A COMPARATIVE CLINICOPATHOLOGICAL STUDY ON THE EFFECT OF FUCOIDAN AND LEVAMISOLE ON SOME HEMATOLOGICAL AND BIOCHEMICAL PARAMETERS IN BOTH NORMAL AND HEAT STRESS RABBITS

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ABSTRACT

This study was planned to investigate the effect of fucoidan and levamisole on some hematological and biochemical parameters in growing rabbits, in both normal and heat stress conditions. One month aged rabbits were orally treated with fucoidan at a dose of 100 and 200 mg/kg body weight daily for 4 weeks and levamisole with 8 mg/kg as a single dose every 2 weeks. This study was conducted at winter and summer. Fucoidan and levamisole treated groups returned the increased RBCs count and Stress leukogram picture to normal at the end of the study. Biochemical profile showed significant decrease in ALT, AST, glucose, urea and creatinine with increased level of total protein and globulin . We concluded that fucoidan express good immunomodulating, hepatoprotective and renoprotective effect against stress induced by high temperature.

INTRODUCTION

Fucoidan refers to a type of polysaccharide containing substantial pereentages of L-fucose and sulfate ester groups mainly derived from brown seaweed and some marine invertebrates (such as sea urchins and seacucumbers) **(Bo et al., 2008 and Oliver and Barbra, 2003)**. Now it is named as "fucoidan" according to IUPAC rules, but some also called it fucan, fucosan or sulfated fucan **(Bo et al., 2008)**.

Chemical compositions of most fucoidans are complex, mainly being composed of fucose and sulfate. They also contain other monosaccharides (mannose, galactose, glucose, xylose, ete.) and uronic acids, even acetyl groups and protein. Furthermore, the structures of fucoidans from different brown algae vary from species to species **(Olivier and Barbara, 2003 and Bo et al., 2008)**.

For the past decadc fucoidans isolated from different species have been extensively studied due to their varied biological activities, including anticoagulant and antithrombotic, antiviral, antitumor and immunomodulatory, anti-inflammatory, blood lipids reducing, antioxidant, antieomplementary properties, activity against hepatopathy, urop-

athy & renalpathy, gastric protective effects and therapeutic potential in surgery **(Bo et al., 2008, Cumashi et al., 2007; Mourão 2004 and Oliver and Barbra, 2003)**.

Levamisole is a synthetic imidazothiazole derivative which is a highly acceptable antinematodal drug because of its broad range of activity in a large number of hosts **(Nicholas and Lealie, 2005)**. The drug appears to restore depressed immune function rather than to stimulate response to above normal levels. Levamisole stimulate formation of antibodies to various antigens, by stimulating T-cell activation and proliferation, potentiate monocyte and macrophage functions including phagocytosis and chemotaxis and increase neutrophil adherence. **(Louis, 1997, Robert & Robert., 2009 and Abbas et al., 2010)**. The drug is well absorbed and widely distributed and can be detected in all tissues and fluids, with the highest levels in liver and kidneys **(Robert and Robert., 2009)**. Our work was planned to study the effect of fucoidan and levamisole on some hematological and biochemical parameters in growing rabbits, in both normal and heat stress conditions.

MATERIALS AND METHODS

2.1. Experimental rabbits:

Eighty (80) unsexed one month old apparently healthy rabbits were obtained from a local commercial farm in Mansoura governorate. The rabbits were housed in batteries and fed commercial diet (table 1) and water which were supplied all the day along four weeks (the duration of experiment).

2.2. Treatment drugs

1- Fucoidan extracted from brown algae Laminaria species, (Leili Natural Products Co., Ltd, China).

2- Levamizole , (ADWIA Co., Egypt)

2.3. Experimental design:

Two experiments were conducted to investigate the effect of fucoidan and levamisole on rabbits. The first one was during winter (optimum temperature for raising rabbits) while the second was in summer where heat stress is prevalent.

2.3.a. First experiment:

The experiment was applied to determine the clinico-pathological changes in one month old rabbits after treatment with fucoidan and levamisole in winter (January) and extended for four weeks. Forty (40) rabbits were assigned randomly and divided into four groups, where a group was kept as negative control, non treated (Control), and another three groups treated orally with fucoidan (F 100), (F 200) and levamisole (Leva.) in a dose (100, 200 and 8) mg/kg body weight respectively .

2.3.b. Second experiment:

The experiment was performed to determine the clinico-pathological changes in one month old rabbits exposed to heat stress after treatment with fucoidan and levamisole in summer (July) and extended for four (4) weeks. Forty (40) rabbits were assigned randomly and divided into four groups, where a group was kept as positive control, non treated heat stressed (H stress), and another three groups treated orally with fucoidan (HS+F100), (HS+F200) and levamisole (HS+Leva.) in a dose (100, 200 and 8) mg/kg body weight respectively .

