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Effect of Abamectin on Biochemical, Immunological and Histological Parameters of Hamster Infected with *Schistosoma mansoni*

Amira I. El-Kabbany[1, *], Rania S. Hamza[2], Somaya M. Ismail[3, 4, *], Khaled I. Ghaled[5, 6]

[1]Department of Zoology, Faculty of Science, Zagazig University, Zagazig, Egypt

[2]Department of Medical Parasitology, Faculty of Medicine, Zagazig University, Zagazig, Egypt

[3]Zoology Department, Faculty of Science, Cairo University, Giza, Egypt

[4]Faculty of Science and Home Economics, Bisha University, Bisha, Saudi Arabia

[5]NCI, Cairo University, Giza, Egypt

[6]Faculty of Applied Science, Bisha University, Bisha, Saudi Arabia

Email address:

aza201477@gmail.com (A. I. El-Kabbany)

[*]Corresponding author

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Abstract: Abamectin (avermectin) is a natural fermentation product of *Streptomyces avermitilis* and is widely used as a pesticide. Recently, it has been used as an antiparasitic agent. This study aims at assessing the impact of abamectin on hamsters infected with *Schistosoma mansoni*. Parasitological, histopathological parameters, glycolytic enzymes, liver function enzymes and cytokines were assessed in an infected hamster model. The data indicated that a significant decrease in the number of worms in Abamectin treated group as well as in the number of mature and live ova in the treated group. Also, treatment of the infected hamster with Abamectin recorded no significant difference in all glycolytic enzymes (PK, GPI and HK). Furthermore, Abamectin recorded no significant difference in the level of LDH, AST and ALT (liver function enzymes) as compared to *S. mansoni* infected group. In addition, immunization caused a slight decline in granuloma diameter, an increase in the immunoglobulins and cytokines. Also, histopathological results showed that Abamectin caused multinucleated histolytic inflammatory giant cell with cytoplasmic engulfed foreign bilharzial pigment in the liver tissue without viable bilharzial egg. In conclusion, the present data indicated that significant decline of parasitological parameters and no side effects of most parameters compared to the normal healthy control group.

Keywords: Abamectin, *Schistosoma mansoni*, Product of *Streptomyces avermitilis*, Liver Function Enzymes, Glycolytic Enzymes

1. Introduction

Schistosomiasis is one of the tropical diseases most widely, which is focused mainly in sub-Saharan Africa's burden and impact of approximately 207 million people [1-4]. The main treatment of schistosomiasis is the drug, praziquantel (PZQ, which affects the membrane permeability of the parasite cells to calcium ions [5], which makes treatment with praziquante) key component of schistosomiasis control programs [6-8]. However, while PZQ effectively kills adult schistosomes and the very young stages shortly after skin penetration, its efficacy against schistosomula is minimal with only a 25-30% reduction in worm burdens [9, 10]. Nassauw et al. [11] assessed the therapeutic effects of racemic mefloquine in *Schistosoma mansoni*-infected mice and stated that a dose of 150 mg / kg of body weight gave a significant reduction of burden of eggs in the *Schistosoma mansoni* - infected mice. The investigation also disclosed that the mefloquine has good *in vivo* effectiveness, with a single oral dose of 200 mg / kg, which

resulted in a reduced high burden of worms from 72.3% in *S. mansoni* infected intestinal mice. An interesting aspect of mefloquine is its effectiveness against the juvenile, immature stage [12]. However, the efficacy of mefloquine against adult worms was not satisfactory (42-68%) when used in its reduced and higher dose respectively. A combination of Artemether and PZQ in humans and animals showed that combination therapy resulted in a significantly higher reduction in worm burden than administration of either drug alone [10]. Acute bilharzias have a major impact on the functions of the liver and specific alterations in defining protein isoforms and upregulation of the unique proteins that may be of value as markers of a new disease [13]. It may of value as new signs of disease [13]. Bilharzias disease is a direct result of the immune response to lay eggs in the host tissues, especially the liver. The associated liver injury usually with the infiltration of inflammatory cells, lead to cirrhosis [14].

Investigators have concentrated on various preventive method against schistosomiasis using several fractures soluble egg antigen (CEA) which have been identified and tested in the experimental models with induces at various levels of protection against infection [15]. Immunisation of mice stimulates specific immunity which causes reduction in worm burden, intestinal egg load and liver pathology [16]. Until recently, none of immunization fractions were able to induce more than 67% protection, partially protective immunity would make a logical complement to drug therapy [17].

