Effect of black seed oil supplementation on selected immunological, hematological and Iron status parameters in ribavirin treated female albino rats

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Abstract: Ribavirin has been found to enhance the anti HCV potential of pegylated interferon and sovaldi. However its use was associated with impact on the hemopoietic system and iron status. The hemopoietic toxicity, sometimes forced patients to reduce the dosage or to discontinue treatment in rare occasions. The main purpose of the present study was to assess the potential of black seed oil, a known potent antioxidant, to ameliorate the negative impact of ribavirin on hematological indices, iron status and natural immunity in rats. Twenty four female albino rats were equally divided into four groups as follows: Group1, served as negative control and received an oral dose of (0.5 ml) saline. Group 2, served as positive control and were given 30 mg/kg/day doses of Ribavirin for / 5 days/ week for 4 weeks. Group 3, which were orally fed a 1ml/kg/ of black seed oil for 5 day/week for 4 weeks. Group 4, which were orally given the above mentioned doses of black seed oil plus ribavirin / 5 days/ week for 4 weeks. The results demonstrated that treatment with ribavirin induced significant decrease in absolute neutrophils count, RBCs count, haemoglobin concentrations (Hb), Packed Cell Volume percentage (PCV%) and liver total iron binding capacity (TIBC). On the other hand, it induced significant increases in serum and liver iron, liver ferritin, transferring saturation % compared to control group. Black seed oil treatment increase absolute neutrophil count and restored RBCs count, Hb concentration and PCV percentage to normal control level. It also significantly reduced serum iron and liver total iron in animals treated ribavirin. Black seed oil supplementation also enhanced serum IgM and IgG concentrations in ribavirin treated rats. In conclusion, black seed oil had the potential to ameliorate the negative effect of ribavirin on the hemopoietic system offering better chances for completion of HCV treatment course with full dose. It also has proven to have the ability to reduce serum and liver iron load and enhance natural IgM and IgG levels.

Keywords: Ribavirin, Black seed oil, Hematological indices, Iron status, Natural immunity, Female rats

INTRODUCTION

Ribavirin (1-β-d-ribofuranosyl-1,2,4-triazole-3-carboxamide) is a synthetic nucleoside analog with a broad-spectrum antiviral activities. It has been reported that ribavirin has the ability to prevent the replication of a large number of RNA and DNA viruses by inhibiting the enzyme inosine monophosphate dehydrogenase (Cameron and Castro, 2001). Inhibition of this enzyme blocks the conversion of inosinate to xanthylate and prevents the biosynthesis of guanine nucleotides, which are essential components of nucleic acids. The spectrum of ribavirin antiviral activities involves the adenovirus 2, 3, 5 and 19, herpes simplex, varicella zoster and influenza type A and B (Knowles *et al*., 2003; Muller *et al*., 2007). Ribavirin has been successfully used in the treatment of chronic hepatitis C in combination pegylated interferon. Data from a number of studies showed that the rates of normalization of aminotransferase values, viral eradication, and histologic improvement were higher when ribivirin was administered with pegylated interferon than when it was used alone (Wartelle-Bladou *et al*. 2006). Recently, ribavirin has been advocated to be used in combination with sovaldi as the most effective therapeutic modality against chronic hepatitis C (Ruane *et al*., 2013).

Unfortunately, peg. interferon alfa plus ribavirin and sovaldi plus ribavirin combination therapy were not without side effects. Fatigue, anemia, neutropenia, insomnia, headache and nausea have been reported along with the use of these medications (Gane *et al*., 2013). A major side effect of ribavirin is hemolytic anemia that accompanies long-term administration of the drug. Ribavirin mediates its toxicity through the inhibition of intracellular energy metabolism and oxidative membrane damage, leading to accelerated extravascular hemolysis by the reticuloendothelial system (Russmann *et al*., 2006). Anemia during combination therapy with pegylated interferon plus ribavirin for chronic hepatitis C virus patients usually force physicians to ribavirin dose reduction or discontinuation of treatment which hampers their trials to eliminate the virus. In the mean time, Isabel Fiel *et al* (2000) showed that ribavirin associated hemolysis increases iron deposition in hepatocytes. Augmentation of liver iron load has been assumed to influence the patient's response to interferon-alfa therapy (Olynyk *et al*., 1995). Actually in one study conducted by Barton *et al* (1995) the latter demonstrated that total hepatic iron scores were higher in patients with

