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RESEARCH ARTICLE

Protective Effect of Echinacea purpurea Plant Extract Against Pasterullosis in Rabbits: Hematological, Biochemical and Oxidative Stress Studies

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Abstract

Echinacea purpurea (E. Purpurea), as one of the most important plants, has been used in prevention and control of infectious diseases of respiratory systems.In this study,we investigated the effect of Echinacea andenrofloxacin on Pasteurella multocida type A infection in male white New Zealand rabbits through evaluation of the hematological, biochemical, phagocytic activities, and oxidative stress markers.Fortymale white New Zealand rabbits were divided intofour equal groups; group 1 was kept as a control,group 2was intranasally infected with P.multocidatype A(4x107 CFU/mL/rabbit) at the 14th dayfrom beginning of experiment (FBE), group 3 was administrated E.Purpure orally (130mg/kg body weight "B.W.") day after day from 1st day to the 35th day and infected with P. multocidaat the 14th day FBE and group 4was intranasally infected with P. multocida at the 14th day FBE, then treated with enrofloxacin(10 mg / kg B.W. in drinking water) after the appearance of the clinical signsfrom the 18th-20th day.The results revealed that P.multocida infection in rabbits produced macrocytic hypochromic anemia (RBCs = 5.26 x106/µL, MCV = 76.06 Fl , MCHC = 24.99%), leukocytosis (14.09x103/µL) with a reduction in the phagocytic percent (51.60 %) and phagocytic index (0.26). We observed decrease in serum levels of total protein, albumin, and globulin. Moreover,significant increase in serum alanine aminotransferase (ALT, 34.4 U/L)and alkaline phosphatase (ALP, 27.80 U/L)were recorded.Also, the serum bilirubin (total bilirubin = 1.03mg/dL, direct bilirubin = 0.61 mg/dL and indirect bilirubin = 0.42 mg/dL)levels were significantly elevated. Serum urea (47.32mg/dL) and creatinin levels (2.10 mg/dL) were significantly increased. Furthermore, P.multocida infection in rabbits induced oxidative stress,which observed in a significant reduction in the serum catalase (CAT,3.13 nmol/L)with elevation in the lipid peroxidation (MDA, 3.46 nmol/L). In conclusion, Echineceatreatment before and after rabbit infection with P. multocida type Ais able to ameliorate the alterations in all studied parameters compared to enrofloxacin treated rabbits.

Key words: Rabbits, Echinaceapurpurea, Enrofloxacin,Pasteurellamultocida,Oxidative stress.

Introduction

*Echinaceapurpurea*is one of the most important medicinal herbs of the genus *Echinacea*[1].It is a purple cone flower that is widely used as a medicinal plant in the United States and Europe. The main active principles are alkamides, glycoproteins, caffeic acid derivatives and polysaccharides.*Echinacea purpurea* has immunostimulatory,immunomodulator, antibacterial, anti-inflammatory, wound healing, antiseptic and antineoplastic properties and growth promoting effects. Moreover, it has some short term effects against herpes, vesicular stomatitis and *influenza* viruses [2- 7]. *Echinacea*

improves the immunity,decreasesthe blood sugar levels, anxiety, and inflammation.Also, it has anti-cancer and, skin health improvement effects as well as it was documented to be effective inprevention and complextreatment of Corona virus[8]. *Echinacea purpurea(E. Purpurea)*is one of the most promising herbal medicine for improving the immunity of various species of animals and humans [9].

Enrofloxacin is the first fluoroquinolone of second generation quinolones[10]. It acts by inhibiting the DNA gyrase, which is essential for the coiling and uncoiling of bacterial DNA and packing it within the cell [11]. Enrofloxacin is indicated for the treatment of bacterial infections of the alimentary and respiratory tracts; it is rapidly distributed through the tissues before being eliminated [12].