Abamectin (avermectins) is insecticidal and antihelmintic compounds derived from various laboratory broths, fermented by the soil bacterium *Streptomyces avermitilis* and used as a pesticide. It has many different agricultural uses [18]. It has been tested in acute and subacute toxicity and genotoxicity in different vertebrate and invertebrate animals [18, 19]. In a recent study, Mohamed et al. [20] found that Abamectin has a high molluscicidal activity against the intermediate host for *Schistosoma*.

This work aims to assess the impact Abamectin on infection of hamsters with *S. mansoni* cercariae intestinal and liver enzymes in some *S. mansoni* infected hamsters representing glycolytic enzymes and liver function path. Moreover, parasitological, histopathological parameters and the dynamics of serum-specific immnoglobulins and splenic cytokines associated with changes in hepatic pathogenesis and granuloma diameter were assessed in an attempt to study the effect of treatment with Abamectin on infected hamster model.

2. Material and Method

2.1. Abamectin

Abamectin was obtained from Merck and Co.. (USA). A stock solution of 18 ppm based on the active ingredient of avermectin was freshly prepared on the basis of the weight / size by using dechlorinated water (pH 7.5-7.7). It has been preparing a series of concentrations that would allow calculation LC_{50} and LC_{90} values accordance with the World Health Organization [21]. Sublethal concentrations were calculated from the lethal-dose probability lines designed according to the procedure of Litchfield and Wilcoxon [22].

2.2. Parasites and Study Animals

Schistosoma mansoni cercariae was acquired from Schistosome Biological Supply Program (SBSP), Theodor Bilharz Research Institute (TBRI, Giza, Egypt). Male hamsters, *Mesocricetusauratus,* of the same age and weight (100-120 g) were selected for this study. They were obtained from the laboratory of animal house (TBRI). The animals have been retained in the animal room at controlled temperatures of 24°C± 2, whiles permitted free access to the diet and water throughout the study period.

2.3. Experimental Design

The animals were split into five groups of equal number (n=6), Those in the first group (control) were orally administered on a daily basis an equivalent amount of distilled water (50ml) for two weeks. Animals in the second group (control plus abamectin) were given distilled water with LC_{25} of Abamectin during two weeks of oral and daily administration. The third group was exposed to 120 *S. mansoni* cercariae/animal subcutaneously in abdominal skin, according to the method of Xue et al. [23]. The fourth group was exposed to 120 *S. mansoni* cercariae/animal and was given drinking water with LC_{25} of Abamectin during two weeks of oral and daily administration. The fifth group was immunized with soluble egg antigen (SEA) (10 µg) 6 weeks before infection and treated with Abamectin. Forty-five days after exposure to cercariae, 6 hamsters from each infected group of the experiments were sacrificed individually and dissected. The worm load in each hamster was carried out by perfusion according to the method of Kloetzel, [24]. The different developmental stages of *S. mansoni* ova (the oogram) have determined the following method described by Pellegrino et al. [25]. The ova count/g tissue (digestion of the liver) was calculated according to Cheever [26] and Kamel *et al*. [27]. Biochemical and histopathological studies were also done.

2.4. Biochemical Studies

The dissected livers were divided into sections of 0.25 g each, and wrapped in aluminum foil prior to storing at -20°C, even are used for smoothing and biochemical assays.

Enzymatic assays included Hexokinase (HK) assayed according to the method described by Uyeda and Raker, [28]. Pyruvatekinase (PK) [29], Lactate dehydrogenase (LDH) activity [30], Glucose phosphate isomerase (GPI) [31]. Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) activities [32] and the Acid phosphatase and alkaline phosphatase activities by Fishman and Ferner [33]. It determined spectrophotometrically using using reagent kits purchased from BioMerieux Company, France.

2.5. Immunological Study (45 Days Post Infection)

2.5.1. Serum-specific Immunoglobulin Isotypes

Serum-specific immunoglobulin isotypes has been measured anti-SEA immunoglobulin subclasses IgG1, IgG2 and IgG4 by using the indirect enzyme-linked immunosorbent assay (ELISA), based on the method described by Engvall and Perlman, [34]. ELISA microtiter plates were coated with 100 µL / beer 30 µg / ml of SEA. Sera were diluted (1:20) and subcategories of anti-mouse IgG (binding site, Birmingham, UK) and used in the dilution of 1: 500 measuring absorbance at 492 nm.