In both experiment light was supplied continuously and rabbits were fed commercial diet (table 1) and all rabbits have free access to feed and water, with regard that neither the diet nor the water contains any drug.

2.4. Blood Sampling:

At the end of the 2nd, 4th two separate blood samples were collected. One sample was taken in epindorf tubes at which mixed with EDTA (0.5mg/ml blood) as anticoagulant for hematological examination RBCs, Hb, PCV, MCV, MCH, MCHC, TLC and differential leucocytic count). The second sample was taken in test tubes without anticoagulant for clear serum seperation which is carefully collected and stored in epindorf tubes at - 20°C until estimation of serum chemistry including ALT, AST, glucose, creatinine, total protein, albumin, globulin, A/G ratio, urea which estimated spectrophotometer by commercial kits (spine react Co. Spenish).

2.5. Statistical Analysis

Hematological values and serum biochemical parameters were analyzed by one way analysis of variance followed by Dunn's multi range test (ANOVA) using **(State View 1993)**.

RESULTS AND DISCUSSION

Optimal temperature for raising in rabbits is 15-18°C. Rabbits exposed to the ambient temperature of 25°C for 12h daily had lower weight gains than rabbits kept at 15°C. Environmental temperatures above 28°C cause heat-induced physiological stress **(Skřivanová et al., 1999)**.

Our erythrogram data for the rabbits treated with fucoidan (F100 and F200) showed insignificant change between all experiment groups. In the same aspect, erythrogram date revealed insignificant change for rabbits treated with levamisole in the 2nd week. However, in the 4th week RBCs count was increased significantly for rabbits treated with levamisole our results partially agreed with **Zia et al., (2003)** who observed an increase in RBC on day 7 of levamisole administration with an increasing trend in RBCs value throughout the experimental period.

In this work erythrogram results revealed insignificant change between heat stress group and control group in the 2nd week while RBCs count in the 4th week was increased in heat stress group, this may be attributed to role of glucocorticoids and ACTH in stimulation of erythropoiesis in animals, where cortisol has a stimulatory effect on erythropoietin Glucocorticoid may stimulate the proliferation of hemopoietic precursors, change the hemopoietic microenvironment **(Rania et al., 2008 and David et al., 1976).** Cortisone stimulates erythropoiesis possibly by increasing the oxygen consumption of tissues and thereby promoting tissue hypoxia which in turn stimulate erythropoietin **(Bijlani 2004)**. From erythrogram results in our work, it was obvious that both (HS+F100) and (HS+F2 00) groups were insignificantly changed from (H stress) group or control group along the whole experiment and the same did (HS+Leva.) group.

Our leukogram data for the rabbits treated with fucoidan (F100 and F200) showed insignifieant change from the control along the whole experiment except for the lymphocytosis in (F200) which may be due to the immu-

nostimulant effect of fucoidan. Fucoidan of L. japonica can restore the immune functions of immunosuppressed mice, and it was an immunomodulator acting directly on macrophage and T lymphocyte. **(Bo et al., 2008).** This result is in conformity with **El-Bouahy and El-Ashram., (2007)** who recorded significant increase in lymphocytes fucoidan treated groups after 21 days compared with cadmium immunosuppressed group in catfish Clarias garieflmus. In the same line fueoidan increased the number of circulating mature white blood cells and enhanced phagocytosis in monkey and mouse **(Sweeney et al., 2002)**. Our results agreed with **Gregory (2005)** who reported that sheep feed on ANOD (an extract from brown seaweeds Ascophyllum nodosum) tended to have higher lymphocyte counts than the control sheep.

