Mansoura Veterinary Medical Journal 21:4 (2020) 180-187

DOI: 10.35943/MVMJ.2020.142626

Original Article *Pharmacology*

Immunomodulatory effect of Echinacea purpurea and Curcuma longa in rabbits

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ARTICLE HISTORY

Received: 18.02. 2020

Revised: 22.9.2020

Accepted: 27.9.2020

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ABSTRACT

Objectives: This study was delineated to investigate the protective and ameliorative effects of *Echinacea purpurea* and *curcuma longa* against immunosuppressive effect of dexamethasone.
Design: Randomized controlled experimental study.
Animals: Twenty male rabbits were used in this study.
Procedure: Rabbits were randomly categorized into 4 equal groups (5 rabbits/each group). G1 was not treated at all and was kept as a control non-treated, G2 was medicated with dexamethasone intramuscularly (2 mg/kg) for 3 successive times at 6 hours intervals. G3 was medicated with dexa and *Echinacea purpurea* (130 mg/kg body weight) orally day after day for 2 weeks. G4 was medicated with dexa and *Curcuma longa* (400 mg/kg body weight) every day for 2 weeks. Blood and serum samples were collected 1, 7 and 14 days post treatment for the determination of some hematological, biochemical and immunological variables. Two weeks post treatment, liver, kidney and spleen were collected for histopathological examination.
Results: At the 7th day post treatment, both *E. purpurea* and *C. longa* improved total and differential leucocytic count in treated rabbits, but the improvement was higher in case of treatment with *Curcuma longa* ($P < 0.05$). At the 14th day post treatment, both *Echinacea purpurea and Curcuma longa* improved total and differential leucocytic count ($P < 0.05$), however the improvement was higher in case of treatment with *Echinacea Purpurea*. *Echinacea purpurea and Curcuma longa* increased serum lysozymes activity and NO concentrations ($P < 0.05$). Similarly, at the 1st and the 7th days post treatment, both *Echinacea purpurea* and *Curcuma longa* increased serum catalase activity and depleted MDA levels ($P < 0.05$). Dexamethasone decreased serum levels of total protein, albumin and globulin compared to their corresponding values in the negative control group ($P < 0.05$). These parameters were significantly increased after treatment with *Echinacea purpurea* and *Curcuma longa*. Both plants showed a protective effect to liver, kidney and spleen against histopathological alterations caused by dexamethasone.
Conclusion and clinical relevance: Echinacea purpurea and *Curcuma longa* have ameliorative effect against immunosuppression induced by dexamethasone, however the effect appeared more superior in case of *Curcuma longa*.
Keywords: *Echinacea purpurea*, *Curcuma longa*, immunomodulatory, rabbit.

1. INTRODUCTION

Rabbit's industry plays an important role in Egyptian economic development, as they provide a high-quality flesh that is characterized by a low fat content, ease of digestibility and high nutritional value. Rabbits also contribute to fur production, and are used for production of antibodies, antisera and other research aspects [1].

Medicinal plants are extensively used nowadays to cure many diseases [2]. Natural products are considered of a great value for the production of many drugs, and are characterized by minimal adverse effects. Medicinal plants are used also as an immune modulator such as *Echinacea*, Curcumin, Garlic, Onion, Ginger and Astragalus [3].

Echinacea purpurea (*E. purpurea*) is a medicinal herb that has an immune-stimulant effect and anti-inflammatory effect. The phytochemical composition of *Echinacea purpurea* includes polysaccharides, flavonoids, caffeic acid derivatives (cichoric acid), essential oils, polyacetylenes and alkyl amides. The polysaccharides and cichoric acid have a primary immunostimulatory effect stimulating the lymphocytes activity. However, the immunomodulatory effect of Echinacea purpurea is considered to be non-specific, as it stimulates the activity of phagocytic and natural killer cells [4].