Pasteurellosis is a common andhighly contagious disease in domestic rabbits thattransmitted by direct contact and aerosol transmission. It is characterized by high morbidity and mortality rates [13]. About 30–90% of apparently healthy rabbits may be a symptomatic carrier[14]. It is one of the main causes of economic losses in rabbits [15]. *Pasteurella* infection is depending on age and stress factors [16].It has three forms in rabbitariesin Egypt. The1st one is, subacute form during first two days post infection (PI). This form manifested by drowsiness, sneezing, pyrexia and anorexia. In the third day, they became off food with lacrimation and mild diarrhea. In the later stages, infected rabbits showed dullness, emaciation, coughing and breathing with a sound "snuffling". Also nasal discharge became turbid and sticky[17].The subclnical infection was established in the upper respiratory tract. After colonization, the infection extends to the rest of respiratory tract and can cause clinical rhinitis, conjunctivitis, pneumonia, tracheitis or otitis media[14].The 2nd form is characterized by abscess formation at any part in the body and the case is terminated with septicemia[18]. Otitis media or interna form includes accumulation of pus or fluid in the middle or inner ear, so the rabbit twist its head e.g "wry neck" or torticollis. Also, subcutaneous and visceral abscesses may be clinically silent for long periods and spontaneously rupture[19]. The third form manifested by urogenital infection, mastitis, pyometra, orchitis, infertility, abortion and meningitis [20].

Thisstudy aimed to investigate the efficacy of*E. Purpurea* plant and enrofloxacin incontrolling*P.multocida*experimental infection in rabbits.

Material and Methods

Experimental animals

A total number of forty, 30 days old, apparently healthy male white New Zealand rabbits (750-1000g) were purchased from the Faculty of Agriculture, Zagazig University, Egypt. These rabbits were kept under good hygienic conditions, housed in clean metal cages, kept at 24 ± 2 °C with a 50–60% humidity and a 12-hour light:dark cycle, fed on well balanced commercial ration and water was provided *ad-libitum*. Rabbits were kept for 2 weeks before starting the experiment.The management and treatment procedures were done according to the Guidelines for the Care and Use of Laboratory Animals of the National Institutes of Health

Chemical treatment agents

Enrofloxacin (Opitryl)was manufactured by El-Obour Modern Pharmaceutical Industries Co, Egypt. Each 100 mL contains 10g enrofloxacin, it was given as a 10% oral solution.*Echinacea purpurea* dry extract capsules (each one contains 175mg) were purchased from Arab Company for

Pharmaceuticals andMedicinal Plants, Purpureaaco-Egypt. All the biochemical tests were performed using test kits of Diamond Diagnostics, Egypt.

Bacterial strain

Pasteurullamultocida typestrain C51-17 (capsular type A) was obtained from the Animal Health Research Institute, Dokki, Giza, Egypt. Rabbits were infected intranasally by a dose of 1mL with a final concentration of $4x10^7$ colony forming unit (CFU).

Experimental design

Fortyapparently healthy male,white New Zealand rabbits, were randomly classified into four equal groups (each group contains10 rabbits). Group 1 was given1 mL phosphate buffer saline(PBS)intranasal (IN) and kept as a negative control. Group 2 was infectedwith *P. multocida* type A ($4x10^7$ CFU/mL/rabbit)at the 14^{th} day [21], from the beginning of the experiment (FBE) (a positive control). Group 3 was orally administrated*E.purpurea*(130 mg/kg B.W.) day after day [22] from 1^{st} day to the 35^{th} day and infected with the above mentioned dose of *P. multocida*type A at14^{th} day FBE. Group 4 was infected IN with *P.multocida*type Aat the 14^{th}day, and treated with enrofloxacin (10mg/kg B.W.), orally by gavag for 3 days after the appearance of the clinical signs [23].

Samples collection and preparation

Blood samples were collected from 3 rabbits in each group under anesthesiaon the 35^{th} dayFBEfrom the ear vein. TwomL of the blood was collected in a heparinized test tube for evaluation of phagocytic activities, 0.5mL of the blood collected in a test tube with ethylene diamine tetra acetic acid (EDTA) for hematological examination, and 5mLwas collected inserum separation glass tubewithout anticoagulant to measure biochemical parameters.

Hematological assay

Collected blood samples on EDTA (10%) were used for the eval

uation of total erythrocyte count, packed cell volume (PCV), hemoglobin (Hb), white blood cells (WBC) and differential leukocyte counts (DLC) according to Coles[24]. Mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC) values were calculated.