2.5.2. Cytokine Assay

Serum IFN-γ, IL-4 and IL-10 levels were measured by a sandwich ELISA technique. Plates were coated with capture antibodies and 100 µl of serum samples. Following the addition of the biotinylated detection antibody and streptavid in alkaline phosphatase conjugate, the reaction was developed with paranitrophenyl phosphate (Sigma) the absorbance was measured at 405 nm.

2.6. Histological Studies

Forty-five days after the exposure to cercariae and drinking water with LC_{25} Abamectin, hamsters in each group of the experiments were sacrificed individually and dissected. After sacrification of animals, part of the liver from each mouse was removed, constant in dissected liver samples from the study, hamsters were fixed in bruin's fixative for about five hours, then transferred to the 70% alcohol. The samples were dehydrated in a graded series of ethanol, cleared in xylol, then embedded in paraffin. Four sections (5 microns in thickness) were taken from each liver sample, each section being at a distance of at least 500 µm from the preceding one. Sections were stained with haematoxylin and eosin and were examined under polarized light microscope.

Granuloma measurement: The hepatic granuloma diameter has been measured according to the procedures described by Von Lichtenberg [35]. The percent reduction calculated in granuloma diameter relative to the infected control

2.7. Statistical Analysis

The student's t-test and the chi square test [36] have been used in the comparison between the experimental methods and rates of experimentation and the control group statistically

3. Results

3.1. Parasitological Studies

The effect of sublethal doses of abamectin (LC_{25}) on the number of *S. mansoni* worms in infected hamsters are shown in Tables 1 and 2. The results showed a 79.3% reduction in worm number and lower mean number of ova per female worm in treated animals compared to the control.

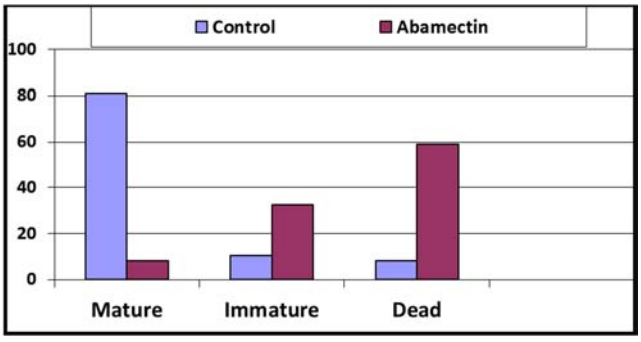

Figure 1. *Number of worms in hamster infected with Schistosoma mansoni cercariae and exposed to Abamectin.*

Table 1. *Number of worms in hamster infected with Schistosoma mansoni cercariae and exposed to Abamectin.*

	Mean number of worms/hamster±SD			Total mean number of worms /hamster ±SD	Percent worm of reduction %
	Male	Female	Pairs		
Control infected	10.4±0.33	4.8±0.25	2.5±0.66	(17.7)± 1.2	
Abamectin treated	1.2±0.21***	0.8±0.32***	0.8±.1.4***	(2.8)±1.4***	(79.3)

*P<0.05, **P< 0.01& ***P< 0.001

Table 2. *Development stages of ova (oogram) in the intestine of infected hamster with Schistosoma mansoni cercariae and exposed to Abamectin.*

	% of different developed stages of ova					
	mature	Percent	immature	Percent	Dead	Percent
Control infected	9453.2±144.23	81, 1	1233±152	10.6	966.8±43.2	8.3
Abamectin treated	966±43***	(8.6)	3377±43**	(30.1)	6885±82.1***	(61.3)

**P<0.01& ***P<0.001

3.2. Biochemical Studies

The data in the table 3 showed a significant induced in Lactate dehydrogenase (LDH) enzyme activity in *S. mansoni* infected group compared to the control, while a significant increase was observed in other glycolytic enzymes Hexokinase (HK), Pyruvatekinase (PK) and Glucose phosphate isomerase (GPI) as compared to the normal healthy control. Also, treatment of the uninfected hamster with Abamectin recorded no significant difference in all glycolytic enzymes (LDH, PK, GPI and HK) as compared to the normal healthy control. Treatment of the infected hamster with Abamectin recorded no significant difference in all glycolytic enzymes (LDH, PK, GPI and HK) as compared to the normal infected hamster. A noticeable remark on the impact Abamectin pointed out to that there is no side impact

on all glycolytic enzymes (LDH, HK, PK& GPI) as compared to the control group.