From leukogram results in this work, leukocytosis and heterophilia were prevailed in heat stress group along the whole experiment in addition to lymphopenia in the 4th week. This is attributed to the effect of stress induced by exposure of animals to heat (stress leukogram) in addition to the role of increased corticosterioides associated with heat stress. Our results agreed with **Tara et al., (2005)** who reported that summer stress significantly raised the heterophil: lymphocyte (H:L) ratio in rabbits in the period from March to July. In the same line **Özge et al., (2000)** who reported an increase in heterophil and basophil rattos and H/L ratio and decreased monocyte and lymphocyte proportions after the exposure of broilers to acute heat stress. A corrective effect for the stress leukogram was obvious along the whole experiment in fucoidan treated groups which may be due to the antioxidant and immunomodulating effect of fucoidan on decreasing corisole level. Our results partly agreed with **Gregory (2005)** who reported that the control sheep had significantly higher cortisol concentrations than the sheep fed ANOD (an extract from brown seaweeds Ascophyllum nodosum) during the hottest part of transport. In this work leukogram showed leukocytosis in the 2nd week and lymphocytosis along the whole experiment in levamisole (Leva.) treated groups. Also a corrective effect of levamisole was observed in the 2nd week in (HS+Leva.) group, while in the 4rth week there were insignificant change in TLC but with lymphocytosis and decrease in heterophils which may be due to the immunomodulatory activity of levamisole. Our results are in accordance with **Zia et al., (2003)** who recorded that lymphocyte percentage and neutrophils decreased monocyte count increased on days 7 and 14 after levamisole (single dose) administration while. Also, we agreed with **Khanna et al., (1993)** who recorded absolute lymphocyte count (ALC) was significantly increased in vesicular mole after levamisole (LVM) treatment and marked improvement of T cell rosette count. In the same line **Alvarez-Pellitero et al., (2006)** reported the leucocytes/thrombocytes ratio was significantly higher in juvenile turbot fish treated with 500 mg/kg dry food levamisole at 14 days p.t.

Our results revealed that ALT and AST serum levels were significantly elevated in the Heat stress (H stress) groups along the whole expertment indicating heart and or liver damage this is may be due to the damaging effect of oxidative stress caused by heat stress. In addition to other stressful stimuli, can induce

the metabolic changes that are involved in the induction of oxidative stress **(Saeed et al., 2009)**. Heat stress increases ROS generation and radical-mediated tissue injury **(Hannah et al., 2003)**. Oxidative stress may exacerbate psychological and physiological demands brought about by stressful conditions. It has been proposed to play a role in the pathogenesis of several infectious diseases of domestic animals. It is extremely dangerous because it does not exhibit any symptoms and is recognizable with great difficulty by means of common methods of analysis. Oxidative stress promotes the insurgence of serious pathologies as a result of the degenerative damage of cellular structures **(Saeed et al., 2009)**. Lipid peroxidation with significantly higher levels present in the livers. The peroxidation of polyunsaturated fatty acids ean lead to ehanges in cellular membrane permeability and even membrane leakagc in assoeiation with the increased steady-state levels of ROS and oxidative damage. Liver had extensive injury after heat stress. Besides direct damage to membranes, lipid peroxidation products such as 4-HNE have been implieated in the activation of stress-response signal transduetion pathways. For instanee, the activation of these signaling pathways is critical in liver fibrosis and proinflammatory responses **(Hannah et al., 2003)**. Our result is approved histopathologically by hemorrhage, edema and local neerotie area.among the cardiac muscle fibers as well as dilation and congestion of eentral vein besides, hydropic degeneration and focal hepatic necrosis of the hepatic parenchyma in the second week and fibrosis and degenerative changes and necrosis of the periportal hepatocytes in the fourth week. Similar result was reported by many authors as **Nazifi et al., (1999), Sevi et al., (2001), Nazifi et al., (2003) and Chin et al., (2007).**

Crude commercial fucoidan was more active than the purified fucoidan at inhibiting the proliferation of vascular smooth muscle cells, and then they speculated that a specific structure in the crude fucoidan may mediate its biological activities. Indeed, the content of the sulfated groups in fucoidan determines its anti-proliferative and anti-coagulant activities in fibroblasts. Identification of the structures of fucoidan that proteet hepatoeytes from hepatotoxins and that inhibit hepatic stellate cell growth is needed for the development of fucoidan as an anti-fibrotic agent **(Shinji et al., 2008)**. In this work, fucoidan treatment significantly reduced ALT and AST serum levels in heat stressed rabbits. This is may be due to the hepatoprotective effect of fucoidan and its antioxidative effect. This results are approved histopathologically by apparently normal hepatic architecture exeept few degenerative. Our result agreed with **Ako et al., (2006)** who reported that fucoidan administration dose-dependently prevented the elevation of plasma ALT induced by concanavalin A (Con A) injection in mice. In the same aspeet **Kawano et al., (2007)a and Kawano et al., (2007)b** reeorded repressive effects against D-GalN-hepatopathy which determined by the serum transaminase activities (ALT and AST) and lactate dehydrogenase (LDH) due to the protective effect of the three kinds of brown seaweeds Laminaria sp., Sargassum fulvellum and Eisenia bicyclis against D-GalN-hepatopathy. In the same line **Kum et al., (2008)** reported that fucoidan extracted from Undaria pinnatipida sporophylls and Laminaria japonica and each were injected intra-