Phagocytic percent and index

The heparinized blood samples were used for leukocytes separation. *Candida albicans* (*C.albicans*) was prepared at Animal Health Research Institute Zagazig and used for determination of the phagocytic activity according toWilikinson[25]. Macrophages (monocytes and lymphocytes) number containing *C.albicans* (phagocytic %) that were engulfed by 100 phagocytes in each individual preparation was examined under light microscope under oil immersion lens. The phagocytic index was calculated through evaluating the average number of attached and ingested*C. albicans* multiplied by the phagocytic %[26].

Biochemical assay

Serum samples were analyzed for determination of alanine aminotransferase (ALT)by the method of Reitman and Frankle[27] and alkaline phosphatase (ALP) according to a previously published protocol[28]. Total protein and albumin levels were measured described elsewhere[29,30]. The globulin level was calculated by subtracting the obtained albumin level from obtaining total protein level according to Doumas and Biggs[31]. Serum bilirubin (total and direct) was determined according to Colombo [32] and the indirect bilirubin level was calculated as the difference between total and direct bilirubin. Urea and creatinine were determined documented previously [33, 34].

Oxidative stress markers assay

Serum samples were used to determinethe catalase (CAT) activity which was measured by an enzymatic colorimetric method using ready-made kitsprovided by BiodiagnosticEgypt,CAT. No.CAT 25 17according to Aebi [35], and lipid peroxidation (MDA) was determined depending on the thiobarbeturicacid reactivityof ***Satoh***[36], CAT.No. 25 29.

Statistical Analysis

The obtained data was statistically analyzed using "F" test one wayanova according to Tamhans and Dunlop (37) using "MSTAT-C" computer program. Means in the same column followed by different letters were statistically significant at P <0.05 and the highest values were represented with the letter (a).

Results

Clinical signs and mortality rate

Negative control rabbits appeared healthy without any clinical signs of illness and no mortalities were recorded. On the other hand, rabbits in positive control group showed ruffled fur, sneezing, nasal discharge, purulent exudates from nose, abnormal respiratory sound and mortality rate reached60%.Both rabbits treated with *Echinacea purpurea*and enrofloxacin then infected with *P.multocida*showed mild clinical signs with mortality rates of 33.33%.and 20% in groups3and 4, respectively.

Hematological findings

Rabbits infected with *P. multocida*showed a significant decrease*(*P < 0.05*)*in RBCs count, Hb concentration, PCV and MCHC, with a significant increasein MCV (macrocytic hypochromic anemia) compared with the control. While rabbits infected and treated with *E. purpura* and enrofloxacin showedimprovement inRBCscount,Hb concentration,PCVandMCHCwith significant decrease (P < 0.05) in MCV in comparison with infected rabbits(Table 1).

In comparison to negative control rabbits, infected rabbits showed asignificant increase (P < 0.05)in the counts of leukocytes, granulocytes and monocytes with non-significant change in lymphocytic count.While *E. purpure* and enrofloxacin treated rabbits showed a significant decrease (P <0.05) in total leukocytes counts, granulocytic count and monocyte count with non-significant change in lymphocyte count when compared to the infected group (Table2). Moreover,*P. multocida* infected rabbits showed a significant decrease (P < 0.05) in phagocytic percent and phagocytic index compared to control negative rabbits, while *E. purpure* and enrofloxacin treated rabbits showed a significant increase (P < 0.05)in phagocytic percent and phagocytic index comparing with infected rabbits(Table2).

Biochemical findings

Serum activities of ALT, ALP and bilirubin (total, direct and indirect) levels showed a significant increase (P < 0.05) in rabbits infected with *P.multocida* compared to the negativecontrol, while treated groups 3 and 4 showed a significant decrease (P < 0.05) in serum ALT, ALP activities and bilirubin levels when compared to infected rabbits (Table 3). Serum urea and creatinine levels showed a significant increase (P < 0.05) in group2 compared with the negative control, while groups3and 4 showed a significantdecrease(P < 0.05) compared with the infectedgroup(Table4).

Antioxidant and oxidative stress findings

Rabbits infected with *P. multocida*showed a significant increase (P < 0.05) in serum CAT activity and significant decreased (P < 0.05)in MDA level compared to the negative control.

While rabbits treated with *E.purpura*and enrofloxacin (groups 3 and 4) showed a significant increase (P < 0.05)in serum CAT activity with a significant decrease(P < 0.05)in MDA level compared to infected rabbits(Table 5).