Curcuma longa (*C. longa*) is a yellow chemical compound produced by *Curcuma longa* plant that has a strong anti-oxidative, anti-inflammatory effect, with a protective effect on both liver and kidneys. It also has an immunostimulant effect by modulating T cells, neutrophil, B cells, dendritic cells and macrophages. *Curcuma longa* has the ability to promote the antibody response. It can improve and regulate the expression of cytokines and chemokines proinflammatory [5].

The aim of this study was to investigate the effects of *Echinacea purpurea* and *Curcuma* on dexamethasone-treated rabbits through the evaluation of hematological, biochemical, immunological parameters, and the associated histopathological changes.

2. MATERIALS AND METHODS

2.1. Plant extract

Echinacea purpurea dry extract capsules, each contains 175 mg, were purchased from Arab Company for Pharmaceuticals and Medicinal Plants,-Egypt. *Curcuma longa*, in bottles each contain 10 gm of curcumin extract, was purchased from EL-Gomhoria Company, Mansoura, Egypt.

2.2. Drugs

Dexamethasone sodium phosphate ampoules (each ampoule contains 8 mg) were purchased from AMRIYA for Pharmaceutical Industries, Alexandria, Egypt.

2.3. Animals

This study was performed on twenty clinically healthy white New Zealand rabbits with an average body weight of 1.8-3.2 Kg. After one week of adaptation, the animals were randomly allocated into 4 equal groups: a non-medicated negative control group (G1), a dexamethasone-treated group (G2) that was injected intramuscularly with dexamethasone (2 mg/kg body weight) 3 times at 6 hours intervals [6], (G3) a *Echinacea purpurea*-treated group that was injected with dexamethasone, and was also supplemented with *Echinacea purpurea* (130 mg/Kg body weight) by oral gavage day after day for 2 weeks [7], and (G4) a *Curcuma longa*-treated group that was injected with dexamethasone, and was also supplemented with *Curcuma longa* at a dose of 400 mg/kg diet for 2 weeks [8].

2.4. Collection of Samples

Two blood samples were collected from ear vein of all rabbits of each group at 1st day, 7th day and 14th day of the drug administration. The first blood sample was collected on EDTA and was used for hematological studies**.** While the second blood sample was collected for serum separation by centrifugation at 3000 rpm for 15 min and was used for the determination of immunological variables, oxidative stress markers and biochemical variables.

2.4.1. Total and differential leucocytic count

Total and differential leucocytic counts were determined by automatic cell counter (Celtac alfa, Japan) [9].

2.4.2. Serum immunological parameters

Serum lysozyme activity was assayed using lysozymes assay kit (ab2111113) according to Metcalf and Deibel [10] and serum nitric oxide concentration was determined using (NO) colorimetric assay kit (E-BC-K035-M) according to Montgomery and Dymock [11].

2.4.3. Serum antioxidant and oxidative stress markers

Catalase activity was determined using catalase colorimetric activity kit (EIACATC) according to Aebi and Bergmeyer [12], while Malondialdehyde concentration was determined using MDA Assay kit (ab118970) according to Kei [13].

2.4.4. Serum total protein profile

Serum total protein concentration was determined using TP colorimetric assay kit (E-BC-K318-M) according to Grant et al. [14], serum albumin using albumin assay kit (fluorometric) (ab241017) according to Drupt [15] and calculation of serum globulin according to Doumas et al. [16].

2.5. *Histopathological analysis*

Liver, kidney and spleen specimens from rabbits of each group were carefully examined by naked eye for detection of any abnormalities. Small specimen of liver, kidney and spleen were taken and immediately fixed in 10% formalin for histopathological examination [17].

2.6. Statistical analysis

Data were analyzed using one way ANOVA and at each time point with post hoc. Duncan multiple comparison test at ($P < 0.05$) was carried out to determine differences between groups.