peritoneally at dose of (100 mg/kg) caused significant decrease in serum ALT and AST levels in rats exposed to CCl4-induced oxidative stress due to role of fucoidan as a potential scavenger of free radicals generated by lipid peroxidation of the liver cells of CCl4-treated rats. In the same aspect, **Shinji et al., (2008)** noticed significant decrease in levels of ALT and AST in fucoidan (crude) treated mice against CCl4-induced acute (IV injection of fucoidan 25 and 50 mg/kg body weight) and chronic (IV injection of fucoidan 50 mg/kg body weight twice a week for 8 weeks). The anti-fibrogenic activity of fucoidan is due, at least in part, to attenuation of hepatic stellate cell activation by inhibition of transforming growth factor-β and/or by scavenging of reactive oxygen species, which can suppress the cascade of events that leads to hepatic stellate cell activation. This besides that there is no significant toxicological changes when fucoidan was administered to rats at dose of 300 mg/kg body weight per day **(Ning et al., 2005)**.

Levamisole treatment signifieantly reduced ALT and AST serum levels this is may be due to the hepatoprotective effect of levamisole and its antioxidant effect of levamisole where **guifeng et al., (2006)** recorded significant increase in SOD and lysozyme activities but decrease MAD aetivity.

Our result revealed hyperglycemia in heat stress group in the 2nd and 4th week. This may be due to the Inereased level of glucoeorticoids associated with heat stress. Our results are in accordance with **Soleimani and Zulkifli., (2010)** who recorded elevation in blood glucose level may be attributed to increase in glucocorticoids secretion which plays a major role in glucose metabolis. In the same line, **Helal et al., (2010)** reportcd that the increase in plasma glucose during hot conditions may be due to the decrease in glucose utilization, depression of both catabolic and metabolic enzymes secretion and subsequent reduction of metabolic rate. Our results showed significant decrease in serum glucose level in heat stress fucoidan treated groups (HS+F100) and (HS+F200) along the whole experiment. This may be due to anti-hyperglycemic effect of fucoidan. We agreed with **Gregory (2005)** who reported control sheep also had significantly higher cortisol concentrations than the sheep fed ANOD (an extract from brown seaweeds Ascophyllum nodosum) during the hottest part of transport. In the same line, **Apostolidis and Lee., (2010)** reported that Ascophyllum nodosumis a brown seaweed nutraceutical potential of A.nodosumbased on phytochemical antioxidant and antihyperglycemia activities.

Levamisole treatment significantly reduced ALT and AST serum levels this is may be due to the antioxidant effect of levamisole **guifeng et al., (2006)** which make the treated group less stressed.

The major site of plasma protein synthesis is the liver and the second major site is the immune system consisting of lymphoid and plasma eells. **(Kaneko et al., 1997)**. Our results showed significant decrease in serum total protein level in heat stress group along the whole experiment which associated with decrease in both albumin and globulin in the 4th week only. This may be associated with decreased feed intake associated with high

environmental temperature and also, may be due to liver damage which eonfirmed histopathologically by hyperplasia of the epithelial lining of the bile duct , degenerative changes and necrosis of the periportal hepatocytes. Our results showed significant increase in globulin (HS+F100) (HS+F200) in the 2nd week and in (F100), (F200), (HS+F100) and (HS+F200) in the 4th . Fucoidan has both humoral and cell-mediated immune responses under in vitro and in vivo conditions. A higher population of large B cells in spleen could be observed after treatment with the fucoidan, in mice infected with herpes simplex virus type 1. These results imply that the fucoidan enhance B cell blastogenesis. Therefore, the fucoidan was expected to promote the maturation of B cells that might result in the stimulation of antibody secreting activity **(Kyoko et al., 2008).** In the same line **Hayashi et al., (2008)** reported that the production of neutralizing antibodies in the mice inoculated with HSV-1 was significantly promoted during the oral administration of the fucoidan for 3 weeks. Our finding revealed that levamisole treated groups showed significant increase in globulin level in (Leva.) and (HS+Leva.) along the study. Levamisole raised all the serum immunoglobulins in both vesicular mole and choriocarcinoma **(Khanna et al., 1993)**. Also, levamisole improved the humoral immune response where both IgM and IgG were elevated **(Pekmezci and Cakiroglu 2009)**.

Our results showed significant increase in serum urea and creatinine indicating renal damage in heat stress groups which is confirmed histopathologically by hyperplasia of the mesangial cells of the glomerular tufts with narrowing of the urinary space in addition to cloudy swelling and coagulative neerosis of the renal tubules. Our results agreed with **Helal et al., (2010), Nazifi et al., (1999), (2001) and Nazifi et al., (2003).** Fucoidan treatment groups showed significant decrease in serum urea and creatinine level (F200) in the 4th week, (HS+F100) and (HS+F200) along the whole experiment this may be attributed to the renoprotective effect of fucoidan which approved histopathologically by apparently normal renal architecture except for some degenerative changes. Our results agreed with **Zhang et al., (2003)**[a] who reported that fucoidan showed renoprotective effects. Also, we agreed with **Zhang et al., (2005)** who revealed that the elevated urinary protein excretion and plasma creatinine due to the induction of Heymann nephritis were significantly reduced by fucoidan at doses of 100 and 200 mg/kg. In addition, we agreed with **Coothan et al., (2006); Veena et al., (2007)**[a] **and Veena et al., (2007)**[b]. Our results showed significant decrease in serum urea and creatinine level in levamisole treated group (Leva) in the 4th week and (SH+Leva.) which may be due to the immunostimulant effect and the antioxidative effect of levamisole.