Table (1): Erythrogram (mean value ±SE) of rabbits' groups at the 35 th day from the beginning of the experiment.

Groups	Parameters					
	RBCs Count x10^6/µL	**Hb g/dL**	**PCV %**	**MCV Fl**	**MCH pg**	**MCHC (%)**
GP1 (Control)	6.48^a ±0.30	12.50^a ±0.37	43.15^a ±0.98	66.92^b ±1.04	19.38^a ±0.13	28.96^a ±0.27
GP2 (*P.multocida*)	5.26^b ±0.14	10.00^c ±0.33	40.00^b ±0.85	76.06^a ±1.83	19.00^a ±0.46	24.99^b ±0.14
GP3 *(Echinacea+P.multocid*a)	6.10^a ±0.18	12.00^{ab} ±0.48	42.00^{ab} ±1.00	68.85^b ±0.88	19.67^a ±0.15	28.57^a ±0.15
GP4 *(P.multocida*+Enrofloxacin)	6.21^a ±0.22	12.20^a ±0.23	42.70^a ±0.24	68.76^b ±0.60	19.46^a ±0.37	28.57^a ±0.92

Means within the same column carrying different letters are significantly different at P < 0.05

RBCs Count : Red blood cell count;MCV : Mean corpuscular volume;Hb: Hemoglobine;MCH: Mean Corpuscular Hemoglobin;MCHC: Mean Corpuscular Hemoglobin Concentration;Fl : femtoliters (one thousand trillionths of a liter) per/cell

PCV: Packed Cell Volume;pg: picograms/ cell (one trillionth of a gram);x10^6/µL: millions of cells per microliter;g/dL: grams per deciliter

Table (2): Leukogram and phagocytic activity (mean value ±SE) of rabbits' groups at the 35 th day from the beginning of the experiment.

Groups	TLC (x10^3/µL)	Differential leukocytic count			Phagocytic %	Phagocytic Index
		Granulocytes (x10^3/µL)	Lymphocytes (x10^3/µL)	Monocytes (x10^3/µL)		
GP1 (Control)	12.74^b ±0.12	5.63^b ±0.11	6.56^a ±0.29	0.55^b ±0.02	59.30^a ±1.76	0.60^a ±0.04
GP2 (*P.multocida*)	14.09^a ±0.17	6.80^a ±0.03	6.43^a ±0.21	0.85^a ±0.06	51.60^b ±0.88	0.26^c ±0.03
GP3 *(Echinacea+ P.multocid*a)	13.14^b ±0.14	6.00^b ±0.09	6.56^a ±0.11	0.58^b ±0.03	60.12^a ±0.44	0.50^{ab} ±0.08
GP4 *(P.multocid*+Enro floxacin)	12.89^b ±0.16	5.80^b ±0.17	6.54^a ±0.13	0.55^b ±0.05	58.25^a ±1.06	0.51^{ab} ±0.14

Means within the same column carrying different letters are significantly different at $P< 0.05$, TLC : Total Leukocytic Count, $x10^3/\mu L$: Thousand per microliter

Table (3): Some serum biochemical parameters (mean value ±SE) of rabbits' groups at the 35 th day from the beginning of the experiment.

Groups	Parameters				
	ALT U/L	**ALP U/L**	**Total bilirubin mg/dL**	**Direct bilirubin mg/dL**	**Indirect bilirubin mg/dL**
GP1 (Control)	23.60^{c} ±0.45	18.80^{c} ±0.25	0.56^{c} ±0.02	0.31^{cd} ±0.01	0.25^{c} ±0.01
GP2 *(P.multocida)*	34.40^{a} ±0.87	27.80^{a} ±0.72	1.03^{a} ±0.06	0.61^{a} ±0.04	0.42^{a} ±0.03
GP3 *(Echinacea+P.multocid*a)	27.20^{b} ±0.55	21.00^{b} ±0.30	0.82^{b} ±0.03	0.41^{b} ±0.02	0.35^{b} ±0.01
GP4 *(P.multocida*+Enrofloxacin)	24.10^{c} ±0.95	20.00^{bc} ±0.28	0.62^{c} ±0.05	0.35^{bc} ±0.02	0.27^{c} ±0.02

Means within the same column carrying different letters are significantly different at $P< 0.05$
ALT: Alanine transaminase, mg/dL: milligramper deciliter, ALP: Alkaline Phosphatase U/L: international units/liter.