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incomplete response of chronic hepatitis C to interferon-alfa. In the mean time pathological accumulation of iron is expected to exacerbate oxidative stress resulting in increased lipid per oxidation. This leads to destruction of organelle membranes and in turn, cell death via hepatocyte necrosis or/and apoptosis. Products of oxidative stress induce a focal inflammatory reaction that plays a role in the stimulation of liver macrophages and release of profibrogenic cytokines (Videla *et al*., 2003). Those mechanisms trigger the activation of hepatic stellate cells (HSCs), which are major sources of collagen and other extra cellular matrix elements that gradually accumulate in the peri sinusoidal spaces of liver parenchyma (Hübscher,2003) and accelerate the HCV associated cirrhosis.

In addition to hematotoxic effect of ribavirin, it has been shown that the drug is able to exert unfavorable effect on the immune response. Peavy *et al* (1981) reported that ribavirin has inhibited humoral response and antibody production by plaque-forming cells in vivo. The immunosuppressive potentials of ribavirin have also been documented in other studies (Heagy *et al*. 1991).

Black seed oil *(Nigella sativa)* is used as a food additive in the Middle East. It has been known to have immunomodulatory effects, anti-inflammatory, and therapeutic properties for the treatment and prevention of a number of diseases (Ali and Blunden, 2003). Most properties of whole seeds or their extracts are mainly attributed to quinine constituents, of which, thymoquinone is more abundant compound (Filippo D Antuono *et al*., 2002). The antioxidant activity of black seed oil and its ability to act as scavenger of oxygen free radicals have also been documented (Ali and Blunden, 2003). Osman *et al* (2012) concluded that black seed oil has ability to improve hematological indices in animals exposed to hemopoietic damage.

In view of the high prevalence rate of HCV infection among the Egyptians (El-Zanaty and Way, 2009; Lavanchy, 2011) and the increasing number of population that are expected to consume ribavirin for viral eradication, looking for agents that ameliorate the negative effect of ribavirin on the hemopoietic system, the natural immunity and iron status is becoming an urgent necessity. The main purpose of the present study is to assess the potential of black seed oil supplementation to ameliorate the negative impact of ribavirin on hematological indices, iron status and natural immunity in rats.

MATERIALS AND METHODS

Chemical

Ribavirin was obtained from (October Pharma Company). The entire content of one capsule of ribavirin (400 mg) was dissolved in 50 ml saline to obtain a freshly prepared solution of 0.8% concentration.

Black seed oil was obtained from (Imtenan Health Shop Company for health and functional food, Cairo- Egypt).

Animals

Twenty four female albino rats, weighting about 100-117gm were obtained from the animal house facility of Application Department of the Egyptian Atomic Authority at Inshas Egypt. All animals were housed in stainless steel cages with wire mesh lid and allowed balanced standard rodent diet and water *ad libitum* for one week for accommodation. Rats were exposed to 12h light: 12h dark cycle and a room temperature of 18-22°C. They were randomly and equally divided into four groups. Group1 (G1): served as negative control, female rats from this group received an oral dose of (0.5ml) saline. Group 2(G2) served as positive control. Rats were given orally 30 mg/kg/day doses of Ribavirin for / 5 days/ week for 4 weeks by oral tube according to Motor *et al*. (2014). Group 3(G3): Rats were orally fed a black seed oil (1ml/kg/5 day/ week for 4 weeks using oral tube according to Juma and Abdulrahman (2011). Group 4 (G4): Rats were treated with ribavirin and black seed oil as shown in group 2 and group 3 respectively 5 days/ week for 4 weeks.

