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Effect Of Curcumin On Hematological , Biochemical And Antioxidants Parameters In Schistosoma Mansoni Infected Mice

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Abstract: The present study aims to investigate the effect of curcumin on treatment of *schistosoma mansoni* infected mice. Sixty mice were used in this experiment were divided equally into four groups ,the first kept as control, the second supplemented with curcumin , the third infected with *schistosoma mansoni* and the fourth infected and treated with curcumin. Our results emphasized on the presence of anemia, leucopenia , neutropenia and eosinophilia in infected groups either treated or non-treated with an improvement in the treated group. The biochemical parameters; ALT, AST, ALP, total protein, albumin, AFP, TNF- α and lipid profile (TC, TG, HDL-C &LDL-C) improved significantly in infected treated mice compared with infected one. By the same way, results showed an improvement of some anti-oxidant parameters (MAD, GSH, CAT and SOD) in *Schistosoma mansoni* infected treated mice.

Key words: *Schistosoma mansoni*, Curcumin, Erythrocyte, Lucocytes, Liver enzymes, Antioxidant enzymes, Lipid profile.

Introduction

There is no doubt that schistosomiasis is one of the major communicable diseases which affecting human and animals either domestic or wild, as it comes secondly to the malaria with socio-economic and health importance in the developing world (**Bergquist & Colley 1998**). Schistosomiasis is a chronic debilitating parasitic disease in tropical and subtropical countries caused by *Schistosoma* species (**Gryseels *et al.*, 2006**). It is affecting about 200 million people infected worldwide and almost 600 million at risk.

There are two types of schistosomiasis: urinary and intestinal schistosomiasis. Four major species are involved in the pathogenesis of Schistosomiasis, three of which, *S. japonicum, S. mansoni and S. interculatum*, cause intestinal schistosomiasis, while the fourth, *S.haematobium*, causes urinary Schistosomiasis (**Sekou *et al.*, 2006**).

Schistosoma is still one of the most prevalent epidemic disease in Egypt and in other developing countries in spite of many attempts to control this parasitic infection over many years (**El-Khoby *et al.*, 2000**). Schistosomiasis mostly affecting the liver and intestine causing granuloma formation, fibrosis and certain necrotic changes in the hepatic tissues (**Elbanhawey *et al.*, 2007**)

Current treatment relies on praziquantel (PZQ) (**Zhang & Coultas 2013**), The drugs of choice for treatment of schistosomiasis which was developed in the late 1970s (**Seubert *et al.*, 1977**). However, praziquantel does not treat early infection or prevent reinfection (**Magnussen, 2003**). In addition to, Numerous evidences indicates to increasing the emergence of strains of *Schistosoma mansoni* resistant to praziquantel (**Melman *et al.*, 2009**, **Van der Werf, 2003** and **Zhang & Coultas 2013).**

In the last few years, there is an obvious increase in searching for antiparasitic drugs from natural sources, especially from plants, which are the main source of biologically active compounds for the development of new treatments (**Magalhães *et al.*, 2009 and Silva *et al.*, 2009)**. One of these compounds is curcumin.

Curcumin is a yellow pigment from rhizomatous plant turmeric (*Curcuma longa*) widely cultivated in tropical and subtropical regions throughout the world, **(Cerny *et al.* 2011).** Curcumin is widely used as a spice and coloring agent in several foods such as curry, mustard and potato chips as well as cosmetics

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and drugs (**Okada *et al.*, 2001 and Joe *et al.*, 2004**). Extensive in vitro and in vivo studies have indicated that curcumin has a potent antitumor, anti-viral, anti-oxidant, and anti-inflammatory properties (**Aggarwal & Harikumar, 2009 and Tu *et al.*, 2011**). Moreover, several recent reports showed that curcumin exerts beneficial effects in animal models of liver toxicity, inflammation and cirrhosis (**Chen & Zheng, 2008 and Fu *et al.*, 2008**).

Several reports revealed that curcumin enhances the hepatic detoxification by acting as a free radical scavenger, increases the glutathione/glutathione disulfide ratio to reduce oxidative stress and inhibits the activation and nuclear translocation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) (**Leclercq *et al.*, 2004 and Reyes-Gordillo *et al.*, 2007**). Recent study postulated that curcumin protects against hepaic fibrosis by inactivating Hematopoietic stem cells (HSCs) through activation of peroxisome proliferator-activated receptor γ, which interrupts platelet-derived growth factor and epidermal growth factor signaling in activated HSCs, (**Lin & Chen ,2008).**

Moreover, the use of curcumin as parasiticidal agents has been extensively studied. It has an activity against *Leishmania* (**Koide *et al.*, 2002 and Das *et al.*, 2008),** *Giardia lambia* (**Perez-Arriaga *et al.*, 2006**) and *Trypanosoma* (**Nagajyothi *et al.*, 2012**). The first studies about the curcumin effects on *Schistosoma mansoni* showed the schistosomicidal effect of the oil extract of *C. longa* against *S.mansoni* infected mice (**El-Ansary *et al.*, 2007**). **Morias *et al.*, (2013)** and **Allam (2009)** described in vitro and in vivo Schistosomicidal activity of curcumin against *S. mansoni* adult worms. Recently, **El-Agamy *et al.*, (2011)** showed that curcumin has a potent anti-fibrotic activity in suppressing and reversing *S. mansoni*-induced liver fibrosis.

On the basis of anti-protozoal and anti-parasitic activity of medicinal plants and natural products, the aim of the present work was to evaluate the antishistosomal activity of curcumin against *Shistosoma mansoni.*

Materials and Methods

Chemicals

All common chemicals used were purchased from one of the following suppliers Sigma Co. (St. Loius, MO, USA). All other chemicals and reagents were of the highest purity commercially available and were purchased from the British Drug Houses (BHD), Poole Dorset, UK. The diagnostic kits are purchased from Human Company (Germany).

Experimental animals

Sixty male CD-1 Swiss albino mice (8-10 weeks of age) used throughout the present study. Thirty mice infected with eighty *Schistoma mansoni* cercariawere. The experimental animals were purchased from Theodore Bilharz Research Institute(TBRI, Imbaba, Giza, Egypt). All animals were maintained on standard commercial diet and water ad libitum.

Experimental design:

Animals were divided into four groups with 15 mice in each group, as the following:

Group I: healthy control group received normal diet (non-infected non-treated).

Group II: healthy received normal diet mixed with curcumin (600 mg/kg/diet) (non-infected treated) from the 15 th day after receiving the animals and continue for 6weeks.

Group III: infected and received normal diet (infected non-treated) .

Group IV: infected and received normal diet mixed with curcumin (600 mg/kg/diet) (infected treated) from the 15 th day after receiving the animals and continue for 6weeks.

Five animals from each group were sacrificed for sampling at the 2nd , 4th and 6th week post treatment.