Abamectin recorded no significant difference in all glycolytic enzymes as compared to the normal control. A noticeable remark on the impact Abamectin pointed out to that there is no side impact on all glycolytic enzymes (LDH, HK, PK& GPI) as compared to the control group.

Table 4 indicated significantly reduced in Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) enzymes in infected group. While significant increase was observed in the acid phosphatase (ADP) and alkaline phosphatase (ALKP) level as compared to the control group. Furthermore, treatment of the uninfected hamster with Abamectin recorded no significant difference in the level of AST and ALT (liver function enzymes) as compared to the normal, healthy control. Treatment of the infected hamster with Abamectin recorded no significant difference in the level of AST, ALT, ADP and ALKP (liver function enzymes) as compared to the normal infected hamster. Although the serum biochemical parameters of infected mice treated with Abamectin were ameliorated in comparison with those of an infected untreated control group.

Table 3. *Effect of Abamectin on some glycolytic enzymes in hamster liver.*

Groups	Enzyme activity μmol/min/mg protein			
	LDH	HK	GPI	PK
Control	40.2± 1.6	0.020±0.14	80.4±1.2	6.4±1.65
Infected control	28.4 ± 2.6**	0.028± 0.4***	110.2±3.6**	10.26±1.8**
Abamectin+ non-infected	39.5 ± 1.2	0.019±0.32	81.4±1.4	7.9± 0.43
Infection+Abamectin	30.4 ± 1.6	0.030±0.4	109.1±1.8	10.8±1.2

**P< 0.01

Table 4. *Effect of Abamectin on liver function enzymes in hamster.*

Groups	Enzyme activity μmol/min/mg protein			
	Aspartate amino transferase (AST))	Alanine amino transferase (ALT)	Acid phosphatase (ADP)	Alkaline phosphatase (ALKP)
Normal control	34.5± 3.1	24.2± 2.26	7.2± 1.6	7.2± 0.34
Infected control	24.2±1.03***	15.4± 0.54***	10.5± 0.4***	9.2±0.23**
Abamectin+ non-infected	34.2± 0.04	25.1+0.27	8.5±0.32	7.2±0.26
Infection+Abamectin	23.3± 12	23.6..2± 1.8	11.6± 0.07	9.8± 0.80

***P< 0.001

3.3. Imnunological Parameters

3.3.1. Serum-specific Immunoglobulin Isotypes

There was no significant change in IgG isotypes in the infected control group when compared to normal control. Nevertheless, there is a significant increase in IgG isotypes in immunized infected control and Abamectin treated group when compared to normal control. Serum-specific immunoglobulin isotypes showed no significant change level of IgG isotypes in the treated groups as compared to immunized infected control. Contrarily, there was a highly significant increase in IgG2 level in Abamectin treated group (p<0.001) (Table 5).

Table 5. *Serum anti-SEA IgG subclasses levels in hamster immunized with SEA, 6 weeks before infection and treated with Abamectin.*

Animal Group	X` O. D ± SEM Ig G1	X` O. D ± SEM Ig G2	X` O. D ± SEM Ig G4
Normal control	0.28 ± 0.2	0.47 ± 0.3	0.32 ± 0.4
Infected control	0.33 ± 0.2	0.50± 0.2	0.38 ± 0.4
Immunized infected	0.77 ± 0.5**	0.61 ± 0.5**	.74 ± 0.3**
Abamectin treated	0.70 ± 0.2**	0.94± 0.3***	0.93 ± 0.5***

** P < 0.001, ** P < 0.01

3.3.2. Serum Cytokines Level

There is a significant increase in the profile of Th-1 related cytokine IFN-γ in the infected (p< 0.001) compared to the control. From another side, Cytokine IFN-γ showed a slight increase in the immunized infected control compared to infected control. Abamectin indicated a significant decrease in the treated group compared to the immunized infected control (p< 0.01).

There is a highly significant increase in the cytokines IL-4 in the infected control as compared to the control (p< 0.001). Serum cytokines level for cytokines IL-4 demonstrated a significant reduction in the immunized infected control and Abamectin treated group (p<0.01) as compared to infected control. The cytokine IL-10 level showed a slight increase in the infected control compared to the normal control and a highly significant increase in the immunized infected control and Abamectin treated group (p<0.001) compared to the infected control. It also showed that a slightly significant increase in the treated group compared to immunized infected control (Table 6).