3. RESULTS

3.1. *Effect of Echinacea purpurea and Curcuma longa on total and differential leucocytic count*

Rabbits of dexamethasone-treated group (G2) showed a reduction in WBCs count in 1st, 7th and 14th days post dexamethasone treatment compared to those of the negative control group (G 1) (Table 1). In addition, *E. purpurea*-treated group (G3) and *C. longa*-treated group (G4) showed a marked decrease in WBCs count in 1st day post-treatment, however a marked ($P < 0.05$) increase in the 7th and 14th day compared to dexamethasone-treated group.

Rabbits of the dexamethasone-treated group (G2) showed a decreased lymphocyte count in 1st, 7th and 14th day post-treatment. Both *E. purpurea*-treated group (G3) and *C. longa*-treated group (G4) showed a significant reduction in lymphocyte counts in 1st day, but showed a significant increase in 7th and 14th days compared to dexamethasone-treated group (Table 1).

Dexamethasone-treated group (G2) displayed a decrease in neutrophils count in 1st and 7th day compared to the negative control group (G1). *E. purpurea*-treated group (G3) and *C. longa*-treated group (G4) displayed a significant increase in neutrophils count in the 7th day (Table 1).

Table 1. Effects of Echinacea purpurea (130 mg/kg) and curcumin (400mg/kg) on total and differential leucocytic count of dexamethasone injected rabbits.

variable		G1	G2	G3	G4
Total leucocytic count (10^9 /L)	1st day	12.2±0.1^a	10.5±1.1^b	10.9±0.3^b	**10.2 ±0.2^b**
	7th day	12.5±0.1^a	10.4±0.1^c	11.6±0.1^b	**10.9±0.2^a**
	14th day	11.3±.2^b	10.7±0.1^c	11.9±0.1^b	**12.4±0.2^a**
Lymphocytes %	1st day	58.4 ±0.1^a	45.3±0.06^b	43.6±1.8^b	**46.6±1.8^b**
	7th day	59.9±0.2^a	46.3±.04^c	52.9 ±0.7^b	**51.9±0.1^b**
	14 day	61.3±3^a	48.7±2^c	59.2±0.7^a	**57.9±0.9^{ab}**
Neutrophils %	1 day	37.4±0.2^a	31.2±.04^b	33.4±0.2^{ab}	**32.8 ±0.07^b**
	7 day	38.1±0. 3^a	32.3±01^b	36.9±0.8^a	**37.8 ±0.2^a**
	14 day	38.9 ±.2^a	34.1±2.9^{ab}	37.9±5^a	**38.9±0.4^a**
Monocytess %	1st day	3.2±0.2^a	2.2±0.3^b	2.8±0.3^{ab}	**2.5±0.2^b**
	7th day	3.6±0.06^a	1.7±0.05^c	2.9 ±0.02^b	**2.8 ±0.01^b**
	14th day	3.4±0.1^a	1.8 ±0.03^b	3.3±0.01^a	**3.1±0.02^a**
Eosinophils %	1st day	0.08±0.03^a	0.00±0.00^a	0.00±0.00^a	**0.02±0.01^a**
	7th day	0.4±0.02^a	0.00±0.00^a	0.06±0.04^a	**0.00±0.00^a**
	14th day	0.03 ±0.02^a	0.02 ±0.01^a	0.03±0.02^a	**0.01±0.01^a**
Basophils %	1st day	0.06 ±0.04^a	0.00±0.00^a	0.00 ±0.00^a	**0.02±0.02^a**
	7th day	0.4 ±0.02^a	00±00^a	0.04±0.01^a	**0.03±0.02^a**
	14th day	0.06±0.01^a	0.01±0.08^a	0.1±0.01^a	**0.01±0.03^a**

Means within same column carrying different superscripts are significantly differ at (P<0.05).

Table 2. Effects of Echinacea purpurea (130mg/kg) and curcumin (400mg/kg) on lysozymes activity and nitric oxide of dexamethasone injected rabbits.