Hematological examination:

Whole blood samples were collected from retro-orbital venous plexus of mice in EDTA tube for determination of erythrocytic count (RBCs), haemoglobin concentration (Hb), haematocrit value (PCV), mean cell volume (MCV), mean cell haemoglobin (MHC), mean cell hemoglobin concentration(MCHC), total (TLC) and differential leucocytic count according to **Feldman *et al.*, (2000).**

Biochemical Analysis

Serum and liver homogenate were taken for all measurements. Serum samples were collected and stored at -20^{o} C until used. The liver was dissected out, washed in ice-cold saline, blotted dry, and weighed. Then homogenate was prepared in phosphate buffer 0.1M, pH 7.4 and used for the biochemical analysis.

Serum hepatic enzymes

Activities of serum Aspartate transaminase (AST) and Alanine transaminase (ALT) were assessed according to **Reitmans & Frankel (1957).** alkaline

phosphatase (ALP) was assayed by the kinetic methods of human kits (Germany) according to **EDKC (1972)**. Activities expressed as IU/L. Total protein and albumin were measured according to **Doumas *et al.*, (1981).**Serum globulin was calculated by subtracting the obtained albumin value from the total protein as described by **Doumas & Biggs (1972).** Tumor necrosis factor-alfa (TNF- α) and Alfa- fetoprotein were assayed using a commercial ELISA kit.

Estimation of serum lipids

Total cholesterol (TC), Triglycerides (TG) and high density lipoprotein cholesterol (HDL-C) were measured according to **Richmond (1973**), **Wahlefeld & Bergmeyer(1974) , Warnik *et. al.*, (1983)** respectively by the human kits (Germany). Low density lipoprotein cholesterol (LDL- C) was estimated by the formula of **Friedewald *et al.*, (1972).**

LDL- C= (total cholesterol) − (HDL-C) − (triglycerides/5)

Estimation of lipid peroxidation

Quantitative estimation of lipid peroxidation was done by determining the concentration of thiobarbituric acid reactive substances (TBARS) in serum and liver tissue homogenates by the method of **Ohkawa et al., (1987).** The amount of malondialdehyde (MDA) formed was quantified by reaction with TBARS and used as an index of lipid peroxidation. The results were expressed as nmol of MDA/g of wet tissue using a molar extinction coefficient of the chromophore (1.56 x10 -5 /M/cm) and 1, 1, 3, 3-tetraethoxypropane as standard.

Determination of non-enzymatic antioxidants

Reduced GSH was determined according to the method of **Ellman (1959)** based on the formation of a yellow coloured complex with Ellman's reagent (0.0198% DTNB in 1% sodium citrate). The color developed was read at 412 nm.

Assay of antioxidants enzymes

Superoxide dismutase was assayed spectrophotometrically according to **Paoletti and Mocali (1990).** This method consists of purely chemical reaction sequence that generates superoxide from molecular oxygen in the presence of EDTA, manganese chloride and mercapto-ethanol. NAD(P)H oxidation is linked to the availability of superoxide anions in the medium. The decrease in absorbance was monitored at 340 nm, One unit of SOD activity is defined as the amount of enzyme required to inhibit the rate of NAD(P)H oxidation of the control by 50%. Catalase assay was carried out according to the method of **Aebi (1974).** One unit was defined as that amount of the enzyme which converts one mole substrate to product in one second.

Statistical analysis

Results were expressed as mean ±standard error (S.E.). One-way analysis of variance (ANOVA) test was first carried out to test for any differences between the mean values of all groups. If differences between groups were established, the values of the treated groups were compared with those of the control group by a multiple comparison t-test. A value of $p < 0.05$ was interpreted as statistically significant **(Tamhane & Dunlop (2000).**

Results and Discussion

The erythrogram ,in the present work, showed microcytic hypochromic anemia in infected non-treated and infected treated group all over the experimental periods (Table 1). This sign marked from a significant decrease in all of the erythrocytic parameters (the mean values of RBCs count, PCV, Hb concentration, MCV, MCH and MCHC) in infected non-treated mice and infected treated group all over the experiment as compared to control group, such decrease was more outstanding in infected non treated group (group III) than infected treated group (group IV). Our results are in agreement with that obtained by **Tjalling *et al.* (2006), Abd EL-Mottaleb *et a.l,* (2008) and Nahla *et al.*, (2008) ,** who recorded a significant decrease in the erthrocytic count and blood indices accompanied with schistosoma infection. On the contrary our results are disagree with that reported by **Bugarski *et al.*, (2006)** who mentioned insignificant changes in any of the erythrogram parameters. This may be attributed to difference in parasitis species and the dose of parasitic infestation.

Administration of curcumin, to non-infected animal group showed an insignificant change in RBC count as compared to control group. The infected mice treated with curcumin, showed an improvement in erythrogram values (PCV, MCV, MCH and MCHC) as compared to infected non-treated group .**Sharma *et al.*, (2011**) proved that curcumin administration to infected mice improved the erythrocytic count, Hb and blood indices.

Decrease in RBCS count may be returned to the reduction in erythropoiesis in bone marrow and faster rate of destruction of peripheral RBC in spleen ***(Coles 1986).*** Decrease in Hb can be related to reduction in

size of RBC, impaired biosynthesis of heam in bone marrow or due to reduction in the rate of formation of RBCS. **Sturrock *et al.*, 1996** attributed the presence of anemia to chronic blood loss that result from the bleeding induced by migration of worms through intestinal wall or due to blood consumption by adult schistosomes .

Table (2) illustrates total (TLC) and differential leukocyte count (Lymphocyte, Neutrophil, Esinophil and Monocytic count) in control and experimental groups of animals. Both of infected non-treated and infected treated groups showed leucopenia as compared to control group although supplimentation of curcumin to non-infected mice improved the WBCs count compared to control group. These results agree with **El-sheikha *et al.* (2008)** who recorded significant decrease in total leucocytic count in infected mice with Schistosomiasis. In contrast to this result, **Abd EL-Mottaleb *et al.*, (2008) and Willingham *et al.* (1998)** who noticed non-significant change in total leucocytic count in all experimental groups. **Allam 2009** demonstrated that infected treated mice showed insignificant alteration in total leukocytic count.

The difference may be due to difference of infestation dose and or experimental period. Supplementation of curcumin to non-infected mice showed insignificant increase in total leucocytes. These results agree with **Antony *et al*.1999** who proved that Curcuma longa extract administration increased the total WBC count in Balb/c mice due to its immune-stimulating activity of Curcumin.

On regarding the differential leucocyte count, our results revealed neutropenia, lymphopenia and eosinophilia in either infected non-treated or infected treated groups when compared with control group (Table 2). Similar results were obtained by **Bugarski *et al.*,(2006)** who reported a significant neutropenia and eosinophilia. Also these results agree with that obtained by **Abd EL-Mottaleb et a.l, (2008), Sharma *et al* 2011, Vercruysse *et al.*, (1988) and Nahla *et al.* (2008)** who found neutropenia, lymphopenia and eosinophilia accompanied parasitic infection**.** Simultaneously, a significant neutropenia and lymphopenia were observed, which could be ascribed to the recruitment of these cells to the site of the infection (**Bugarski *et al.*, 2006).** Otherwhile **Abd EL-Mottaleb *et a.l,* (2008)** mentioned that the eosinophilia may be due to the powerful defense reaction and allergic manifestation against *Schistosoma mansoni* and their eggs. From the same side, animals were primarily characterized by the appearance of eosinophilia, which was not unexpected since eosinophilia is the most frequent response to helminths **Klion & Nutman , (2004).**

Supplementation of curcumin to non-infected mice insignificantly increased neutrophil , eosinophil and lymphocytic count as compared to control group. The results showed insignificant changes of neutrophil, leucocyte and eosinophil in infected treated mice group when compared to infected non-treated group. **Sharma *et al,* 2011** recorded that curcumin may stabilize the cell membrane and restore various blood variables.