Table 6. *Serum cytokine level in hamster immunized with SEA, 6 weeks before infection and treated with Abamectin.*

Animal Group	IFN – γ Pg/ml ± SEM	IL – 4 Pg/ml ± SEM	IL – 10 Pg/ml ± SEM
Normal control	214 ± 43.1	33± 0.24	88 ± 2.3
Infected control	611± 22***	82± 6***	366± 12.3**
Immunized infected	317± 12**	44 ± 2.3 **	622± 12.4***
Abamectin treated	177 ± 38**	48 ± 5.2**	6 88± 223***

*** P < 0.001, ** P < 0.01

3.4. Histological Studies

The present results showed that histological section of the liver of hamster `forms of homogeneous mass of parenchymal cells arranged in hepatic lobules, distinguished by their central vein and separated by a poorly developed interlobular spate. The hepatic lobules are composed of irregular branched and interconnected hepatic strands that anastomose to form a network enclosing a system of tortuous blood sinusoids. Liver of normal hamster. Figure 2 showed preserved normal hepatic lobule with the radial arrangement of hepatocytes around the central vein. No fibrosis, cirrhosis, dysplasia or neoplasia and or degeneration were recorded of hepatocytes. The data in Figure 3 present section in the liver of a hamster exposed to Abamectin. It shows diffuse, tri-zonal mixed both micro & macro-vesicular steatosis "fatty change", but no cirrhosis, dysplasia or neoplasia.

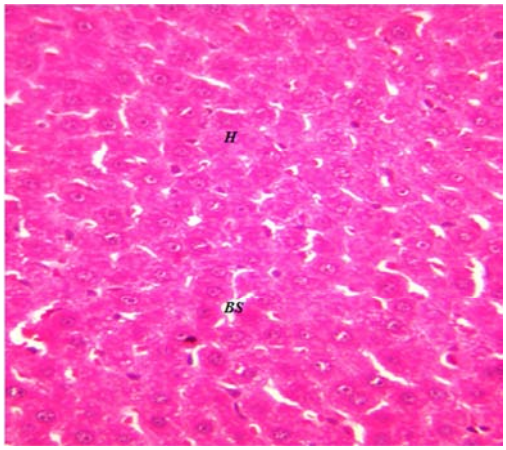

Figure 2. *Section of liver tissue from a healthy hamster (control) showing preserved normal hepatic structure with the radial arrangement of hepatocytes around the central vein and separated by blood sinusoids, H= hepatocytes, BS= blood (H&E x300).*

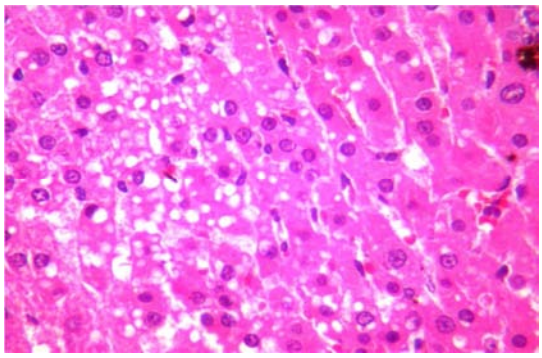

Figure 3. *Section of liver tissue from a hamster exposed to abamectin showing Diffuse, tri-zonal mixed both micro & macro-vesicular steatosis "fatty change", but no cirrhosis, dysplasia or neoplasia (H&E x 200).*

Figure 4 shows viable bilharzial egg deposition, with related granulomas of a chronic inflamatory cellular collection having a portal location in the liver of a hamster infected with *S. mansoni* cercariae, viable eggs appear oval in longitudinal section or round showing the miracidial content in cross-section.

Liver of hamster infected with *S. mansoni* cercariae and exposed to LC_{25} of Abamectin represent multinucleated histolytic inflammatory giant cells with cytoplasmic engulfed foreign bilharzial pigment, but they do not contain viable bilharzial egg, dilated vascular spaces (central vein) of portal circulation, but no cirrhosis, dysplasia or neoplasia is noticed (Figures 5 & 6).