Group	Lysozymes (mg/dl)			NO (mg/dl)		
G1(control)	**1st day**	**7th day**	**14th day**	**1st day**	**7th day**	**14th day**
	32.3±0.4^a	31.4±0.7^b	31.3±1.8^b	35.6±1.7^a	32.4±1.3^a	34.5±1.1^a
G2 dexa treated	27.6±1.4^b	26.9±1.3^c	27.1±1.1^c	30.6±1.3^b	29.9±1.02^b	28.7±2.3^b
G3 dexa+ Echincea (130mg/kg)	28.1±1.6^b	36.8±1.5^b	43.4±2..9^a	29.3±0.9^b	33.1±1.9^a	33.7±1.3^a
G3 dexa+curcumin (400mg/kg)	26.5±0.9^b	41.5±0.5^a	47.4±1.4^a	29.9 ±1.4^b	34.8 ±2.1^a	36.1 ±1.7^a

Means within same column carrying different superscripts are significantly differ at (P<0.05).

There was also a marked reduction in monocytes count in dexamethasone-treated group (G2) in 1st, 7th and 14th days post dosing compared to the negative control group (G1). On the other hand, (G3) and (G4) showed an increase ($P < 0.05$) in monocytes count at 7th and 14th day post-treatment compared to dexamethasone-treated group.

3.2. Effects of Echinacea purpurea and Curcuma on serum lysozyme activity and nitric oxide levels

3.2.1. Effects on serum lysozyme activity

Serum lysozyme markedly decreased in dexamethasone-treated group (G1) in 1st, 7th and 14th day compared to the negative control group (G1). Meanwhile *E. purpurea* and *C. longa*-treated groups showed a depletion in serum lysozymes activity in 1st day in comparison with the negative control group. Conversely, both groups showed a significant increase in serum lysozymes activity in 7th and 14th days compared to dexamethasone-treated group (Table 2).

3.2.2. Effects on serum nitric oxide (NO) levels

Serum NO level was markedly decreased in dexamethasone-treated group in 1st, 7th and 14th day. Meanwhile *E. purpurea* and *C. longa*-treated groups showed reduced serum NO level in 1st day. On the other hand, both groups revealed elevated NO level at 7th and 14th day post treatment (Table 2).

3.3. Effects of tested plants on serum oxidative stress markers

3.3.1. Effects on serum catalase activity

Rabbits of the dexamethasone-treated group showed decreases serum catalase levels in 1st and 7th day compared to those of the negative control group. On the other hand, *E. purpurea*-treated group displayed decreased activity of serum catalase in 1st day, then displayed increased values in 7th and 14th days post dosing compared to dexamethasone-treated group. Meanwhile, *C. longa*-treated group showed increased activity of serum catalase on 7th and 14th day after dosing (Table 3).

Table 3. Effects of Echinacea purpurea (130mg/kg) and curcumin (400mg/kg) on serum catalases and MDA of dexamethasone injected rabbits.

Group	Catalases (mg/dl)			MDA (mg/dl)		
G1(control)	**1st day**	**7th day**	**14th day**	**1st day**	**7thday**	**14thday**
	4.4±0.18 a	4.2±0.12 b	3.9±0.05b	1.67±0.04c	1.8±0.02b	1.5±0.1b
G2control +ve	3.3±.03b	2.9±.02c	3.2±0.02b	3.1±0.16a	2.8±0. 8a	1.9±0.02a
G3 (dexa +Echincea (130mg/kg)	3.2±.08b	5.9±0.23a	6.2±0.4 a	1.9±0.12 bc	1.7±0.04b	1.2±0.05b
G4(dexa+curcumin 400mg\kg)	3.9±0.04a b	4.9±0.5a	5.18±0.2 a	2.1±0.02b	1.6±0.3b	1.4±0.01 b

Means within same column carrying different superscripts are significantly differ at (P<0.05).