Table (4): Some renal function tests (mean value ±SE) of rabbits' groups at the 35 th day from the beginning of the experiment.

Groups	Urea mg/dL	Creatinine mg/dL
GP1 (Control)	38.60^{c} ±0.32	1.10^{c} ±0.05
GP2 (*P.multocida*)	47.32^{a} ±0.58	2.10^{a} ±0.04
GP3 *(Echinacea+P.multocid*a)	41.50^{b} ±0.28	1.52^{b} ±0.04
GP4 *(P.multocida*+Enrofloxacin)	39.50^{c} ±0.38	1.25^{c} ±0.09

Means within the same column carrying different letters are significantly different at $P< 0.05$
mg/dL: milligram /deciliter

Table(5): Serum catalase and malondialdehyde (mean value ±SE) of rabbits' groups at the 35 th day from the beginning of the experiment.

Groups	CAT (nmol/L)	MDA (nmol/L)
GP1 (Contro)	4.56^{a} ±0.32	1.86^{b} ±0.19
GP2 (*P.multocida*)	3.13^{b} ±0.17	3.46^{a} ±0.23
GP3 *(Echinacea+P.multocid*a)	4.30^{a} ±0.24	2.04^{b} ±0.05
GP4	4.36^{a}	2.00^{b}

(*P.multocida*+Enrofloxacin)	±0.14	±0.13

Means within the same column carrying different letters are significantly different at $P< 0.05$
CAT : Catalase, MDA: Malondialdehyde, (nmol/L) : Nanomoles Per Liter

Disscussion

Pasteurella multocida is the most commonbacterial pathogen in rabbits. Stress, such as shipping, mating and handling, may cause replication of many serotypes of *P. multocida*. Depression, in appetence, rhinitis,sneezing,coughing, nasal discharge, conjunctivitis, breathing with a snuffling sound, pneumonia and torticollis were recorded in *P.multocida* infected rabbits, thatattributed to theinfection withpathogenvia respiratory route causing inflammation of mucous membranes before spreading through blood [14, 16, 19, 20 and 38]. The high mortality ratewas recorded in the infected rabbits that resulted from the side effect of *P. multocida*endotoxin [15, 17]. Severity of clinical signs and mortality rates was improved in the treated groups (3, 4), which mainly attributed to the presence of alkaloids, tannins and sterols or total phenols and flavonoids in the *E. purpura* that have antimicrobial activity [39] and the antibacterial activities of enrofloxacin[40].

Concerning the erythrogram, *P. multocida* infected rabbits exhibited a significant reduction in RBCs count, Hb concentration and PCV % with the development of macrocytic hypochromic anemia that attributed to the hemorrhagic effect of the bacteria and/ or its endotoxin on RBCs, which led to reduce their life span which stimulate active erythropoiesis that led to reticulocytosis. Our data supported the previously obtained results by Praveena and coauthors[41].Rabbits protected and treated with*E. purpura* before and after*P.multocida* infection (group 3) showed animprovement in the erythrogram. This indicates that using *E. purpura* as prophylactic and treatment is more effectivein protect the cells [42, 43].Enrofloxacin treated rabbits(group 4) also showed animprovement in the erythrogram due to the effectiveness of this antibiotic against*P. multocida*.

Leukocytosis was observed in rabbits infected with *P.multocida* due to heterophilia and monocytosis. Such elevation in heterophils and monocytes counts could be due to the infection and inflammation[24]. Heterophiles and monocytes counts were reduced in rabbits treated with *E. purpura*before and after infection with *P.multocida*due to anti-inflammatory and antibacterial effect of *E.purpurea*[44].Also, there was an improvement in the total leucocytic count, heterophils and monocytes in enrofloxacin treated rabbits.