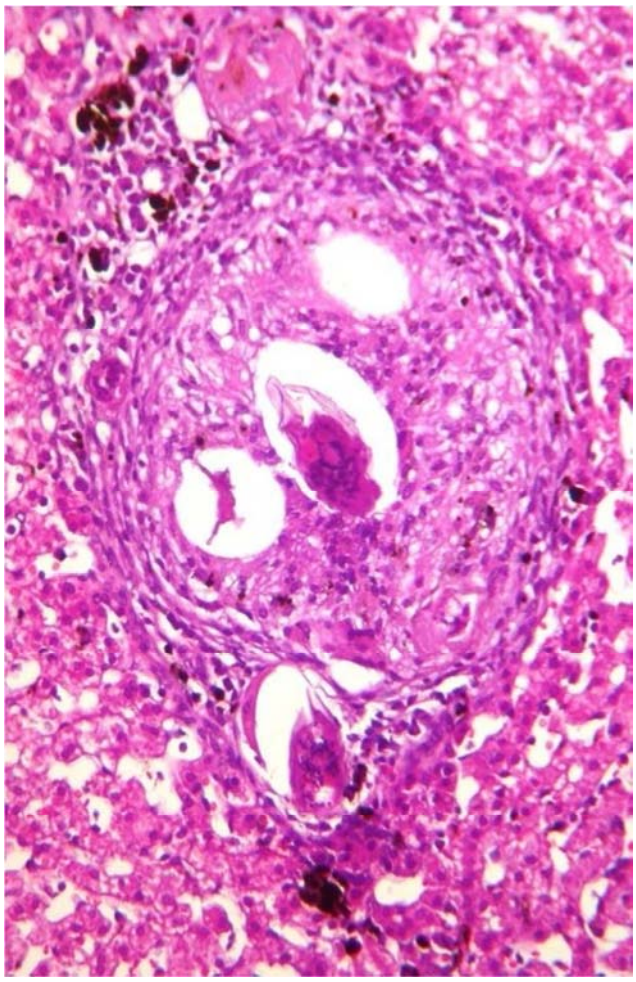

Figure 4. *Section of liver tissue from infected hamster with Schistosoma mansoni cercariae showing Viable Bilharzial egg deposition, with related granulomas of a chronic inflamatory cellular collection having a portal location, circum-oval bilharzial granuloma eggs appear oval in longitudinal section or rounded in shape on cross-section. Bilharzial dark brown to black pigment is also evident (H & E x 300).*

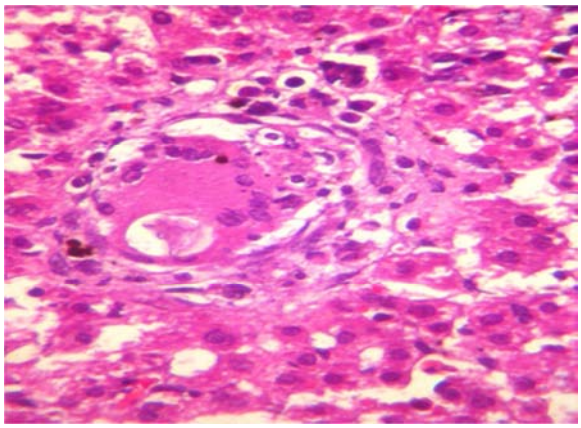

Figure 5. *Section of liver tissue from infected hamster with Schistosoma mansoni cercariae and exposed to abamectin showing showing A multinucleated histiocytic inflammatory giant cell with cytoplasmic engulfed foreign bilharzial pigment, (H & E x 400).*

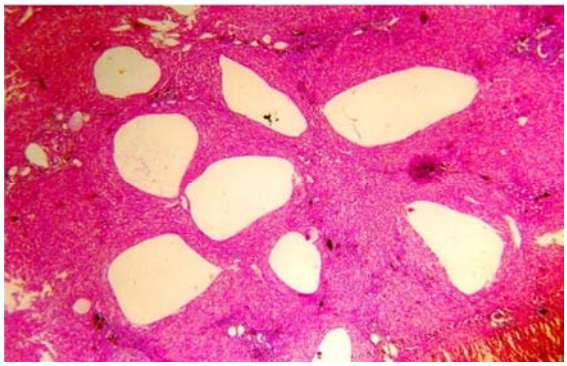

Figure 6. *Section of liver tissue of infected hamster with Schistosoma mansoni cercariae and exposed to Abamectin showing dilated vascular spaces (central vein) of portal circulation, no cirrhosis, dysplasia or neoplasia (H&E x200).*

Granuloma measurement: The present data in Table 7 showed that although all treated groups revealed significant diminution of granuloma diameter, at the same time, the groups treated with Abamectin revealed lower pattern than the other treated groups and this may be due to the effect of previous immunization of the infected animals before treatment.

