changes of rectal temperature of rabbits following TAB vaccine injection 48 2 The changes of rectal temperature of rabbits during the isopropanol/CCl $_{\it A}$ induction of hepatotoxicity and subsequent TAB vaccine injection 53 3 Percentage changes in serum proteins from initial values and the elevations in rectal temperatures of rabbits following the injection of TAB vaccine (low dose 0.4%) 57 4 Percentage changes in serum proteins from initial values and the elevations in rectal temperatures of rabbits following the injection of TAB vaccine (high dose 1.0%) 64 5 Porcentage changes in serumalkaline phosphatase and transaminases (COT & GPT) from the initial values and the elevations in rectal temperature of rabbits following the injection of TAB vaccine (low dose 0.4°)..... 6.7 6 Percentage changes in serum alkaline phosphatase and transaminase (GOT & GPT) from the initial values and the elevations in rectal temperatures of rabbits following the injection of TAB vaccine (high dose 1.0%)..... 71

Fig.	No.	Page
7	Percentage changes in scrum tri- glycerides, bilirubin and creatinine from initial values and the elevations in rectal temperatures of rabbits fol- lowing the injection of TAB vaccine (low dose 0.4%)	73
8	Percentage changes in serum trigly-cerides, bilirubin and creatinine from initial values and the elevations in rectal temperatures of rabbits following the injection of TAB vaccine (high dose 1.0%)	75
9	Percentage changes in serum biochemistry in response to CCl ₄ /isopropanol treatment	78
10	Forcentage changes in serum proteins from hepatotoxic state and changes in rectal temperature of hepatotoxic rabbits (no treatment)	85
11	Percentage changes in serum proteins from hepatotoxic state and changes in rectal temperature of hepatotoxic rabbits following the injection of saline	87
12	Percentage changes in serum proteins from hepatotoxic state and changes in rectal temperature of hepatotoxic rabbits following the injection of TAB vaccine (low dose 0.4%)	88

Fig.No.		Page
13	Percentage changes in serum proteins from hepatotoxic state and changes in rectal temperature of hepatotoxic rabbits following the injection of TAB vaccine (high dose 1.0%)	95
14	Percentage changes in serum alkaline phosphatase and transaminases (GPT & GOT) from hepatotoxic state and changes in rectal temperature of rabbits (no treatment)	98
15	Percentage changes in serum alkaline phosphatase and transaminases (GPT & GOT) from hepatotoxic state and changes in rectal temperature of rabbits following the injection of saline	101
16	Percentage changes in serum alkaline phosphatase and transaminases (GPT & GOT) from hepatotoxic state and changes in rectal temperature of hepatotoxic rabbits following the injection of TAB vaccine (low dose 0.4%)	104
17	Percentage changes in serum alkaline phosphatase and transaminases (GPT & GOT) from hepatotoxic state and changes in rectal temperature of hepatotoxic rabbits following the injection of TAB vaccine (high dose 1.0%)	10 9
18	Section from normal untracted walling	

- x -

Fig.	No.	Page
19	Section from liver of rabbit receiving TAB vaccine	112
20	Section from liver of hepatotoxic rabbit.	113
21	Section from liver of hepatotoxic rabbit receiving TAB vaccine	114

INTRODUCTION