Rabbits infected with *P.multocida* revealed a reduction in the phagocytic percent and phagocytic index, which attributed to the effect of oxidative stress that exhaust the body immune response resulted from infection and /or *P. multocida* endotoxin [45].Phagocytosiswas inhibited by*P.multocida* capsular polysaccharides [46].While, rabbits treated with *E.purpurea* revealed a significant improvement in the phagocytic percent and index,attributed to the glycoprotein rich fractions of *E.purpurea* that enhances the phagocytic activity[47, 48], also the immune-stimulatory effects of lipophilic alkylamides, polar caffeic acid derivative and cichoric acid of *E.purpurea* [49, 50].The improvement of phagocytic percent and index was recorded in enrofloxacin treated rabbits due to the effectiveness of this antibiotic against *P. multocida* so reduces its negative impact on phagocytic percent and index.

Regarding to the biochemical results, rabbits infected with *P. multocida*showed reduction in the total protein and albumin with an elevation of globulin levels,which

may be due to areduction in feed intake by diseased animal and / or protein synthesis by damaged liver. Also, it may be due to increase protein loss nephropathy [14]. While the hyperglobulinemia indicated the immune defense of rabbits due to respiratory infection and increase the level of antibodies to combat this infection[51, 52]. Hepatic enzymes (ALT and ALP) significantly elevated in the infected rabbits[53],such elevation in ALTactivity due to the hepatocellular damage resulted from the infection and subsequent liberation of these enzymes from damaged hepatocytes into the circulation, also serum ALP elevation is associated with cholestasis [54].

Rabbits received *E.purpura* before and after *P.multocida* infection showed an elevation in the protein levelwithreduction in serum activities of ALT and ALP that attributed to the hepato-protective effect of *Echinacea* [7 and 55], also *Echinacea* species stimulate the immune response of the body [56].Moreover, rabbits treated with enrofloxacin showed a significant improvement in the total protein, albumin, globulin and hepatic enzymes. Fluoroquinolones act by interfering with bacterial DNA synthesis so preventing the growth and replication of *P.multocida*[57]reducing the damaging effect of it.Furthermore, serum total, direct and indirect bilirubin were elevated in infected rabbits,thatattributed to hepatocellular damage resulted from the effect of *P.multocida* and/or its toxin on hepatocytes [17]. Thus, all major excretory steps of bilirubin may be distributed and resulted in an elevation in total bilirubin [54], these findings agree withGlavits and Magyer[58]. Administration of *E.Purpurea* before and after *P.multocida* infection induced reduction in total, direct and indirect bilirubin, which attributed to the presence of large amount of chicoric acid and caftaric acid in *E.Purpurea*, which had a role in inhibition of hyaluronidase enzyme, that secreted by bacteria to facilitate penetration into tissue [59], so treatment with*E.Purpurea*protect hepatic cell and reduce the elevated bilirubin[55]. Moreover, usingenrofloxacin could counteract the effect of *P. multocida* and reduce the level of bilirubin.

Concerning the kidney function tests, *P.multocida* infected rabbits exhibited a significant elevation in the levels of serum urea and creatinine levels,which attributed to the renal damage induced by *P. multocida*and /or its endotoxin on renal tissue. Also, the circulating toxin may lead to reducethe renal blood flow and glomerular filtration rate leading to accumulation of serum nitrogenous end products[60], our results run on the same ground with those reported byGaber[15].

Rabbitsadministered *E.purpura* before and after infection revealed amelioration of renal function,whichconfirms the ability of *E.purpura* to protect the renal tissue against infection and toxins due to its high content of natural metabolites that have antibacterial activity [61], also the alkamides content of *E.Purpure* down regulates inflammatory responces in the tissue [62]. Our results are in accordance withpreviously publishedresearches[54, 63].Moreover, enrofloxacin administered rabbits showed improvement in the serum urea and creatininlevels, whichattributed to its antibacterial activity, which suppress bacterial infection and decreasing the damaging effect on the kidney[64].

Concerning the oxidative stress marker evaluation, infected rabbits showed a significant reduction in serum activity of CAT with elevation MDA level. From our opinion, this may be due to endotoxin effect of *P.multocida*which increased the oxidative stress and exhausting the antioxidant defense system, leading to decrease of CAT enzyme and increase of lipid peroxidation [37and65]. Rabbits treated with *E.purpurea* showed a significant elevation in the serum CAT level with the reduction MDA level,

which may be due to thenatural components found in *E.purpurea* (echinacoside, caffeic acid, total phenols, and flavonoid), which have antioxidant activities by elimination of free radicals and subsequently preventdestruction of cell [7, 39,66, 67, 68]and the alkamides contents decreases the proinflammatory cytokines and TNF-alpha [62].Enrofloxacin improved the antioxidant status of infected rabbits through its ability to reduce bacterial replication, as it is effective against *p. multocida* infection, so reduces the oxidative stress resulted from infective microorganism and its toxin.