Samples

At the end of the experiment (4 weeks) the animals were sacrificed. Blood samples were collected into plain tubes and tubes with EDTA. Blood with EDTA were used for investigating the blood picture and the plain blood was centrifuged at 3000 rpm for 15 minutes to obtain serum for the determination of the biochemical parameters. The animals abdominal cavities were exposed, livers were excised and 1 gm of the liver tissue was obtained from each animal. The liver tissue samples were homogenized in 10 ml (0.9%) saline solution and the homogenate was centrifuged at 10,000xg for 20 min at 4C° and the resultant supernatant of the liver was used for the determination of iron parameters.

Total counts of erythrocytes (RBCs) and leucocytes (WBCs) were performed using an improved Neubauor chamber. Differentiation of white blood cells were carried out according to Carleton (1976).Hemoglobin content (Hb by g/100ml blood) was determined using Hemoglowiner Laboratory Kit and the resulting cyanmethemoglobin was measured spectrophotometrically at 546nm. The hematocrit value (HCT) was determined in duplicate samples by microhaematocrit centrifuge at 3000 rpm for 15 minutes. Mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and blood platelet counts were estimated according to Dacie and Lewis, (1991). The quantitative measurement of serum and liver

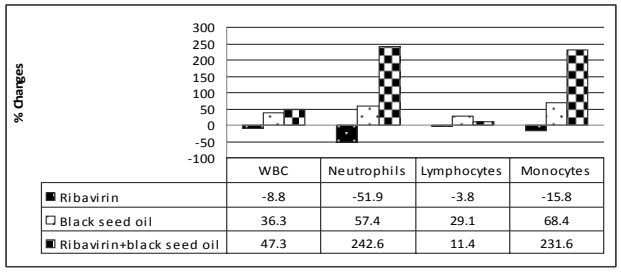
iron, ferritin and total iron binding capacity (TIBC) were performed on Cobas e411 (Roche Diagnostics International Ltd, Switzerland) according to the manufacturer protocol. Transferrin Saturation was calculated as follow: (Serum iron/TIBC) X100. Serum immunoglobulin (IgG, and IgM) were measured by single radical immunodiffusion (RID) method.

STATISTICAL ANALYSIS

The obtained data was presented as means ± SD. One-way analysis of variance (ANOVA) was carried out. The statistical comparisons among the groups were performed with Duncan's test, using a statistical package program (COSTAT). Differences among the groups were considered significant at $P<0.05$.

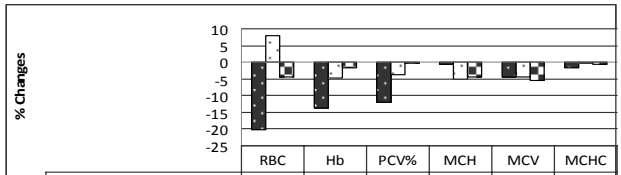
RESULTS

Results of table (1) and fig. (1) show the effect of black seeds oil, ribavirin and both on total white blood cell (WBC), neutrophil, lymphocyte and monocyte counts. These results demonstrated significant increase ($p>0.05$) in WBCs in G3 (black seed oil) and G4 (ribavirin +black seed oil) compared to control and ribavirin treated group. Neutrophilis count experienced a significant decrease in the group of rats treated with ribavirin (G2) and this decrease was over corrected by black seed oil supplementation.



	WBC	Neutrophils	Lymphocytes	Monocytes
Ribavirin	-8.8	-51.9	-3.8	-15.8
Black seed oil	36.3	57.4	29.1	68.4
Ribavirin+black seed oil	47.3	242.6	11.4	231.6

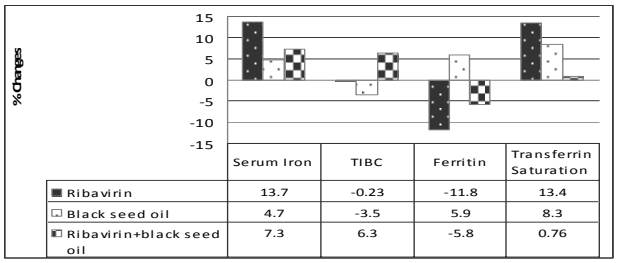
Fig. 1: illustrates the percent of change of WBC, neutrophils, lymphocytes and monocytes in ribavirin, black seed oil and ribavirin +black seed oil treated animals in comparison to normal controls.