Hepatic damage can affect the metabolic processes in the body due to the role of liver in general metabolism. Enzymes are necessary for normal cellular metabolism including that of the liver **(Rajamanickam & Muthuswamy, 2008).** Hepatoprotective activity of curcumin was evaluated on *Schistosoma mansoni* infected mice by estimation of serum hepatic enzymes. Hepatic cells appear to participate in a variety of enzymatic metabolic activities. Infection of *Schistosoma mansoni* damages the hepatic cells leading to a significant increase in serum levels of AST, ALT ,and ALP respectively (Table 3). The significant ($p<0.05$) increase of serum AST, ALT, and ALP levels were observed in infected non-treated mice when compared with control group. On the other hand, the infected treated mice (group IV) showed reduction in the serum enzymes level as compared to infected non-treated mice (group III).

These results are in agreement with previously reported by **El-Gowhary *et a.l,* (1993). Allam (2009)** reported that, infected mice treated with curcumin restore the hepatic ALT and AST activities that were decreased by *S. mansoni* infection. This amelioration in the activities of liver enzymes could be attributed to the reduction in hepatic granuloma size and fibrosis as well as absence of necrotic hepatic tissue in infected treated mice **(Allam , 2009).** Apparently it appears that the membrane damage seems to be the prime culprit for the marked increase in the serum marker enzymes, AST, ALT, and ALP **(Naik et *al*., 2011).**

Serum levels of total protein, albumin and globulin were reduced significantly in infected non-treated (group III) as compared to control group (Table 3). However Supplementation of curcumin to infected mice (group IV) resulted in elevation of total protein, albumin and globulin levels compared with infected non treated mice. Similar observations were noticed

by **El-Ansary *et al.*, (2007)** and **El-Emam *et al.*, (2011)**. These results supported through the work of **El-Heig *et al.*, (1977)** who recorded a marked decrease of protein content in *S. mansoni* infected mice.

Alfa-fetoprotein (AFP) is a glycoprotein, of unknown function, normally produced during neonatal development by the liver and in small concentrations by the gastrointestinal tract **(Abelev *et al.*, 1963).** Abnormal serum level of AFP has been reported in patients with liver cirrhosis and hepatocellular carcinoma **(Gupta *et al.*, 2003)**. So our work was extended to observe the effect of both *Schistosoma* infection and administration of curcumin on serum alfa-fetoprotein (AFP) and, tumor necrosis factor-alfa (TNF- α) (Table 4). Infected non treated mice showed significant increases of AFP and TNF-a compared with control group. However supplementation of curcumin to infected mice improved the both AFP and TNF- α levels as compared to infected non-treated mice. These results agreed with that observed by **El-Rigal *et al*, (2011)** , Who recorded elevated level of AFP in sera of *S. mansoni* infected mice which may be considered as an index for liver fibrosis related to Schistosomiasis.

Tumor necrosis factor-alpha (TNF-α) is a cytokine involved in systemic inflammation and is a member of a group of cytokines that stimulate the acute phase reaction. **Torben & Hailu (2007)** stated that increased level of this inflammatory cytokine after egg excretion may be an indication of its effect in complications of Schistosomiasis, it is capable of inducing tissue injury and fibrosis. The results showed in table (4) indicated that, TNF-α is increased in serum of infected non treated mice compared to control group. The infected mice group treated with curcumin showed an improvement in serum TNF-α level compared with infected non treated mice. These results agree with that obtained by **El-Rigal *et al* 2011** and **Allam 2009** who observed that infected mice treated with curcumin revealed low serum level tumor necrosis factor alpha (TNF- α).

In order to investigate the hypolipidemic effects of curcumin on *S. mansoni* infected mice, quantitative assay of lipid profile was conducted by measuring the concentrations of serum TC & TG , HDL-C and LDL-C. The infected non treated mice showed increased levels of serum TC &TG and LDL-C as compared to control group (Table 5). There were insignificant differences in HDL-C among all groups.

On the other hand, curcumin supplementation to the infected mice lowered the serum TC &TG and LDL-C concentrations as compared to infected group. These results are in accordance with that obtained by **Arafa (2005)** while opposite to that reported by **Baum *et al.*, (2007)**. Similar observation were recorded by **Godkar *et al.*, (1996**) who investigated that supplementation of curcumin in diet of Swiss mice caused a marked decrease of serum TC &TG level. The mechanism by which curcumin decreased serum cholesterol in previous study is not known. One hypothesis is that curcumin prevents the increase in serum cholesterol in the animal studies by inhibiting dietary cholesterol absorption **(Arafa, 2005).** Curcumin was reported to cause a little increase of plasma HDL-C in rats **(Arafa , 2005).** Otherwise **Kang & Chen (2009)** provide a novel insights into the roles and mechanisms of curcumin in lowering the level of LDL-C that include curcumin suppressed LDL-R receptor gene expression in activated hepatic stellate cells.

The amount of malondialdehyde (MDA) formed was quantified by the reaction with TBARS and used as an index to lipid peroxidation. Results shown in (Table 6) indicated that MAD level was significantly ($P < 0.05$) increased in serum and liver tissue homogenate of infected non treated mice. However MAD level in serum and hepatic tissue homogenate in infected treated group significantly decreased as compared to that of infected non treated group. The decreased MDA formation in various target tissues following curcumin treatment confirms its anti-oxidant property (**El-Demerdash *et al.*, 2009)**. In such types of proliferative process, excessive formation of free radicals occurs, that triggers membrane damage and also augments activation of membrane bound enzymes **(Yadav *et al.*, 2005).** The study applied by **(Naik *et al.*, 2011)** showed that, curcumin treatment inhibited the lipid peroxidation process, which results in decreased MDA formation in edematous and granulomatous, liver, and cardiac tissue.

Reduced glutathion (GSH) are thought to play a vital role in protecting cells against reactive oxygen. During the metabolic action of GSH, its sulfhydryl group becomes oxidized resulting with the formation of corresponding disulfide compound, GSSG. Thus depletion of GSH content is associated with an increase in GSSG concentration resulting with the depletion in GSH/GSSG ratio. The content of reduced glutathione was significantly ($P < 0.05$) decreased in serum and hepatic tissue of infected non treated mice group compared to control group (Table 6). Supplementation of diet with curcumin (group II) caused a significant ($P < 0.05$) increase in the content of reduced glutathione compared with both of

control and infected non-treated groups (group I and group III). Infected mice supplemented with curcumin (group IV) partially restored the content of reduced glutathione to the normal values. Similar protective effect of curcumin pretreatment that showed a powerful antioxidant effect; it notably inhibited MDA production, elevated GSH concentration and attenuated cellular ALT and AST released from hepatocytes reported by **Naik *et al.*, (2004**). The decreases in GSH level of infected mice is in agreement with the findings of **Leelank & Bansal (1996)** , who reported GSH depletion decreases the GSH/GSSG ratio and production of free radicals. These free radicals interact with membrane lipids leading to the production of lipid hydroperoxides.