Conclusion

Our results indicate that using of *Echinacea*for prophylactic and treatment of *Pasteurella* infection returned the altered hematological, biochemical and oxidative stress markers nearly to the normal.

Conflict of Interest

The authors have no conflict to declare.

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الملخص العربى

التأثير الوقائي لنباتالإشنساعلي خلايا الدمو كيمياء الدم والقدرة على الإلتهام ومضادات الأكسدة فى الأرانب المعدية تجريبيا بالباستيريلا مالتوسيدا.

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الإشنسا هي واحدة من أهم النباتات، وقد إستخدمت في الوقاية والعلاج من الأمراض المعدية التي تصيب الجهاز التنفسي. في دراستنا، قمنا بدراسة تأثير الإشنسا والإنروفلوكساسين على الأرانب المعدية تجريبيا بالباستيريلا مالتوسيدامن خلال تقييم خلايا الدم وكيمياء الدم والقدرة على الإلتهام ومضادات الأكسدة. فتم تقسيم أربعين أرنب نيوزلندى أبيض من الذكور البالغ متوسط أوزانهم (750-1000 جرام) ومتوسط أعمارهم شهرإلى 4 مجموعات متساوية، وتم الإحتفاظ بالمجموعة الأولى كمجموعة ضابطة، و المجموعة الثانية تلقت عدوى تجريبية للأرانب بالباستيريلا مالتوسيدا (1مللى تحتوى على710x4 ميكروب حى)عن طريق الأنف فى اليوم الرابع عشرمن بدأ ألتجربة (مجموعة ضابطة معدية)،والمجموعةالثالثة تم إعطاء نبات الإشنسا(130ملليجرام/كيلوجرام وزن) للأرانب عن طريق الفم يوم بعد يوم من اليوم الأول وحتى نهاية التجربة وتم إجراء عدوى تجريبة بالباستيريلا مالتوسيدا(1مللى تحتوى على710x4ميكروب حى) عن طريق الأنففى اليوم الرابع عشرمن بدأ التجربة.والمجموعةالرابعةتم إجراء عدوى تجريبية للأرانب بالباستيريلا مالتوسيدا(1مللى تحتوى على710x4ميكروب حى) عن طريق الأنف فى اليوم الرابع عشرمن بدأ التجربة وبعد ظهور الأعراض تم العلاج بالإنروفلوكساسين (10ملليجرام/كيلو جرام وزن حى) فى ماء الشرب لمدة 3 أيام.

أوضحت النتائج أن عدوىالباستيريلا مالتوسيدا في الأرانب أدت إلى نقص معنوي فى عدد كرات الدم الحمراء والهيموجلوبين وحجم الخلايا المضغوطة وحدوث فقر دم من النوع كبير الخلايا الناقص الصباغ وزيادة عدد الكريات البيضاء مع إنخفاض في مؤشرالإلتهام. لاحظنا انخفاضًا في مستويات البروتين الكلي والألبومين والجلوبيولين في الدم. وعلاوة على ذلك، تم تسجيل زيادة كبيرة في إنزيم الألانين أمينو ترانسيفيريز والألكالين فوسفاتيز, كما إرتفع مستوى الصفراء الكلية والمباشرة والغير مباشرة في الدم بشكل ملحوظ وتم زيادة مستويات اليوريا والكرياتينين بشكل ملحوظ. علاوة على ذلك، تسببت عدوى الباستيريلا مالتوسيدا في الأرانب في حدوث الإجهاد التأكسدي الذي أظهره انخفاض كبير في إنزيم الكتاليزوزيادة معنوية فى الملون داى ألديهيدووجد ان علاج الإشنسا قبل وبعد عدوى الباستيريلا مالتوسيدا في الأرانب قادره على تحسين قياسات جميع العوامل المختبرة مقارنة بالأرانب المعالجة بالإنروفلوكساسين.