	RBC	Hb	PCV%	MCH	MCV	MCHC
Ribavirin	-20.3	-13.7	-12.1	-0.8	-4.4	-1.6
Black seed oil	7.8	-4.9	-3.7	-5.03	-4.4	-0.3
Ribavirin+black seed oil	-4.3	-1.5	-0.2	-4.5	-5.3	-0.7

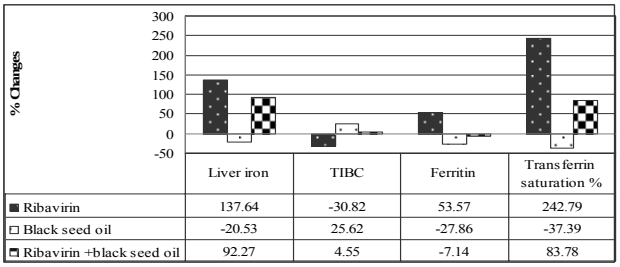
Fig. 2: illustrates the percent of change of RBC, Hb, PCV%, MCH, MCV and MCHC in ribavirin, black seed oil and ribavirin +black seed oil treated animals in comparison to normal controls.

Data presented in table (2) and fig. (2) illustrate the changes of the hemogram pattern in response to ribavirin, black seed oil and both in female rats. These data demonstrated the negative impact of ribavirin on erythrocytic series in treated animals. This was evident from the significant ($p>0.05$) decrease in RBCs count, Hb concentration and PCV% induced by ribavirin. Data also showed that black seed oil treatment restored the negative effect of ribavirin treatment on these parameters to almost the control level.



	Serum Iron	TIBC	Ferritin	Transferrin Saturation
Ribavirin	13.7	-0.23	-11.8	13.4
Black seed oil	4.7	-3.5	5.9	8.3
Ribavirin+black seed oil	7.3	6.3	-5.8	0.76

Fig. 3: illustrates the percent change of serum iron, TIBC, ferritin and transfirrin saturation %in ribavirin, black seed oil and ribavirin +black seed oil groups, relative to the match normal control group.



	Liver iron	TIBC	Ferritin	Transferrin saturation %
Ribavirin	137.64	-30.82	53.57	242.79
Black seed oil	-20.53	25.62	-27.86	-37.39
Ribavirin +black seed oil	92.27	4.55	-7.14	83.78

Fig. 4: illustrates the percent change of liver iron, TIBC, ferritin and transfirrin saturation % in ribavirin, black seed oil and ribavirin +black seed oil groups, relative to the match normal control group.

Table 3 and fig. 3 mirrors the serum iron status in all tested groups. Data from this table showed that ribavirin treatment significantly increased serum iron concentration ($p>0.05$) without affecting TIBC or serum ferritin level. Black seed oil extract was able to induce a significant ($p>0.05$) reduction in serum iron concentration boosted by ribrvirin treatment.

Table (4) and fig. (4) demonstrate the total liver iron, TIBC, ferritin and transferrin content of control and treated rats. Rats treated with ribavirin experienced a significantly ($p>0.05$) higher levels in liver iron, ferritin and transferrin saturation (%) and a significant decrease in TIBC, while in treated with black seed oil extract experienced a significant ($p>0.05$) decrease in iron, ferritin and transferrin saturation (%) but, significant increase TIBC in comparison to the ribavirin group. Ribavirin treated animals exhibited less liver iron, ferritin, transferrin level and increased TIBC upon black seed supplementation.

Table 1: Effect of ribavirin, black seed oil and both on total white blood cell, absolute neutrophil, lymphocyte and monocyte count per cubic millimiter in female rats.

Groups Parameters	G1 (Control)	G2 (Ribavirin)	G3 (Black seed oil)	G4 (Black seed oil+Ribavirin)
WBC ($x10^3$)/ Cmm	9.1±1.2^b	8.3± 0.9^b	12.4±1.9^a	13.4±0.7^a
Neutrophils ($x10^3$)/ Cmm.	1.08±0.06 ^{c}	0.52±0.1^d	1.7±0.3^b	3.7±0.4^a
Lymphocyte ($x10^3$)/ Cmm	7.9±0.9^b	7.6±0.9^b	10.2±1.8^a	8.8±0.3^b
Monocytes($x10^3$)/ Cmm	0.19±0.04^c	0.16±0.05^c	0.32±0.05^b	0.63±0.1^a

Table 2: Mean ± SD of erythrocyte indices in all study groups.