We concluded that fucoidan express good immunomodulating, hepatoprotective and renoprotective effect in growing rabbits against stress occur due to high temperature.

Table (1): Erythrogram Paramcters (Mean ± S.E.) in Rabbits Treated with Fucoidan and Levamisole in Optimum and Heat Stress Conditions.

Time / Week	Group	RBC $\times 10^6/\mu L$	Hb g/dl	PCV %	MCV fl	MCH Pg	MCHC %
2nd week	Control	4.791±0.31a	10.88±0.52 a	31.8±1.2 a	66.87±2.01a	22.84±0.64a	34.19±0.58 a
	F 100	5.131±0.18 a	10.75±0.18 a	31.4±0.51 a	61.42±1.71 a	21.06±0.86 a	34.25±0.54 a
	F 200	4.927±0.15 a	10.95±0.11 a	31.5±0.45 a	64.13±1.65 a	22.31±0.68 a	34.77±0.25 a
	Leva.	4.814±0.19a	10.71±0.26 a	30.9±0.95 a	64.73±1.44 a	21.97±052 a	33.974±0.89 a
	H stress	4.980±0.11 a	11.34±0.09 a	33.0±0.35 a	66.37±1.35 a	22.81±0.61a	34.36±0.27 a
	HS+F100	5.048±0.23 a	11.12±0.25 a	31.8±0.58 a	63.71±3.88 a	22.29±1.41a	34.96±0.17 a
	HS+F200	5.312±0.30 a	11.32±0.33 a	33.0±1.1 a	62.50±1.84 a	21.46±0.73 a	34.32±0.20 a
	HS+Leva.	5.12±0.15a	11.09±0.29 a	33.0±0.88 a	64.76±0.88 a	21.6±0.41a	33.58±0.01 a
4th week	Control	5.06±0.14 a	10.79±0.14 a	31.90±0.40 a	63.26±1.57 a	21.39±0.46 a	33.84±0.11 a
	F 100	5.27±0.15 ab	10.89±0.33 a	31.95±0.61 a	60.73±0.74 ab	20.67±0.20 ab	34.06±0.56 a
	F 200	5.29±0.13 ab	10.75±0.20 a	32.20±0.37 a	61.01±1.75 ab	20.33±0.41 ab	33.38±0.68 a
	Leva.	5.20±0.19 b	10.93±0.17 a	32.20±0.86 a	62.13±1.98 ab	21.13±0.85 ab	34.01±0.78 a
	H stress	5.56±0.11 b	11.10±0.20 a	32.60±0.51 a	58.67±.38 b	19.98±0.08 b	34.05±0.12 a
	HS+F100	5.34±0.19 ab	10.67±0.37 a	31.20±1.07 a	58.50±1.46 ab	19.99±0.41 ab	34.21±0.43 a
	HS+F200	5.49±0.14 ab	10.91±0.21 a	32.40±0.81 a	59.12±1.89 ab	19.92±0.64 b	33.70±0.51 a
	HS+Leva.	5.40±0.184ab	10.86±0.18 a	32.00±0.84 a	59.31±1.06 ab	20.16±0.46 ab	33.98±0.48 a

Means in the same column not followed by the same letter differ significantly ($P<0.05$) .

Table (2): Leukogram Picture (Mean ± S.E.) in Rabbits Treated with Fucoidan and Levamisole in Optimum and Heat Stress Conditions.