Table 4. Effects of Echinacea purpurea (130mg/kg) and curcumin (400mg/kg) on total protein, albumin and globulin of dexamethasone injected rabbits.

Group	Total protein (gm/dl)			Albumin (gm/dl)			Globulin(gm/dl)		
G1	**1st day**	**7th day**	**14th day**	**1st day**	**7th day**	**14th day**	**1st day**	**7th day**	**14th day**
	6.9±0.2 a	6.5±0.4b	6.9 ±0.2b	4.2 ±0.1 a	3.9±0.06 b	3.6 ± 0.3 b	2.8 ± 0.4 a	2.6± 0.3 b	**3.3 ±0.2a**
G2	5.9±0.5c	5.7±0.4c	5.6 ±0.2 c	2.6±0.09 c	2.9±0.42 c	3.1 ±0.6 b	2.6 ± 0.9 b	2.2 ± 0.4c	**2.6 ±0.3b**
G3	6.3 ± 0.1 b	7.4 ±0.3a	7.8±0.1 a	3.4 ±0.1 b	4.3 ±0.12 a	4.5±0.7 a	2.9± 0.1 a	3.1± 0.5 a	**3.3±0.2a**
G4	6.5± 0.3 b	6.9 ±0.2 ab	7.1 ±0.8 a	3.5 ±0.08 b	4.1 ±0. 9 a	4.3±0.9 a	2.8 ± 0.1 a	3.1± 0.5 a	**3.2 ± 0.5 a**

Means within same column carrying different superscripts are significantly differ at (P<0.05).

3.3.2. Effects on serum MDA levels

Animals of the dexamethasone-treated group showed increased serum MDA levels in 1st, 7th and 14th days post-treatments compared to animals of the negative control group. *E. purpurea* and *Curcuma longa*-treated groups showed decreased serum MDA levels in 1st, 7th and 14th day compared to dexamethasone-treated group (Table 3).

3.4. Effect of Echinacea purpurea and Curcuma on serum biochemical parameters

3.4.1. Effect on serum total protein concentration

Dexamethasone-treated animals showed reduced levels of serum total protein in 1st, 7th and 14th. Meanwhile on 1st, 7th and 14th day both *E. purpurea* and *C. longa*-treated groups showed a marked increase in total protein levels compared to the negative control (Table 4).

3.4.2. Effect on serum albumin concentration

There was a significant decrease in the serum albumin level in dexamethasone-treated rabbits compared to those of the negative control in the 1st and 7th day, while *E. purpurea* and *C. longa*-treated groups showed increased ($P < 0.05$) levels of serum albumin in 1st, 7th and 14th day compared to dexamethasone-treated group (Table 4).

3.4.3. Effect on serum globulin concentration

Results revealed reductions in serum globulin level in 1st, 7th and 14th days in dexamethasone-treated animals compared to those of the negative control. On the other hand, both *E. purpurea* and *C. longa*-treated groups showed increased serum globulin levels in 7th and 14th day post dosing compared to the negative control group (Table 4).

3.5. Histopathological findings

3.*5.1. Liver lesions*

Histopathological examination of liver sections of rabbits in the negative control group showed normal hepatocyte (Fig. 1A). Liver of the dexamethasone-treated rabbits revealed degenerative changes in hepatocytes, intralobular fibroblastic proliferation forming bridging fibrosis (Fig.1C). Examination of liver of *E. purpurea*-treated rabbits showed normal hepatocytes radially arranged around the central vein (Fig.1E). Examination of liver of *C. longa*-treated rabbits revealed normal hepatocytes with very mild degenerative changes (Fig.1G).

3.5.2. Kidney lesions

Histopathological examination of kidney sections of rabbits in the negative control group showed normal renal tubular epithelium (Fig. 2A). Whereas, kidney of the dexamethasone-treated rabbits revealed congestion in glomeruli, degenerative changes in renal tubular epithelium, and proliferation in mesangial cells (Fig.2 C,D). *E. purpurea*-treated rabbits showed mild proliferation of glomeruli and normal renal tubular epithelium (Fig. 2E). *C. longa*-treated rabbits showed normal glomeruli and normal renal tubular epithelium (Fig.2 G).