Groups Parameters	G1 (Control)	G2 (Ribavirin)	G3 (*Black seed*oil)	G4 (*Black seed*oil+Ribavirin)
RBCs (x10 6 /µl)	7.42±0.6^b	5.9± 0.13 ^{c}	8.0± 0.41 ^{a}	7.1±0.24 ^{b}
Hb (g/dL)	13.1± 0.55^a	11.3 ± 0.35^b	12.45 ± 0.66^a	12.9± 0.67^a
PCV (%)	42.8± 2.05^a	37.6± 1.72^b	41.2±3.2^a	42.7±1.5^a
MCH (pg)	19.06±0.9^a	18.9±1.3^a	18.1±0.8^a	18.2±0.2^a
MCV(pg/dL)	64.1±0.7^a	61.2±4.1^a	61.3± 1.3^a	60.7± 0.4^a
MCHC	30.6±0.6^a	30.1±0.7^a	30.5±0.8^a	30.4±0.7^a

Table 3: Serum iron parameters in all study group

Groups Parameters	G1 (Control)	G2 (Ribavirin)	G3 (*Black seed*oil)	G4 (*Black seed*oil+Ribavirin)
Iron (µg/dL)	204.8±13.7^b	232.9±15.7^a	214.3± 7.8^b	219.5±9.2^b
TIBC (µg/dL)	520±58.7^a	518.8± 29.9^a	501.6 ± 47.7^a	552.7± 55.9^a
Ferritin (ng/mL)	1.7± 0.9^a	1.5± 0.3^a	1.8± 0.2^a	1.6±0.5^a
Transferrin Saturation (%)	39.6±2.1^c	44.8±2.5^a	42.9±2.6^{ab}	39.9±2.7^{bc}

Table 4: Liver iron parameters in all study groups

Groups Parameters	G1 (Control)	G2 (Ribavirin)	G3 (Black seedoil)	G4 (Black seedoil+Ribavirin)
Iron (µg/dL)	78.9±6.3^c	187.5±11.7^a	62.7± 5.9^d	151.7± 6.8^b
TIBC (µg/dL)	356.3±35.6^b	246.5± 12.6^c	447.6 ± 11.1^a	372.5± 15.2^b
Ferritin (ng/mL)	2.8± 0.2^b	4.3± 0.8^a	2.02± 0.5^c	2.6±0.7^{bc}
Transferrin Saturation (%)	22.2±1.9^c	76.1± 2.8^a	13.9±1.1^d	40.8± 2.4^b

Table 5: Immunoglobolins (G &M) in all study groups

Groups Parameters	G1 (Control)	G2 (Ribavirin)	G3 (Black seed oil)	G4 (Black seed oil+Ribavirin)
Ig G (µg/dL)	111.7± 6.8^c	105±4.5^c	200.7± 15 ^{a}	126.7±13.7^b
Ig M (µg/dL)	49.1±6.5^{ab}	44.3±3.9^b	52.03± 3.6^a	50.8±2.4^a

Values are shown as means ± SD of N=6.
Different small letters in the same row indicate significant difference at P< 0.05

Data of table (5) and fig. (5) show the effect of ribavirin, black seed oil and both on serum immnoglobulins (IgG & IgM) levels in rats. Data showed that black seed oil administration was able to counteract the negative impact of ribavirin on serum IgG and IgM levels in treated animals. Data also showed a profound ability of black seed oil to boost serum IgG level in ribavirin non-treated animals.

DISCUSSION

Egypt has the highest prevalence rate of HCV infection and the total Egyptian HCV carries outnumber their peers in the European Content (Proceedings of the International Workshop on Epidemiology, Diagnosis and Management of Hepatitis C Infection. Medicine and the Community, 1996). Co administration of ribavirin with peginterferone or sovaldi has markedly enhanced their antiviral potentials, however, the combination therapy was found to be associated with numerous undesirable side effects. These side effects include neutropenia, anemia, and iron overload in liver (Heagy *et al*., 1991; Isabel Fiel *et al*., 2000; Russmann *et al*., 2006).