Time /W eek	Group	TLC $10^3/\mu L\times$	Lymphocytes $\times10^3/\mu L$	Heterophils $\times10^3/\mu L$	Eosinophils $\times10^3/\mu L$	Basophils $\times10^3/\mu L$	Monocytes $\times10^3/\mu L$
2nd week	Control	8.43±0.85 a	4.86±0.57 a	3.17±0.24a	0.03±0.02 a	0.06±0.04 a	0.31±0.03ac
	F 100	8.73±0.55 a	5.46±0.33 ab	2.81±0.16a	0.06±0.04 a	0.07±0.03 a	0.33±0.03ac
	F 200	9.40±0.09 ad	6.09±0.12 bc	2.84±0.09a	0.04±0.02 a	0.06±0.02 a	0.38±0.004a
	Leva.	10.62±0.67 bd	7.24±0.63 c	2.87±0.56a	0.04±0.02 a	0.06±0.03 a	0.42±0.03a
	H stress	19.65±0.53 c	5.86±0.26abd	13.71±0.38b	0.12±0.05 a	0.08±0.05 a	0.12±0.08b
	HS+F100	11.50±0.77 b	5.82±0.42ab	5.24±0.45c	0.06±0.03 a	0.11±0.03 a	0.18±0.05b
	HS+F200	11.83±0.68 b	5.89±0.31ab	5.64±0.37c	0.09±0.04 a	0.05±0.03 a	0.22±0.05bc
	HS+Leva.	12.08±0.71 b	6.89±0.31cd	4.84±0.33c	0.05±0.03 a	0.13±0.09 a	0.36±0.02a
4th week	Control	10.19±0.29 a	6.05±0.19 a	3.83±0.12 a c	0.040±0.02 a	0.041±0.025 a	0.224±0.059 ad
	F 100	10.54±0.44 a	7.08±0.86 a b	3.07±0.78 a c	0.046±0.03 a	0.046±0.028 a	0.299±0.050 ab
	F 200	11.53±0.65 a b	8.48±0.71 bd	2.59±0.43 a	0.048±0.03 a	0.066±0.027 a	0.346±0.019 bc
	Leva.	11.64±0.78 a b	7.79±0.43 b	3.21±0.44 a c	0.062±0.04 a	0.041±0.025 a	0.453±0.038 c
	H stress	13.42±0.91 b	4.25±0.36 c	8.89±0.86 b	0.088±0.04 a	0.122±0.055 a	0.115±0.054 a
	HS+F100	10.721±1.33 a	6.32±0.71 ad	4.17±0.79 a c	0.043±0.03 a	0.035±0.023 a	0.160±0.016ae
	HS+F200	10.821±1.01 a	6.67±0.53 ad	3.86±0.52 a c	0.058±0.02 a	0.039±0.024 a	0.187±0.014 ad
	HS+Leva.	12.461±0.701a h	7.53±0.60 a b	4.56±0.29 c	0.044±0.03 a	0.053±0.033 a	0.268±0.042 ae

Means in the same column not followed by the same letter differ significantly ($P<0.05$) .

Table (3): Some Biochemical Parameters Mean (±S.E.) in Rabbits Treated with Fucoidan and Levamisole in Optimum and Heat stress Conditions.

Time / W eek	Group	A LT U/L	AST U/L	Glucose mg/dl	T.Protein g/dl	Albumin g/dl	Globulin g/dl	A/G Ratio	Urea mg/dl	creatinine mg/dl
2nd week	Control	26.0±0.71 a	20.25±0.71ac	101.9±2.87 a	6.897±0.19ab	3.48±.07 a	3.42±.13 a	1.02±.02 abc	23.6±1.3 a	0.63±.02 a
	F 100	26.2±1.43 a	19.60± 0.93ac	104.4±2.71 a	6.764±0.04ab	3.49±.03 a	3.27±.03 a	1.07±.01 ae	24.8±1.4 a	0.66±.01 a
	F 200	24.8±1.35 a	18.80±1.49 a	105.4±1.86 a	6.816±.12 ab	3.46±.05 a	3.35±.12 ac	1.04±.05 ab	23.2±1.1 a	0.61±.02 a
	Leva.	26.4±2.06 a	19.40±1.08 ac	100.4±1.44 a	7.165±.17 a	3.49±.11 a	3.67±.08 b	0.95±.02 bcd	22.0±.71 a	0.66±.02 a
	H stress	30.2±0.78 b	25.40±0.93 b	145.4±2.93 b	6.529±.17 b	3.43±.14 a	3.10±.04 a	1.11±.04a	36.4±1.01b	0.86±.03b
	HS+F100	20.2±0.80 c	22.00± 0.76c	134.4±1.72cd	7.065±.19 a	3.37±.05 a	3.69±.19 b	0.92±.05 cd	30.6±.92c	0.76±.03c
	HS+F200	18.4±0.68 c	15.50±0.85d	131.6±1.21 c	6.891±.083ab	3.26±.13 a	3.63±.14 bc	0.90±.07d	28.2±1.01c	0.76±.01c
	HS+Leva.	20.0±1.0 c	21.00± 0.89ac	138.0±1.41d	6.819±.078ab	3.36±.02 a	3.44±.06 b	0.98±.01de	28.5±1.1c	0.79±.02c
4th week	Control	24.6±1.21 a	23.60±1.03 ad	103.6±3.19 a	7.094±.12 a	3.74±.10 ab	3.350±.07 a	1.12±.04a	36.20±1.15 a	0.75±.01 a
	F 100	25.2±1.53 a	20.8±1.16ac	106.0±3.98ad	7.798±.08b	3.99±.09 a	3.810±.08b	1.05±.04 ab	34.17±.5 ad	0.73±.01 a
	F 200	26.0±0.71 a	24.40±2.5 ad	103.0±3.63 a	7.490±.05bd	3.81±.04 a	3.678±.04b c	1.04±.16 ab	31.08±.8 b	0.71±.02 a
	Leva.	24.1±0.95 a	26.20±1.42bd	102.4±2.21 a	6.951±.10 a	3.53±.06b c	3.423±.08 a c	1.03±.32 ab	33.42±1.05bd	0.74±.004 a
	H stress	39.4±1.1 e	28.80±0.86b	127.8±2.35 b	6.450±.26 e	3.37±.18 e	2.992±.14d	1.14±.09 a	39.96±.71 e	0.92±.02 b
	HS+F100	23.4±0.93 a	25.6±1.08bdf	119.0±1.70 e	6.996±.09 a	3.44±.06 e	3.552±.03 ab	.969±.11 b	32.20±1.02bd	0.80±.008 e
	HS+F200	18.0±0.89 b	22.2±1.16acf	113.6±1.33cd	7.124±.15 ad	3.38±.07 e	3.744±.11 b	.905±.03 c	25.80±.8e	0.75±.18 a
	HS+Leva.	25.6±0.51 a	18.60±0.51c	121.4±1.60 b	7.086±.12 a	3.45±.03 e	3.632±.13 b c	.956±.04 b	31.00±1.0 bd	0.80±.006 e