Table 7. *Hepatic granuloma diameter and % reduction in hamster immunized with SEA (10 µg x3) 6 weeks before infection and treated with Abamectin.*

Animal Group	Hepatic granuloma diameter Mean µm± SEM	% Reduction
Infected control	266.2 ± 2.6	
Immunized infected	288 ± 3.2*	8.2%
Abamectin treated	122 ± 9.2***	54.2%

*** P <0.001, * P <0.05

4. Discussion

In this study, the experiments were carried out to test the infectivity of *S. mansoni* exposed to LC_{25} of Abamectin to hamster. The data indicated that, the mean number of worms per hamster in the Abamectin treated group (exposed to the dose level LC_{25}) was less than that of the non treated group with a reduction of 79.3%. Similar results obtained by Ritchie et al. [37], that showed infectivity of *S. mansoni* cercariae was inhibited after treatment with 100 ppm of bis tri-nbutyltin oxide for 5 min. The same finding was observed by Viyanant et al. [38] that used sublethal concentrations of copper sulphate and tributyltin fluoride and Gawish, [39]. Who used sublethal concentrations of Niclosamide.

In the present work, the total number of ova per gram tissue was decreased significantly in hamsters infected with the *Schistosome* cercariae and exposed to Abamectin. This is in agreement with the findings of Viyanant et al. [40] who observed a significant decrease in the number of recovered worms per infected mouse and number of ova in liver tissue after exposure of *S. mansoni* cercariae to 0.25 ppm of copper sulfate for 15-60 mintutes. The reduction in the number of ova explained by WHO, [30]. That, could infect the exposed mice and developed to adult worms that laid low numbers of ova. This may be due to disturbance in their physiological activities as Bayluscide affects the respiratory enzymes, which are essential factors in physiological processes of cercariae and adult worms. Eggs appeared oval in longitudinal section or rounded in shape in cross-section. This agrees with Rollino et al., [41] found that egg production of schistosome starts 4-6 weeks after infection and persist for the life of the worm. Eggs go through from the lumen of blood vessels into the nearby tissues. Spicher et al. [42] reported that the eggs of schistosome can either succeed in access to the lumen of the organ (intestine) and leave the body with urine or feces or remain trapped in the body tissues, where they die and to urge the granuloma formation or even be transported in the blood flow to warded the other organs (including peritoneum) where they determine granulomas.

In this study, a significant increase in the glycolytic enzymes PK, GPI and HK were noticed in both in infected and treated infected groups, while the activity of the enzyme LDH showed a significant decline. This can be attributed to the promotion of the activities of glycolytic enzymes in the infected hamster to increase metabolic tissues of infected liver activity to make up for the inhibition of host crep cycle resulting from parasitic infection [43].

The reduction in the activity of LDH enzyme as an important glycolytic enzyme may be attributed to the change that occurred in the permeability of the plasma membrane as a result of egg and worm toxins in necrotic which lead to changes in integrity of cell membranes and discharge of the enzyme [44].

LDH inhibition revealed the aerobic –anaerobic switch, resulting from the developing parasite [43]. Decreased activity in LDH in the direction of lactate oxidation can be easily connected to the impact of schistosomiasis [43]. Where the accumulation of lactate and consequential glycogen depleted confirms the inhibition of aerobic respiration and stimulate anaerobic glycolysis through hexokinase [45].

Concerning AST and ALT enzymes activities, a significant

decrease was observed in both infected hamster groups. The decrease noted in AST and ALT may be due to the hepatocellular damage resulting from egg deposition. The transaminases level showed an intimate relationship to cell necrosis and/or an increased in cell membrane permeability that may lead to the performance of the enzyme to the blood stream [46, 47]. The decrease in transaminases level may give additional side effect, as a result of the *S. mansoni* infection on the mitochondria of the hepatic cells as it is the supcellular localization of transaminases [48].

In this study, acid phosphatase and alkaline phosphatase (ALKP) show significantly increased in both in infected and in infected but treated hamster groups. Higher levels of acid phosphatase and alkaline phosphatase (ALKP) in tissue were observed by authors such as Abdel-Rahman et al. [49]. This elevated level may be attributed to the irritation of liver cells through toxins or metabolic products of growing schistosomoules of adult worms and eggs or because of It may also be the result of the increased loss of intracellular enzyme by diffusion through cell membranesthat seem to act as an incentive for the production of more enzyme.