Table (6) showed that the activities of serum and liver tissue SOD and CAT of infected non treated mice significantly decreased ($P < 0.05$) as compared to control group. Treatment of non-infected mice with curcumin (group II) significantly increased the activities of both serum and liver tissue SOD and CAT as compared to that of infected mice. In addition, a significant recovery relating to serum and liver tissue SOD and CAT was observed in infected mice supplemented curcumin **(El-Demerdash *et al.*, 2009)**. Also, **Rizk (1998) and Allam (2009)** reported that catalase activity was enhanced in infected mice treated with curcumin. The antioxidant enzymes superoxide dismutase and catalase play an important role in keeping homeostasis and protection against oxidative damage by removing the toxic free radicals in vivo **(EI Shenawy *et al.*, 2008 and Jia *et al.*, 2009)**. Recently, **Rizk *et al.*, (2012)** noticed that the reduction in catalase activity could be attributed to its utilization in scavenging the free radicals overload which generated during Schistosomiasis. A decrease of SOD activity can be resulted from increased removal of superoxide anions **(Sharma *et al.*, 2005)**. The levels of antioxidant enzymes are known to be elevated in cells in response to free radical production **(Bandyopadhyay *et al.*, 1999)**.

These results coincide with that of **Cerny *et al.*, (2011)** who observed plasma catalase activity as a marker of oxidative stress was 2.4-fold elevated as compared to control and this level further increased to 3-fold following curcumin treatment. **Priyadarsini, (1997)** and **Masuda *et al.*, (1999)** indicated that the exact mechanism of antioxidant activity of curcumin is not clear, while it is known to react with glutathione and also undergo dimerization by interacting with free radicals**. Naik *et al.*, (2011) and Kurup *et al.*, (2007)** attributed the antioxidant property of curcumin extract to the presence of chemical groups like hydroxyl methoxy and 1,3-diketone conjugated diene system . **Naik *et al.*, (2011**) believed that the antioxidant activity of curcumin might be directly or indirectly associated with the maintenance or preservation of membrane integrity, which might help to prevent the elevation of serum marker enzymes observed during inflammation.

According to our results we concluded that curcumin, could not be used as an anti-parasitic whereas it only improves the alterations of hematological, biochemical ,antioxidants parameters previously induced in *schistosoma mansoni* infected mice.

Table (1) Erythrogram in mice infested with *S. mansoni* and or treated by curcumin (mean ± S.E):

groups / parameters		Non infected non treated control	Non infected treated	Infected non treated	Infected treated
2 nd WEEK post treatment	RBCS (X10 6 / UL)	6.56 ±0.05	6.61±0.06	4.74±0.06 ab	5.21±0.4 ab
	Hb (g/dl)	12.30±0.07	12.57±0.04	7.44±0.17 ab	7.30±0.33 ab
	PCV (%)	41.38±0.06	40.97±0.04	27.01±0.19 ab	30.90±0.28 ab
	MCV (fl)	63.13±0.44	61.98±0.61	57.06±0.82 ab	59.34±0.46 ab
	MCH (pg)	19.07±0.20	19.03±0.21	15.73±0.45 ab	14.00±0.55 ab
	MCHC (gm/dl)	30.21±0.17	30.70±0.08	27.54±0.58 ab	23.63±1.10 ab
4 th week post treatment	RBCS (X10 6/ UL)	6.11±0.08	6.09±0.03	4.28±0.05 ab	4.67±0.03 ab
	Hb (g/dl)	12.74±0.12	12.53±0.08	7.23±0.07 ab	7.28±0.15 ab
	PCV (%)	39.38±0.10	39.03±0.09	25.15±0.20 ab	27.22±0.23 ab
	MCV (fl)	64.51±0.67	64.10±0.40	58.72±0.93 ab	58.37±0.91 ab
	MCH (pg)	20.87±0.23	20.58±0.13	16.89±0.27 ab	15.62±0.36 ab
	MCHC (gm/dl)	32.35±0.29	32.10±0.28	28.76±0.37 ab	26.75±1.19 ab
6 th week post treatment	RBCS (X10 6/ UL)	6.23±0.12	6.18±0.02	4.18±0.10 ab	4.76±0.08 ab
	Hb (g/dl)	12.91±0.10	12.70±0.18	6.84±0.36 ab	7.91±0.45 ab
	PCV (%)	39.95±0.75	39.85±1.03	24.58±0.62 ab	27.64±0.89 ab
	MCV (fl)	64.16±0.74	64.47±0.58	58.98±1.40 ab	58.08±0.62 ab
	MCH (pg)	20.75±0.32	20.54±0.13	16.43±0.61 ab	16.63±0.39 ab
	MCHC (gm/dl)	32.34±0.49	31.88±0.43	27.84±0.72 ab	28.66±1.12 ab

a, b, c Significantly difference at P≤ 0.05. a : compared to control, b : compared to non-infected treated. C : compared to infected non treated

Table(2) leukogram in mice infested with *S. mansoni* and or treated by curcumin (mean ± S.E):

parameters \ groups			Non infected non treated control	Non infected treated	Infected non treated	Infected treated
DIFFERENTIAL LEUCOCYTIC COUNT	2nd week post treatment	TLC (X10 3 / UL)	8.22±0.20	8.45±0.09	6.74±0.12 ab	6.72±0.10 ab
		LYMPHOCYTE (X10 3 / UL)	5.19±0.13	5.22±0.13	4.41±0.08 ab	4.60±0.14
		NEUTROPHIL (X10 3 / UL)	2.85±0.14	3.10±0.06	1.57±0.05 ab	1.69±0.07 ab
		ESINOPHIL (X10 3 / UL)	0.13±0.01	0.20±0.01	0.68±0.02 ab	0.39±0.04 ab
		MONOCYTE (X10 3 / UL)	0.03±0.01	0.02±0.01	0.07±0.01	0.03±0.01
	4th week post treatment	TLC (X10 3 / UL)	6.80±0.34	7.18±0.64	5.40±0.53 ab	5.78±0.36
		LYMPHOCYTE (X10 3 / UL)	4.84±0.33	5.09±0.60	3.11±0.66 ab	3.96±0.69
		NEUTROPHIL (X10 3 / UL)	1.80±0.14	1.88±0.09	1.38±0.18 ab	1.34±0.14 ab
		ESINOPHIL (X10 3 / UL)	0.12±0.01	0.18±0.08	0.81±0.07 ab	0.41±0.07 abc
		MONOCYTE (X10 3 / UL)	0.03±0.01	0.02±0.004	0.09±0.005 a	0.07±0.01
	6th week post treatment	TLC (X10 3 / UL)	7.45±0.23	7.83±0.43	4.38±0.50 ab	4.39±0.40 abc
		LYMPHOCYTE (X10 3 / UL)	5.23±0.38	5.44±0.52	2.90±0.44 ab	3.18±0.22 ab
		NEUTROPHIL (X10 3 / UL)	2.07±0.43	2.21±0.57	0.84±0.33	0.85±0.77
		ESINOPHIL (X10 3 / UL)	0.12±0.10	0.14±0.02	0.55±0.10 ab	0.31±0.04 ab
		MONOCYTE (X10 3 / UL)	0.02±0.01	0.02±0.01	0.09±0.01 ab	0.05±0.01

a, b, c Significantly difference at P≤ 0.05. a : compared to control, b : compared to non-infected treated. C : compared to infected non treated.