3.5.3. Spleen lesions

Histopathological examination of spleen sections of rabbits in the negative control group showed normal lymphoid tissue (Fig.3 A). Whereas, spleen of the dexamethasone-treated rabbits revealed depletion in lymphoid tissue and normal red pulp (Fig.3 C). *E. purpurea*-treated rabbits showed normal lymphoid aggregation and normal red pulp (Fig.3 E). *C. longa*-treated rabbits showed normal lymphoid aggregation and normal red pulp (Fig.3 G).

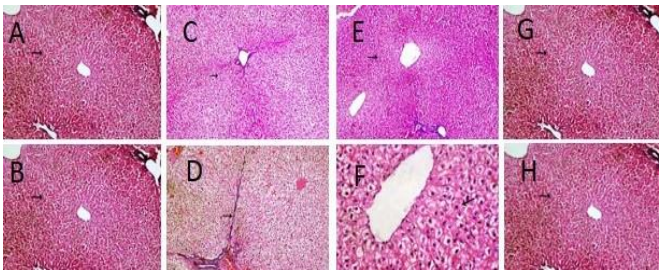

Figure 1. Microscopic picture of liver sections of negative control group (A), (HE, 100x) showed normal histology of hepatocytes in control group (A&B), and intralobular fibroblastic proliferation forming bridging fibrosis (arrow) and normal portal vein in dexamethasone-treated group (C). Liver sections of *E. purpurea*-treated group (E&F) showed normal hepatocytes and normal radial arrangement around central vein (HE, 100x), and liver sections of *Curcuma longa*-treated group (G) showed normal hepatocytes and normal radial arrangement around central vein (HE, 100x).

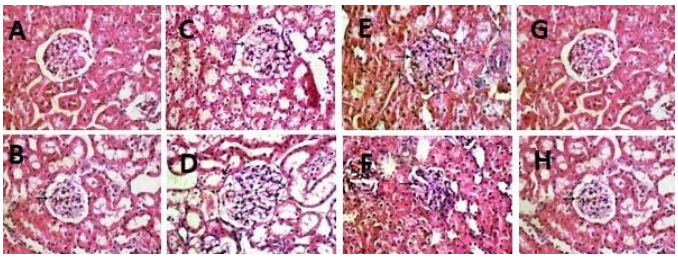

Figure 2. Microscopic picture of kidney sections showing normal histology of renal tubular epithelium in negative control group (A&B) (HE, 100x), and congestion in glomeruli (arrow) and degenerative changes in renal tubular epithelium and proliferation mesangial cells in dexamethasone-treated group (C), kidney sections of *E. purpurea*-treated groups (E) showed mild proliferation of glomeruli (arrow) and normal renal tubular epithelium (HE, 400x), kidney of *Curcuma longa*-treated group (G), showed normal glomeruli (arrow) and normal tubular epithelium (HE, 400x).

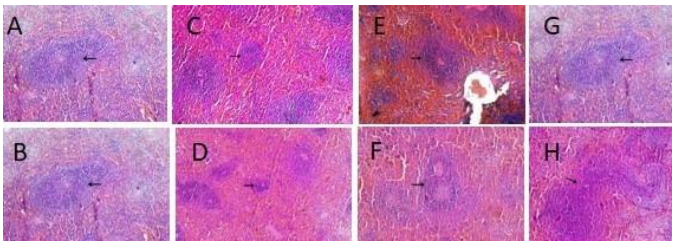

Figure 3. Microscopic picture of spleen sections showed normal lymphoid tissue in control group (A), spleen of dexamethasone-treated group (C) showed depletion of lymphoid tissue (arrow) and normal red pulp (HE, 100x), spleen sections of *E. purpurea*-treated group (E&F) showed normal lymphoid aggregation (arrow) and normal red pulp (HE, 100x), spleen of *Curcuma longa*-treated group (G) showed normal lymphoid aggregation (arrow) and normal red pulp (HE, 100x).