Means in the same column not followed by the same letter differ significantly (P<0.05) .

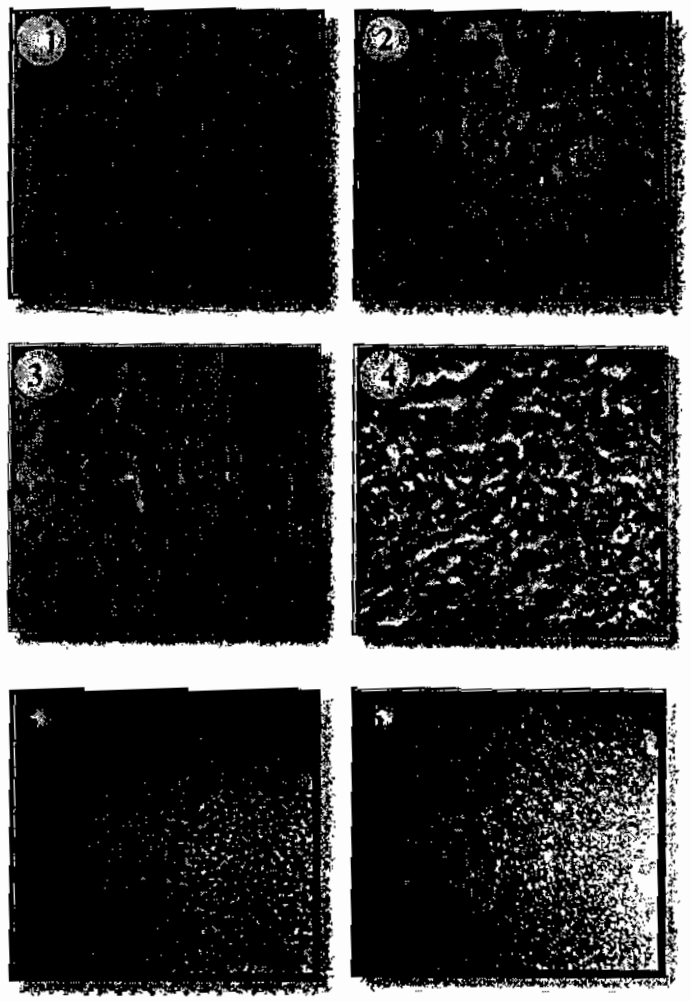

PLATE (1)

Fig. (1) : Liver of heat stress at 4th weeks, showing hyperplasia of the epithelial lining of the bile duct, newly formed bile ductules, fibrosis and degenerative changes and necrosis of the periportal hepatocytes H&E., X520.

Fig. (2) : Kidney of heat stress at 4th weeks, showing focal replacement of the necrotic renal tubules with leukocytes mainly lymphocytes and maerophages H&E., X520.

Fig. (3) : Heart of heat stress at 4th weeks, showing coagulative necrosis of the myocardial fibers with hemorrhage replaced the necrotic fibers H&E., X520.