Table (3) serum liver enzymes and proteinogram of mice infested with *S. mansoni* and or treated with curcumin (mean ±S.E):

groups / parameters		Non infected non treated control	Non infected treated	Infected non treated	Infected treated
2nd week post treatment	AST (IU/L)	22.41± 0.29	21.36 ±0.15	39.66 ±0.13[ab]	28.72±0.25[abc]
	ALT(IU/L)	19.30±0.62	17.75±0.35	29.89±0.63[ab]	22.71±0.58[abc]
	ALP(IU/L)	38.42±0.24	37.44±0.28	58.31±0.36[ab]	44.32±0.23[abc]
	Total protein g/dl	6.68±1.03	6.82±0.73	3.97±0.81[ab]	4.01±0.57[ab]
	Albumin g/dl	2.38±0.84	2.54±0.23	1.01±0.38[ab]	1.42±0.68[ab]
	globulin g/dl	4.30±0.19	4.28±0.50	2.96±0.73[ab]	2.59±0.76
4th week post treatment	AST (IU/L)	34.25±0.74	36.12±.52	67.00±0.65[ab]	45.00±0.92[abc]
	ALT(IU/L)	18.50±1.36	21.00±1.2	68.80±0.5[ab]	32.00±1.17[abc]
	ALP(IU/L)	35.52±0.05	32.08±1.63	72.40±1.8[ab]	46.47±0.45[abc]
	Total protein g/dl	6.49±0.4	6.35±0.1	4.15±0.6[ab]	4.87±0.13[ab]
	albumin g/dl	2.55±0.5	2.60±0.8	1.38±0.14[ab]	1.50±0.12[ab]
	globulin g/dl	3.94±0.59	3.75±0.1.21	2.770.8[ab]	3.37±0.14
6th week post treatment	AST (IU/L)	28.00±1.2	27.14±0.08	55.00±0.05[ab]	31.10±1.02[c]
	ALT(IU/L)	21.16±0.9	21.41±0.19	31.70±0.06[ab]	22.65±0.07[c]
	ALP(IU/L)	36.80±1.5	38.20±1.2	67.43±2.5[ab]	42.25±1.3[c]
	Total protein g/dl	5.84±0.48	5.90±0.70	3.80±0.18[ab]	4.52±0.30[a]
	albumin g/dl	2.89±0.21	2.68±0.83	1.82±0.5[ab]	2.40±0.68
	globulin g/dl	2.95±0.26	3.22±0.13	1.98±0.23[ab]	2.12±0.52

a, b, c Significantly difference at P≤ 0.05. a : compared to control, b : compared to non-infected treated. C : compared to infected non treated.

Table (4) serum AFP and TNF of mice infested with *S. mansoni* and /or treated with curcumin (mean ±S.E):

parameters \ groups		Non infected non treated control	Non infected treated	Infected non treated	Infected treated
2 week post treatment	AFP (ng/ml)	7.62±0.10	7.00±0.39	38.65±0.72 [ab]	30.12±0.54 [abc]
	TNF (Pg/ml)	12.45±0.30	11.48±0.32	33.32±0.50 [ab]	24.71±0.27 [abc]
4th week post treatment	AFP (ng/ml)	8.87±0.47	8.51±0.57	50.44±0.70 [ab]	41.96±0.23 [abc]
	TNF (Pg/ml)	12.35±0.40	10.76±0.37	48.41±0.87 [ab]	40.72±1.08 [abc]
6th week post treatment	AFP (ng/ml)	8.94±0.26	8.23±0.54	57.61±0.31 [ab]	49.46±0.40 [abc]
	TNF (Pg/ml)	11.78±0.64	10.22±0.87	59.87±1.83 [ab]	47.71±2.85 [abc]

a, b, c Significantly difference at P≤ 0.05. a : compared to control, b : compared to non-infected treated. C : compared to infected non treated.

Table (5) serum lipid profile of mice infested with *S. mansoni* and /or treated with curcumin (mean ±S.E):

parameters \ groups		Non infected non treated control	Non infected treated	Infected non treated	Infected treated
2nd week post treatment	Cholesterol (mg/dl)	82.33±0.22	79.83±1.03	111.50±1.97 [ab]	96.83±1.72 [abc]
	triglycerides(mg/dl)	56.00±0.14	49.70±1.87	77.90±0.57 [ab]	65.10±0.16 [ab]
	HDL-C (mg/dl)	15.10±0.18	17.60±0.61	14.20±0.78	14.80±1.2
	LDL-C (mg/dl)	56.30±0.04	52.29±0.60	81.72±1.32 [ab]	69.01±1.10 [ab]
4th week post treatment	Cholesterol (mg/dl)	85.67±2.16	83.17±0.18	138.83±1.22 [ab]	114.33±1.43 [abc]
	triglycerides(mg/dl)	48.00±0.20	45.70±0.3	67.12±0.41 [ab]	50.39±0.43
	HDL-C (mg/dl)	21.82±1.27	22.48±2.18	19.06±1.16	20.13±1.42
	LDL-C (mg/dl)	54.25±1.54	51.55±1.95	106.35±1.14 [ab]	89.12±0.86 [ab]
6th week post treatment	Cholesterol	83.49±2.32	80.57±1.03	104.83±1.72 [ab]	99.50±1.87 [abc]
	triglycerides(mg/dl)	69.67±0.88	60.35±0.28	92.71±0.37 [ab]	89.20±0.81 [ab]
	HDL-C (mg/dl)	17.31±0.73	16.91±1.81	15.85±1.38	16.22±0.92
	LDL-C (mg/dl)	52.24±0.24	51.59±0.49	70.47±0.38 [ab]	65.44±0.89 [ab]

a, b, c Significantly difference at P≤ 0.05. a : compared to control, b : compared to non-infected treated. C : compared to infected non treated