Data from the present study showed that ribavirin treatment induced significant decline in the absolute count

of neutrophils (table-1, fig. 1). This was consistent with data of Weiss *et al* (1993). The latter have attributed the ability of ribavirin to reduce neurophils count in the peripheral blood to its bone marrow-induced toxicity. Neutrophils act as the body's first line of defence against bacterial infections. Hence, significant neutropenia may hamper the body ability to stand bacterial invasion (Ganong, 1991). Data from the present study also showed that black seed oil was able to counteract the negative effect of ribavirin on the neutrophil count even to more than the control level. The present data are in accordance with those from (Paarakh, 2010; Naz, 2011) who demonstrated the increase of WBCs of rats treated with black seed oil or ribavirin plus black seed oil. Recently, Kamil (2013) reported a significant increase WBCs count in mice which have been orally treated with 0.3 ml of crude traditional oil of Nigella sativa. Neutropenia is the most frequently reported hematological adverse event with an overall prevalence of 42% in combination therapy and is rated mild to moderate in most cases. Of the patients that develop neutropenia, 19% need dose drug reduction; 5% require granulocyte-stimulating therapy and 1.7 % are forced to discontinue treatment because of this adverse effect (Manns *et al*., 2001).

Data from table 2 and fig. 2 concluded the ability of ribavirin to reduce RCBs, haemoglobin and PCV% in treated rats. This was expected since anemia has been considered as another possible complication of the ribavrin therapy (Patrick *et al*., 2002). The latter reported that ribavirin-induced anemia is caused by a combination of transient suppression of erythropoiesis and extra vascular hemolysis . The hemolytic element is due to accumulation of ribavirin and its metabolites in human RBCs causing oxidative stress, mitochondrial toxicity and RBCs membrane damage with consequent reduction of their life spans (Van Vlierbergh *et al*., 2001). Black seed oil had the ability to improve hematological indices in animal studies in which it increased RBCs, Hb, and PCV% (table-2). This was in agreement with Ali and Blunden (2003) and Meral *et al*. (2004) they reported that increase in RBCs, Hb and PCV% in treated and diabetic rabbits after administration black seed oil. They have attributed the increase in RBC count to lowering of the membrane lipid peroxide level, leading to decreased susceptibility to hemolysis. Anemia is present in 28% of patients receiving combination treatment. Nine percent of patients experience a decrease in hemoglobin level to the degree that requires a drug dose modification or erythropoietin administration. Anaemia rarely forces therapists to discontinue the combination therapy (Manns *et al*., 2001).

In view of the above and in the results obtained from the present study, the use black seed oil along with patients under goining HCV treatment in which ribavirin constitutes a major part is of utmost importance. The ability of black seed oil to counteract the neutropenic effect of the ribavirin and the sequel of anemia, would offer patients better chances from benefiting of the combined treatment. This would be guaranteed by minimizing the possibilities of dose reduction or drug discontinuation. On the other hand, black seed oil is very much less expensive and more available than either granulocyte stimulating factor or erythropoietin.

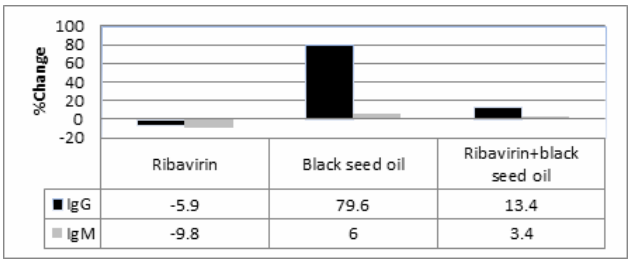


Fig. 5: illustrates the percent of change of circulating IgG and IgM in ribavirin, black seed oil and ribavirin +black seed oil treated animals versus normal non0trated animals.