Fig. (4) : Spleen of heat stress at 4th weeks, showing sever lymphoid depletion of the white pulp besides sever congestion and golden brown pigment (seems to be hemosidern) were seen in the red pulp H&E., X520 .

Fig. (5) : Liver of (HS+F100) group at 4th week, showing apparently normal hepatic parenchyma except for dilatation of the central veins and hepatic siusoides H&E., X52.

Fig. (6) : Kindney of (HS+F100) group at 4th week, showing apparently normal renal architecture except for except for some degenerative changes H&E., X52.

Plate 2

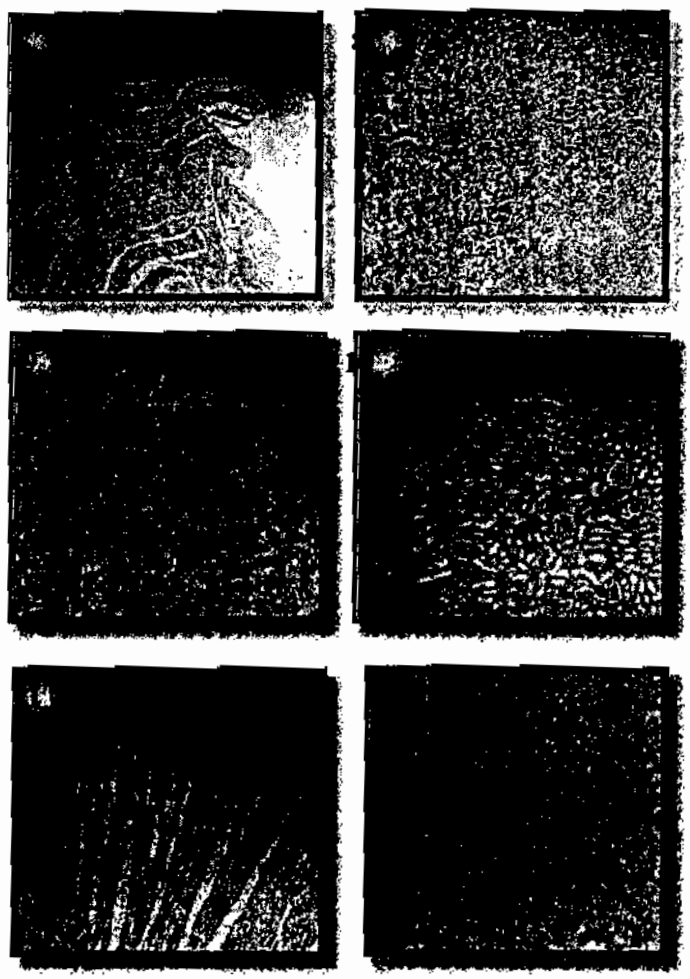

PLATE (2)

Fig (7) : Heart of (HS+F100) group at 4th week, showing apparently normal myocardial fibers H&E., X130.

Fig (8) : Spleen of (HS+F100) group at 4th week, showing congestion red pulp with mild lymphoid depletion of the white pulp H&E., X130.

Fig (9) : Liver of (HS+F200) group at 4th week, showing apparently normal hepatic architecture except few degenerative changes H&E., X130.

Fig (10) : Kidney of (HS+F200) group at 4th week, showing apparently normal renal architecture except some nerotic changes of the epithelial lining of some renal tubules and dilatation of the other renal tubules H&E., X130.

Fig (11) : Heart of (HS+F200) group at 4th week, showing apparently normal cardiac muscle fibersH&E., X130.

Fig (12) : Liver of (HS+Leva) group at 4th week, showing apparently normal hepatic architecture except dilatation of central veins and sinusoids H&E., X52.

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الملخص العربى

دراسات باثولوچيا إكلينيكية مقارنة على تأثير الفيوكدان والليفاميزول فى الأرانب

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أجريت هذه الدراسة على عدد ٨ من الأرانب بهدف معرفة تأثير كل من الفيوكدان والليفاميزول للوقاية من الإجهاد الناجم عن تعرض الأرانب لدرجات الحرارة المرتفعة، وقد لوحظ من الدراسة دور كلاً من الفيوكدان والليفاميزول فى إستعادة خلايا الدم الحمراء والبيضاء إلى عددها الطبيعى وكذلك إنخفاض إنزيمات الكبد وانخفاض الكرياتينين واليوريا والسكر بعد الارتفاع الناشىء عن الإجهاد الحرارى، بينما ارتفع مستوى البروتين والجلوبيولين، ومما سبق نستنتج أن الفيوكدان له تأثير منشط للجهاز المناعى ووقائى للتغيرات المرضية الناتجة عن الإجهاد الحرارى فى الأرانب.