Table (6) levels of GSH, SOD, CAT AND MAD in serum and liver tissue homogenates of (mean ±S.E):

parameters \ groups			Non infected non treated control	Non Infected treated	Infected non treated	Infected treated
2 nd week post treatment	GSH	SERUM	12.88±0.22	12.91±0.46	7.26±0.31 ab	9.70±0.37 abc
		TISSUE	30.47±0.73	32.60±0.23	13.40±0.18 ab	24.15±0.95 abc
	SOD	SERUM	6.94±1.36	7.64±1.43	3.29±0.83 ab	5.72±1.05 abc
		TISSUE	23.50±0.61	24.10±0.37	14.25±0.79 ab	17.70±0.58 ab
	CAT	SERUM	49.10±6.99	48.31±7.89	31.20±8.56 ab	36.29±7.33 abc
		TISSUE	67.80±1.20	70.30±3.42	53.70±3.42 ab	61.94±3.72 abc
	MAD	SERUM	0.13±0.2	0.12±0.01	0.62±0.03 ab	0.39±0.05 abc
		TISSUE	1.06±0.72	1.00±0.18	1.94±0.15 ab	1.25±0.11 ab
4 th week post treatment	GSH	SERUM	14.11±0.95	14.58±0.66	8.62±0.13 ab	10.73±0.32 ab
		TISSUE	34.15±0.41	35.78±0.62	18.71±0.30 ab	25.93±0.43 ab
	SOD	SERUM	6.10±0.59	6.25±0.23	2.62±0.17 ab	5.00±0.19 c
		TISSUE	21.90±0.61	20.34±0.23	11.84±0.74 ab	14.69±0.81 ab
	CAT	SERUM	53.70±7.91	51.30±3.41	23.79±5.87 ab	40.17±6.58 abc
		TISSUE	70.32±3.99	72.85±4.86	48.30±5.64 ab	52.60±8.31 ab
	MAD	SERUM	0.15±0.40	0.16±0. 90	0.87±0.11 ab	0.30±21 abc
		TISSUE	0.92±0.30	0.83±0.11	2.16±0.90 ab	1.72±0.70 abc
6 th week post treatment	GSH	SERUM	16.80±0.95	18.13±1.2	8.42±1.36 ab	12.90±1.13 abc
		TISSUE	33.72±0.93	34.61±0.82	16.32±0.59 ab	21.80±0.36 abc
	SOD	SERUM	9.10±0.45	11.30±0.53	6.37±0.31 ab	8.50±0.39
		TISSUE	25.43±0.16	27.38±0.81	10.93±0.76 ab	18.47±0.51 ab
	CAT	SERUM	48.13±3.43	45.19±6.32	32.81±4.37 ab	36.58±3.45 ab
		TISSUE	69.28±7.31	71.19±6.39	43.64±8.31 ab	50.97±4.53 abc
	MAD	SERUM	0.12±0.31	0.11±0.10	0.46±0.21 ab	0.32±0.34 abc
		TISSUE	1.44±0.31	1.55±0.40	2.87±0.82*	1.92±0.48*

a, b, c Significantly difference at P≤ 0.05. a : compared to control, b : compared to non-infected treated. C : compared to infected non treated. SOD & CAT (U/mg protein in serum &tissue),GSH (mg/dl in serum& nmole/g tissue),MAD(nmole/ml in serum & nmole/g tissue)

References

[1] Abd EL-Mottaleb E M, El-Gharieb H H, Abdel Rahman, M A M .(2008). Parasitological and Clinico-Pathological Studies on Some Herbal Preparations in Mice Experimentally Infected With Schistoma mansoni. Egypt.J.Comp. path&Clinic.Path., 12(2), 269-299.

[2] Abelev, G.1., S.D. Perova, N.1. Khramkova, Z.A. Postnikova and LS. Irlin, (1963). Production of embryonal a-globulin by transplantable mouse hepatomas. Ransplantation., 1,174-180.

[3] Aebi H. (1974). Catalase. Bergmeyer, H.U. (Ed.), Methods of Enzymatic Analysis, vol. 2. Academic Press, New York, pp. 673–678.

[4] Aggarwal B.B, Harikumar K B. (2009). Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. Int. J. Biochem. Cell Biol., 41, 40–59.

[5] Allam G. (2009). Immunomodulatory effects of curcumin treatment on murine Schistosomiasis mansoni. Immunobiology., 214, 712–27

[6] Arafa H M.(2005). Curcumin attenuates diet induced hypercholesterolemia in rats, Med Sci Mon.i, 11,228-34.

[7] Antony S, Kuttan R, Kuttan G. (1999) Imunomodulatory activity of curcumin. Immunol.Invest., 28, 291-303.

[8] Bandyopadhyay U, Das D, Banerjee R K. (1999). Reactive oxygenspecies: oxidative damage and pathogenesis. Current Science., 77, 658–666.

[9] Baum L, Cheung S K, Mok V C, Lam L C, Leung V P, Hui E, Ng C C, Chow M, Ho P C, Lam S, Woo J, Chiu H F, Goggins W, Zee B, Wong A, Mok H, Cheng WK, Fong C, Lee J S, Chan M H, Szeto S S, Lui V W, Tsoh J, Kwok T C, Chan I H, Lam C W. (2007). Curcumin effects on blood lipid profile in a 6-month human study. Pharmacol Res., 56(6), 509-14.

[10] Bergquist N R, Colley D G. (1998). Schistosomiasis vaccines: research to development, Parasitol., 14, 99–104.

[11] Bugarski D, Jov G IC, Katic´-Radivojevic´ S, Petakov M, Krstic´ A, Stojanovic´ A, Milenkovic´ P. (2006): Hematopoietic changes and altered reactivity to IL-17 in Syphacia obvelata-infected mice. Parasitology International., 55,91 – 97.

[12] Černy D, Lekić N, Vaňova K, Muchova L, Kmoničkova E, Zidek Z, Kamenikova L, Hořinek A and Farghali H. (2011). Hepatoprotective effect of curcumin in lipopolysaccharide/D-galactosamine model of liver injury in rats: Relationship to HO-1/CO antioxidant system. Fitorapia., 82, 786-791.

[13] Chen A, Zheng S. (2008). Curcumin inhibits connective tissue growth factor gene expression in activated hepatic stellate cells in vitro by blocking NF-kappaB and ERK signalling. Br. J. Pharmacol., 153, 557–567.

[14] Coles E H .(1986). Veterinary Clinical Pathology 4th ed. W.B. Saunders Company, Philadelphia, London,Toronto, Mexico, Sydney, Tokyo, Hong Kong.

[15] Das R, Roy A, Dutta N, Majumder H K. (2008). Reactive oxygen species and o calcium homeostasis contributes to curcumin induced programmed cell death In Leishmania donovani., Apoptosis., 13, 867–82.

[16] Doumas B T, Baysa D D, Carter R J, Peters T Schaffer R .(1981): Determination of seum total protein. Clin. Chem., 27., 1642.

[17] Doumas B T, Biggs H G. (1972). Determination of serum globulin in: Standerd Methods of Clinical Chemistry Vol. 7 Edited by Cooper,New York ,Academic Press.

[18] EDKC E, der deutschen G FK. (1972). "Kinitic determinations of alkaline phos phatase activity as recom-mended by the German clinical Society." Z. Klin Chem Biochem., 10, 182.

[19] El-Agamy D S, Shebl A M, Said S A. (2011). Prevention and treatment of Schistosoma mansoni-induced liver fibrosis in mice. Inflammopharmacology., 19, 307–16.

[20] El-Ansary A K, Ahmed S A, Aly S A. (2007). Antischistosomal and liver protective effects of Curcuma longa extract in Schistosoma mansoni infected mice. Indian Journal of Experimental Biology., 45,791–801.