This study disclosed that the immunization schedule being used has not caused any significant change in the worm, but a large decline in in the tissue egg load, generally agrees with findings of Botros et al. [50] Abamectin treatment in infected animals gave a similar high percentage of eradication of worms and tissue egg load as indicated by Suleiman et al. [51].

The percentage decrease in the number of eggs in both SEA infected and treated groups was found to be higher in the intestinal tissue than in hepatic tissue. This difference can be attributed to excretion of some ova from the intestine prior to digestion and to hepatic shift of worms after treatment [52]. In SEA experiment, treatment with Abamectin caused a drop in immature egg stages and the number of mature eggs with the large increase in the number of dead eggs compared to the findings of Botros et al. [50]. The parasitological improvement may be due to the effects of Abamectin that causes a direct or indirect toxic effect in combination with the effect of immunization of SEA that to reduction in tissue egg quantity. The combined effects may have attributed to the significant decrease in the number of worm fertility in the disability of the egg-laying process [53] According to Abath et al. [54] the manifestations of schistosomiasis are primarily due to granulomatous inflammation from the parasite eggs. It must be kept in mind that hepatic stellate cells (HSCs) include 10-15% of all liver cells and become activated upon hepatic injury Cassiman et al., [55]. They adopted a myofibroblast–like phenotype, secreting extracellular matrix components [56].

The increase in the production of an immune response an important role in improving liver pathology may play a role in the reduction of the number of *Schistosome* cercariae eggs found, but also in the worm burden [57-59].

In the present study, also indicated a significant diminution in granuloma diameter, with SEA immunization before infection and increased production of IgG1 and IgG4 levels. All the treated groups increased in IgG2 levels, This increase in the immune production of renders an important role in improving the pathology and at the same time, The at the same time, the reduction of the number of eggs and the worm burden [57-59]. Cytokines are of particular interest because of their role in the immune responses [60]. Cheever and Anderson [61] indicated cytokine responses, During schistosomal infection, both Th1 and Th2 respones interferon [IFN-γ] responses to soluble egg antigens and the IL-13, IL-10, and IL-5 response to adult worm antigen [61, 62]. In this study, it may be involved in the production of Th1-cytokine IFN-γ and Th2- cytokine IL-4 in the group immunized in the lower formation of granulomas in response to immunization.

Groups treated with Abamectin showed significant decrease in IFN- γ and IL-4. Recent studies indicate that Treg cells play a key in suppressing Th1 cell development as well as limiting the magnitude of Th2 response against egg antigens dependent upon IL-10 [61]. The increasing level of IL-10 is probably implicated in the down regulation of granuloma as it reduces the inflammatory response in the liver, and therefore an antifibrotic effect [63]. These results indicatedthe importance of the effect of Abamectin having a potent antifibrogenic role.

Hamsters infected with *S. mansoni* cercariae and exposed to LC_{25} Abamectin caused multinucleated histolytic inflammatory giant cells with cytoplasmic engulfed foreign bilharzial pigment. But a result also, shows an inflammatory giant cell, engulfing a recent viable bilharzial egg. These observations agree with that found by Rollino et al. [41]. Michael and Anthony, [64] mentioned that in a granulomatous reaction, the induction of eggs to fibrosis. This in turn may lead to portal hypertension or urinogenital dysfunction, depending on the parasite species. The disease symptoms are therefore attributable mainly toimmunopathology. No cirrhosis, dysplasia or neoplasia were observed in this study.

5. Conclusion

In conclusion, the number of *S. mansoni* worms as well as ova count showed a significant decrease in the infected hamsters treated with abamectin. Moreover, normal control hamster treated with Abamectin did not show any side effects, for most of the parameters, compared to the normal healthy control group. This may give additional support for the protective role of plant extract against schistosomiasis. Treatment with Abamectin in conjunction with immunization resulted in a significant decline in the parasitological parameters; and a rise of specific immunoglobulins. In addition, Abamectin has antifibrotic and antipathology effect, minimizing and ameliorated liver fibrosis by inhibiting the activation of HSC and the reduction of Treg cells effects. Albeit more research are required, Abamectin can possibly be applied, clinically, or in preventive therapy against schistosomiasis, enhanching the positive effects of praziquantel as anti-schistosomiasis drug.

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