Data from the present study demonstrated that ribavirin treatment induced a state of iron overload in treated animals when compared to control. This was mirrored by the changes in blood and liver iron indices shown in tables 3 and 4. The positive iron balance shown here is most likely due shortened life span of the RBCs due to oxidative stress-induced membrane damage. These results seemed in accordance with those from Johnson *et al*., (2002). Di Bisceglie *et al*. (1994) and Isabel Fiel *et al*. (2000) also reported that hepatic iron stores increased significantly in patients treated with ribavirin compared with those treated with placebo. Iron overload and increase in liver iron content has been reported to correlate with the severity of HCV induced liver damage and the progression of the disease (Lin *et al*., 2008; Sikorska *et al*., 2010). Additionally, high serum levels of ferritin have been associated with decrease response to Peg-INF-α based therapy (Lange *et al*., 2012).

Beside the ability of increased liver iron to decrease the response to peg interferon, the pro oxidant activity of liver iron and its role in hepatocyte damage and cirrhosis have been well documented by Shimizu *et al*., (2012). They showed that the primary source of reactive oxygen species (ROS) production is mitochondrial NADPH/NADH oxidase. These oxidase enzymes generate hydrogen peroxide (H_2O_2) which is converted to a highly reactive ROS, the hydroxyl radical, in the presence of iron (+Fe). The hydroxyl radical induces DNA cleavage and lipid per oxidation in the structure of membrane phospholipids, leading to cell death and discharge of products of lipid per oxidation, malondialdehyde (MDA) and 4-hydroxynonenal (HNE) into the space of Disse in which hepatic stellate cells reside. These products induce HSCs activation and overproduction of the extracellular matrix, collagen, fibronectin and laminin characteristic of liver cirrhosis. The ribavirin induced liver iron overload is

expected to aggrevate HCV-induced cirrhosis and retard its resolution despite its ability to eliminated the virus. Therefore, the ability of black seed to ameliorate the liver iron content of ribavirin treated rats (table 4), is expected to minimize its pro cirrhotic potential. In the mean time, it would remove an important element that retard the antiviral response since it has been postulated that the success of the antiviral treatment could be dependent on decreasing iron overload and ferritin levels in the liver.

Data from the present study showed also black seed oil significantly increased serum naturally occurring IgG and IgM levels in comparison to ribavirin treated animals (table 5). The role of natural IgG, which pre-exists in neonates and uninfected individuals, has remained unclear due to the general perception that natural antibodies lack affinity for pathogens for nearly five decades. However, it has been recently demonstrated that natural IgG recognizes a spectrum of bacteria through lectins like ficolin and mannose binding lectin which enable it to play a protective role against bacteria (Panda *et al*., 2013). The same was considered for naturally occurring serum IgM. A growing body of evidence has supported its partial contribution against pathogenic attack. Also, the repertoire of natural IgM antibodies has been postulated to have been selected during immune evolution for their contributions to critical immunoregulatory and housekeeping properties. In other words, it has a pronounced role in the clearance of dying cells and is required to prevent uncontrolled inflammation and autoimmunity (Grönwall and Silverman, 2014). The ability of black seed oil to augment the naturally occurring serum IgG and IgM level may be beneficial in protecting against bacterial infection used to complicate liver cirrhosis.

Finally, it should be noted that the black seed oil constituent, thymoquinone, has recently shown to have a well documented anticirrhotic potential in experimental animal models by inhibiting hepatic stellate cell activation (Bai *et al*., 2013). This latter finding makes it a very suitable candidate for use as a supplement along with the antiviral combination therapy of HCV in which ribavirin is included.

CONCLUSION

In conclusion, data from the present study offer a functional element that is black seed oil, which has multiple beneficial effects in ameliorating the harmful consequences of ribavirin, a drug used in the treatment of HCV infection. Black seed oil seemed to have the ability to minimize the need to reduce the dose or to discontinue the administration of the anti-HCV therapy and replaces other possible expensive medications such as granulocyte stimulating or eryhtropoitein. Black seed oil also has proven to reduce liver iron load and enhance natural immunity. Its valuable protective capabilities demonstrated here beside its previously reported anticirrhotic properties ranks it as an excellent co medicine to ribavirin/peg interferon or ribaverin/sovaldi therapy for HCV infection.

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