[21] El-Banhawey M A, Ashry M A, El-Ansary A K, Aly S A. (2007) Effect of Curcuma longa or praziquantel on Schistosoma mansoni infected mice liver—histological and histochemical study. Indian J Exp Biol., 45(10), 877–889.

[22] El-Demerdash F M, Yousef M I and Radwan F M E . (2009). Ameliorating effect of curcumin on sodium arsenite-induced oxidative damage and lipid peroxidation in different rat organs Food and Chemical Toxicology., 47, 249–254.

[23] El-Emama M, Momeana B M, Wafaa L I, Basma M. AE, Alaa A, Youssef A A. (2011). Biological and biochemical parameters of Biomphalaria alexandrina snails exposed to the plants Datura stramonium and Sesbania sesban as water suspensions of their dry powder. Pesticide Biochemistry and Physiology., 99 (1) 96–104.

[24] El-Gowhary s h, Rahmy A E, El-azzouni M Z, Nagil A I, El-Medany A. (1993). Oral contraceptive pills in experimental Schistosomiasis manosoni parasitology, biochemical, histopathogical and ultrastructural studies. J Egypt Soc Parasitol., 23, 609.

[25] El-Haieg M O, Ibrahim II, Zanaty M F. (1977). Alpha-fetoprotein in adult normal, bilharzial hepatic fibrosis and viral hepatitis. Egypt. J Egypt Med Assoc., 60,699.

[26] El-Khoby T., Galal N, Fenwick, A, Barakat, R, El-Hawey, A, Nooman, Z, Habib, M, Dewolfe Miller F. (2000). The epidemiology of schistosomiasis in Egypt:summary findings in nine governorates. American Journal of Tropical Medicine and Hygiene., 62, 88–99.

[27] Ellman, G L. (1959). Tissue sulfhydryl groups. Archives of Biochemical and Biophysics., 82, 70–77.

[28] EI-Rigal N S, Nadia M M, Azza M M, Naema Z M and Z. Maha Z R. (2011). Protection against oxidative damage induced by Schistosoma mansoni using susceptible/resistant nucleoproteins from Biomphalaria alexandrina snails. Asian Journal of Biological Sciences.,4 (5), 445-456.

[29] El-sheikha H M, Hussein S , Rahbar M H. (2008). Clinico-pathological effects of *Schistosoma mansoni* infection

associated with simultaneous exposure to malathion in Swiss outbred albino mice. Acta Tropica, 108:11-19.

[30] EI -Shenawy N S, Soliman M F, Reyad S I. (2008).The effect of antioxidant properties of aqueous garlic extract and Nigella sativa as anti-schistosomiasis agents in mice. Rev. Inst. Med. Trop. Sao Paulo., 50, 29-3654.

[31] Feldman B F, Zinkl J G Jain N C. (2000)."Schalm's Veterinary Hematology" 5th Ed., Philadelphia, London.

[32] Friedewald W T, Levy R I, Fredrickson D S. (1972). Estimation of the concentration of low-density lipoproteins cholesterol in plasma without use of the ultracentrifuge. Clin Chem., 18, 499–502.

[33] Fu Y, Zheng S, Lin J, Ryerse J, Chen, A. (2008). Curcumin protects the rat liver from CCl -caused injury and fibrogenesis by attenuating oxidative stress and suppressing inflammation. Mol. Pharmacol., 73, 399–409.

[34] Godkar P B, Narayanan P, Bhid S V, (1996). Hypocholesterolemic effect of turmeric extract on Swiss mice. Indian J Pharmaco., 28(3)171-174.

[35] Gryseels B, Polman K, Clerinx J, Luc K. (2006). Human schistosomiasis. Lancet., 368(9541), 1106–1118.

[36] Gupta S, Bent S, Kohlwes J. (2003). Test characteristics of a-fet.oprotein for detecting hepatocellular carcinoma in patients with hepatitis C: Asystematic review and critical analysis. Ann. Internal Med., 139, 46-50.

[37] Jia J, Zhang X, Hu y, Wu y, Wang Q. (2009). Evaluation of in vivo antioxidants activities of Ganoderma lucidum polysaccharides in STZ-diabetic rats. Food Chern., 115, 32-36.

[38] Joe B, Vijaykumar M, Lokesh B R. (2004). Biological properties of curcumin-cellular and molecular mechanisms of action. Critical Review in Food Science and Nutrition., 44, 97–111.

[39] Kang Q , Chen A .(2009) . Curcumin suppresses expression of low density lipoprotein (LDL) receptor, leading to the inhibition of LDL-induced activation of hepatic stellate cells British Journal of Pharmacology., 157,1354–1367.

[40] Klion A D, Nutman T B. (2004) The role of eosinophils in host defense against helminth parasites. J Allergy Clin Immunol., 113, 30 – 7.

[41] Koide T, Nose M, Ogihara Y, Yabu Y, Ohta N. (2002). Leishmanicidal effect of curcumin in vitro. Biological and Pharmaceutical Bulletin., 25,131–3.

[42] Kurup V P, Barrios C S, Raju R, Johnson B D, Levy M B, Fink J N.(2007) Immune response modulation by curcumin in a latex allergy model. Clin Mol Allergy., 5, 1

[43] Leclercq I A, Farrell G C, Sempoux C, dela Pena A, Horsmans Y.(2004). Curcumin inhibits NF-kappaB activation and reduces the severity of experimental steatohepatitis in mice. J Hepatol., 41, 926–34.

[44] Leelank B N, Bansal M P. (1996). Effect of selenium supplementation on the glutathione redox system in the kidney of mice after chronic cadmium exposures. Journal Applied Toxicology., 17, 81–84.

[45] Lin J, Chen A. (2008). Activation of peroxisome proliferator activated receptor-gamma by curcumin blocks the signaling pathways for PDGF and EGF in hepatic stellate cells. Lab Invest., 88, 529–40.

[46] Magalhães L G, Machado C B, Morais E R, Moreira E B, Soares C S, da Silva S H, Da Silva F A A, Rodrigues V. (2009). In vitro schistosomicidal activity of curcumin against Schistosoma mansoni adult worms. Parasitol Res., 104(5), 1197–1201.

[47] Magnussen P. (2003). Treatment and re-treatment strategies for schistosomiasis control in different epidemiological settings: a review of 10 years' experiences. Acta Trop., 86, 243–254.

[48] Masuda T, Hidaka, K, Shinohar A, Maekawa T, Takeda Y, Yamaguchi H.(1999). Chemical studies in antioxidant mechanism of curcuminoids: analysis of radical reaction products from curcumin. Journal of Agriculture and Food Chemistry., 47, 71–77.

[49] Melman S D, Steinauer M L, Cunningham C, Kubatko L S, Mwangi I N, Wynn N B, Mutuku M W, Karanja D M, Colley D G, Black C L, Secor W E, Mkoji, G M, Loker E S. (2009). Reduced susceptibility to praziquantel among naturally occurring Kenyan isolates of Schistosoma mansoni. PLoS Negl. Trop. Dis., 3, 504.