4. DISCUSSION

The present study aimed to investigate the possible effects of *Echinacea purpurea* and *Curcuma longa* on dexamethasone injected rabbits through evaluation of hematological, biochemical, immunological parameters and the associated pathological lesions.

Results of the current study revealed an immunosuppressive effect of dexamethasone. These results are similar to those of Abu-Akkada [19] who found that single administration of dexamethasone in rats markedly decreased the number of WBCs, as well as the number of lymphocytes, monocytes, neutrophil and eosinophil, and that these reduction might have resulted due to redistribution of WBCs, a degree of cell death and a decreased regeneration. Similarly, Ahmed et al. [20] demonstrated a decreased number of WBCs and lymphocyte in rabbits treated with dexamethasone.

The findings of the current study revealed a possible role of *E. purpurea* and *Curcuma longa* in modulation of immune state of rabbits treated with dexamethasone. These findings could be supported by those of Torkan et al. [21] who stated that administration of *E. purpurea* to rats produced a significant increase in WBC, neutrophil and monocyte counts, and improved phagocyte activity. Similarly, Sharma et al. [22] reported that supplementation of curcumin to diets of mice increased neutrophil, eosinophil and lymphocytic count.

Kulkarni et al. [23] demonstrated that administration of dexamethasone induced immune suppression by inhibiting the basal mRNA expression of lysozyme and secretory leukocyte peptidase. On the other hand,, Nazerian et al. [24] reported that serum lysozyme activity increased in *E. purpurea*-treated mice.

The findings of the current study are consistent with those of Mondo et al. [25] and Ong et al. [26] who found that levels of plasma nitrate/nitrite, a marker of total body NO synthesis, were reduced in rats and mice made hypertensive by dexamethasone treatment. In addition, Fouad et al. [27] found that dexamethasone administration decreased nitric oxide production finding that the author attributed to decreased iNOS mRNA and protein expression and NO formation.

Several studies demonstrated that E. purpurea stimulated the production of nitric oxide and TNF-α [28 and 29]. Concomitant with that, several studies demonstrated that nitric oxide levels and antioxidant enzymes increased after curcumin feeding [30 and 31]. The findings of the current work are also similar to those of Fouad et al. [27], and Hasona [32] who stated that dexamethasone administration evoked a significant decrease in catalase activity in rats.

The findings of the current study refer to a possible ameliorative effect of *E. purpurea* supplementation. The activity of antioxidant enzymes catalase (CAT) has been shown to increase in rats treated with *E. purpurea* [33]. A protective effect of *E. purpurea* against oxidative stress has also been demonstrated in mice [28]. The findings of the present work are similar to those of Sankar et al. [34] who mentioned that curcumin significantly increased catalase levels and can be a potent protective agent against biochemical alterations and oxidative damage in rats.

The current study demonstrated that dexamethasone-treated rabbits showed elevation in catalase activity, and that concurrent treatment of dexamethasone-treated rabbits with *E. purpurea* and *C. longa* led to a significant reduction in serum MDA levels. El-Sawy et al. [35] demonstrated that dexamethasone-treated rats showed a significant increase in serum MDA levels, and a significant decrease in total antioxidant capacity levels.

Concerning the antioxidants and oxidative stress markers evaluation, rabbits treated with *E. Purpurea*

showed a significant elevation in serum CAT levels, and a significant decrease in serum MDA levels. This effect could be attributed to the antioxidant properties and phenolic compounds of the plants [36].

Beneficial effects of *Curcuma longa* has been suggested to include antioxidant defense system, and scavenging of free radicals via prevention of lipid peroxidation. Curcumin might have a protective effect against cisplatin-induced testicular damage and oxidative stress in rabbit [30, 37].