[50] Morais E R, Oliveira K C, Magalhãe L G, Moreira E B C, Sergi V A, Rodrigues V. (2013). Effects of curcumin on the parasite Schistosoma mansoni: A transcriptomic Approach. Molecular & Biochemical Parasitology.187, 91-97.

[51] Nahla S E, Maha F M S, Shimaa I R. (2008). The effect of antioxidant proper- ties of aqueous garlic extract and Nigella sativa as anti- schistosomiasis agents in mice." Rev. Inst. Med. Trop.S.Paulo., 50, 10.

[52] Naik S R, Thakare V N, Patil S R. (2011). Protective effect of curcumin on experimentally induced inflammation, hepatotoxicity and cardiotoxicity in rats: Evidence of its antioxidant property. Experimental and Toxicologic Pathology., 63, 419-431.

[53] Naik R S, Mujumdar A M, Ghaskadbi S. (2004). Protection of liver cells from ethanol cytotoxicity by curcumin in liver slice culture in vitro. Journal of Ethnopharmacology., 95, 31–37.

[54] Nagajyothi F, Zhao D, Weiss L M, Tanowitz H B. (2012). Curcumin treatment provides protection against Trypanosoma cruzi infection. Parasitology Research. 110(6):2491-9.

[55] Okada K, Wangpoentrakul C, Tanaka T, Toyokuni S, Uchida K. Osawa T. (2001). Curcumin and especially tetrahydrocurcumin ameliorate oxidative stress-induced renal injury in mice. Journal of Nutrition., 131, 2090–2095.

[56] Ohkawa H, Ohoshi N, Yagi K. (1987). Assay for lipid peroxides in animal tissue by thiobarbituric reaction. The Journal of Biological Chemistry., 262, 1098–1104.

[57] Paolett F, Mocali A (1990). Determination of superoxide dismutase activity by purely chemical system based on NAD(P)H oxidation. Methods Enzymol., 186, 209–220.

[58] Perez-Arriaga L, Mendoza-Magana M L, Cortes-Zarate R, Corona-Rivera A, Bobadilla-Morales L, Troyo-Sanroman R. (2006). Cytotoxic effect of curcumin on Giardia lamblia trophozoites. Acta Tropica., 98, 152–61.

[59] Priyadarsini K I. (1997). Free radical reaction of curcumin in membrane models. Free Radical Biology and Medicine., 23, 838–843.

[60] Rajamanickam V, Muthuswamy N. (2008). Effect of heavy metals induced toxicity on metabolic biomarkers in common carp (Cyprinus carpio L.). Maejo Int. J. Sci. Tech., 2(01), 192-200.

[61] Reitmans S, Frankel, S L. (1957). colorimetric method for the determination of serum glutamic oxalacetic and glutamic pyruvic transaminases., Amer. J. Clin. Pathol., 28,56-63.

[62] Reyes-Gordillo K, Segovia J, Shibayama M, Vergara P, Moreno M G, Muriel P.(2007). Curcumin protects against acute liver damage in the rat by inhibiting NF-kappaB, proinflammatory cytokines production and oxidative stress. Biochim Biophys Acta., 1770, 989–96.

[63] Richmond w. (1973). Enzymatic determination of cholesterol. Clin. Chem., 19, 1350-1365.

[64] Rizk M, Ibrahim N ,. El-Rigal I N. (2012). Comparative In vivo antioxidant levels in schistosoma mansoni infected mice treated with praziquantel or the essential Oil of Melaleuca armillaris leaves. Pakistan Journal of Biological Sciences., 15 (20), 971-978.

[65] Rizk M.(1998). Protective effect of Curcuma longa against oxidative stress in Schistosoma mansoni infected mice livers. Egypt. I. Bilh., 21, 1-8.

[66] Sekou B, Drissa D, Seydou D, Berit S P. (2006). Ethnopharmacological survey of plants used for the treatment of schistosomiasis in Niono District, Mali. Journal of Ethnopharmacology., 105, 387–399.

[67] Seubert J, Pohlke R, Loebich, F. (1977). Synthesis and properties of Praziquantel, novel broad spectrum anthelmintic with excellent activity against Schistosomes and Cestodes. Experientia., 33, 1036–1037.

[68] Silva M, Rodrigues V, Albuquerque S, Bastos J K, Silva R, Pereira Junior O S, Bianco T N C, Cunha W R, Santos F F, Donate P M, Magalhaes L G, Pereira A C, Da Silva F A A. (2009) In vitro antischistosomal activities of phenylpropanoids and lignans against Schistosoma mansoni adult worms. Planta Med., 75 (9),945–945.

[69] Sharma V, Sharma C and Sharma C. (2011).Influence of Curcuma longa and Curcumin on blood profile in mice subjected to aflatoxin B. international journal of pharmaceutical science and research., 2(7),1740-1745.

[70] Sharma R A, Gescher A J, Steward W P. (2005). Curcumin: the story so far. Eur J Cancer., 41, 1955–68.

[71] Sturrock R F, Kariuki H C, Thiongo F W. (1996). Schistosoma mansoni in Kenya:relationship between infection and anemia. Trans. Roy. Soc. Trop. Med. Hyg., 90, 48-54.

[72] Tamhane A C, Dunlop D D. (2000). Statistic and data analysis from Elementary to Intermediate. Upper Saddle River, USA.

[73] Torben W, Hailu A. (2007). Serum cytokinese of the 20 Krad-irradiated S. mansoni cercariae vaccinated, primary and superinfected Cercopethicus aethiops aethiops. Exp. Parasitol., 115, 121-126.

[74] Tu C T, Han B, Liu H C, Zhang S C. (2011). Curcumin protects mice against concanavalin A-induced hepatitis by inhibiting intrahepatic intercellular adhesion molecule-1(ICAM-1) and CXCL10 expression. Mol. Cell. Biochem., 358, 53–60.

[75] Van der Werf, M J, de Vlas, S J, Brooker S, Looman, C W, Nagelkerke N J, Habbema J D, Engels D. (2003). Quantification of clinical morbidity associated with schistosome infection in sub-Saharan Africa. Acta Trop., 86, 125–139.

[76] Vercruysse J E, Rollin I S, fMaieleine W. (1988): Clinical pathology of experimental Schistosoma curassoni infections in sheep and goats. Res. Vet. Sci., 44 (3), 273-281.

[77] Warnik G R, Benderson V, Albern N. (1983): estimation of HDL cholesterol and selected methods Clin. Chem., 1, 91-99

[78] Wahlefeld A w, Bergmeye H W. (1974). Triglycereides determination after hydrolysis in methods of enzymatic analysis Berlachmie Zeinheim and academic press inc., NewYourk and London., 1831-1835.

[79] Yadav V S, Mishra K P, Singh K P, Mehrotra S, Singh V K.(2005) Immunomodulatory effects of Curcumin. Immonopharmacol Immunotoxicol., 27, 485–97.

[80] Zhang S, Coultas K A. (2013): International Journal for Parasitology: Drugs and Drug Resistance. International Journal for Parasitology: Drugs and Drug Resistance., 3, 28–34.