In same context, Abd Elazem et al. [38] found that dexamethasone induced a significant reduction in total protein, gamma globulin, total globulin, alongside insignificant reduction in albumin. Furthermore, Hussein et al. [39] recorded a significant increase in total protein and globulin in rabbits given *E. purpurea*. Also, Radwan et al. [40] said that oral administration of *E. purpurea* with dexamethasone resulted in a great normalization in the levels of liver's protein. Similarly, Diab et al. [41] found that curcumin induced a significant increase in total protein level and ameliorated the gentamicin-induced decrease in serum total protein, albumin and albumin/globulin ratio.

Considering histopathological findings, the cross sectioned liver of dexamethasone-treated rabbits showed degenerative changes of hepatocytes and intralobular fibroblastic proliferation forming bridging fibrosis and normal portal vein. These findings are similar to those reported by Hussein et al. [39] and Noel [42] who stated that the liver sections of rabbits treated with dexamethasone showed many histopathological changes including necrosis of hepatocytes and congestion of sinusoids with fatty changes.

The section of rabbits' liver treated with *E. purpurea* and *C. longa* showed an improved histopathological picture of liver tissue with normal hepatocytes and normal radial arrangement around central vein. This finding is similar to that of Rezaie et al. [43] and Hashem et al. [44] who stated that the liver of infected broiler chicks supplemented with *E. purpurea* showed an improvement with slight degeneration of hepatocytes and slight inflammatory cell infiltration. The findings are also similar to those reported by El-Agamy [45] and Kyung et al. [46] who stated that oral administration of *C. longa* ameliorated aflatoxin-B1 induced liver damage in rats and counteracted oxidative stress caused by aflatoxin, suggesting that *C. longa* ameliorated liver cirrhosis by its anti-inflammatory and antifibrotic effect.

Results of the current study showed that the cross sectioned spleen of dexamethasone-treated rabbits showed depletion of lymphoid tissue and normal red pulp. This finding is similar to that of Xiping et al. [47] who reported spotty necrosis in spleen lymphoid nodules with enlargement and congestion of medullary sinuses of dexamethasone-treated rats. It is also similar to that reported by Hussein et al. [39] who reported necrosis and fibrosis in epithelial lining convoluted tubules 9n dexamethasone-treated rats. Similarly, Hashem et al. [44] clarified that kidney of broiler chicks infected with E. coli and supplemented with *E. purpurea* showed apparently normal glomeruli with mild degeneration in epithelial lining of renal tubules. Rezaie et al. [43] demonstrated that *E. purpurea* had a protective effect against diethyl nitrosamine toxicity in rats with less necrotic cells in proximal tubules. Momeni and Eskandari [48] stated that curcumin significantly reversed the adverse effects of sodium arsenite on kidney of mice compared the diameter of glomerulus and proximal tubule.

The examined section of spleen of rabbits treated with E. purpurea and *C. longa* showed normal lymphoid aggregation and normal red pulp. This finding is similar to that of Hashem et al. [44] and Tarasub et al. [49] who indicated that pretreatment of rats with *C. longa* before cadmium application prevented changes in spleen, splenic sinusoids and cells in red and white pulp.

Conclusion

It could be concluded that *Echinacea purpurea* and *Curcuma longa* may have the potential to ameliorate dexamethasone-induced immunosuppression, and that this potential appeared more potent in *Curcuma longa*. Both plant extracts also corrected the leukogram picture highlighting therefore a prominent antioxidant effect.

Conflict of interest statement

The authors declare that there is no conflict of interest in the current research work.

Research Ethics Committee permission

The current research work was permitted by Research Ethics committee, Faculty of Veterinary Medicine, Mansoura University.

Authors' contribution

A.A. and M.A. conducted the experiment, analytical procedures, research writing, A.A. designed the experiment, and revised the manuscript, M.A. revised the manuscript.

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