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IMMUNOMODULATORY EFFECT OF ECHINCAE PURPAREA AND *ORGUINUM VULGARIS* ON SERUM PROTIENS IN RHATTUS

By

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ABSTRACT

Herbal extracts have been reported to modulate immune response to combat immune-related diseases .The present study investigated the effect of *Echincae purparea* extract *; Orguinum vulgaris* extract and mix both of them on serum total protein , albumin and globulin concentrations in rats as animal model .Eighty adult male rats were assigned into four groups (20 rats in each one).The 1st group kept as control ,the 2nd group was given *Echincae purparea* extract in a dose of 300mg/day/rat, the 3rd group was given *Orguinum vulgaris* extract in a dose of 200mg/day/rat , while the 4th groups was given mixture of both extracts in a dose of 100mg/day/bw/rat of *Orguinum vulgaris* and 150mg/day/rat of *Echincae purparea* extract. All herbal extracts were given in drinking water for 15 days .Blood samples were collected from rats on the 1,3,5,7,9,12,15 days following the first day of adminstertion through medial canthus vein of eye, the serum total prorien was increased non significantly (6.20+/-0.2a) in rats treated by mixure of extracts in the fifteenth day post treatment as compared with control group (5.9+/-0.100a) Serum albumin was significantly increased in the 7th and 9th days post treatment with Echniaca extract compared with Organium Vulgaris extract also there was significant decrease in the 15th day post treament with *Oragiumn Vulgaris* with *Echincae purparea* extract and mixure was not significant. Gama globulin was significantly increased in the 15th day Post treatment with mix of *Echniaca* extract and *Organium Vulgaris* extract compared with each extract treatment alone

Keywords:

Echincea purea extract, orgiunm *vulgaris*, serum total protien, albumin, globulin, rats.

INTRODUCTION

Many publications are interested in the application of herbal drugs for their prenevention of some diseases like; cancer, cardiovascular diseases and liver diseases. *Echinacea purpurea* is a phytobiotic ,medicinal plant which has been used as food supplements in animal feed to improve performance also used in infectious diseases in children ,old people and animal **(Ayrle *et al* .,2016)** It's biological activities were anti-inflammation;anti-oxidation;anti-bacteria anti-proliferative,anti-hypertensive immunomodulation effects**(Aarland *et al*. 2017).** The major ingredients of *E. purpurea* are choric acid, caffeic acid other polyphenols and glycoprotiens responsible for their immunomodulatory properties. The immunomodulatory effect of *E. purpurea* was reported to involve biochemical. Changes in immune cells **(Woelkart *et al.*, 2008 and Matthias *et al.*, 2008).** *Oregano* is a worldwide herbal extract drug that is extensively used. **(Habibi *et al*. (2015 a) Habibi *et al*. (2015 b).** Studied the protective effects of *Origanum* Sara Vitalini. Marcello 2017 *O. vulgaris* it suggesting to be immunomodulating agent **(Yesilbag *et al.*, 2013).**The essential oils of *Origanum* have been found to develop strong antioxidant, antimicrobial, insecticidal and genotoxic activities. The major components of the *oragiumn vulgaris* oil, the monoterpenescarvacroland thymol**. (Schefferet *al.*,1986;Sivropoulou*etal.*,1996; Karpouhtsis *et al.*, 1998).**Serum total protien is a biochemical test for measuring the total amount of protien in serum or a test that measure the total amount of two calsses of protein found in fluid protion of the blood usually albumin and gloubin. Protien are necessary for body growth, development and health .Albumin constitsutes about half of blood serum protien and albumin transports horomones, fatty acids, and buffer pH. **(Aja *et al.*, 2015).**Hundreds of proteins is dissolved in the plasma. By measuring the concentration of these proteins, the clinician can obtain information regarding disease status in different organs and systems. The measurement of protein is done on serum, which is the fluid that remains after plasma has clotted, thus removing fibrinogen and most of the clotting factors. Total protein content provides some information regarding patient's general status and more clinically useful data are obtained from fractionating the total protein. The normal serum protein level is 6 to 8 g/dl. Albumin makes up 3.5 to 5.0 g/dl, and the remainder is the total globulins. These values may vary according to the individual laboratories. Albumin makes up more than half of the total protein present in serum. Approximately 30 to 40% of the body's total albumin pool is found in the intravascular compartment.

The remainder is extravascular and is located in the interstitial spaces, mainly of the muscles and skin. Albumin is also found in small amounts in a variety of body tissue fluids such as sweat, tears, gastric juice, and bile. Albumin does not diffuse freely through intact vascular endothelium. Hence, it is the major protein providing the critical colloid osmotic or oncotic pressure that regulates passage of water and diffusable solutes through the capillaries. Albumin accounts for 70% of the colloid osmotic pressure. It exerts a greater osmotic force than can be accounted for solely on the basis of the number of molecules dissolved in the plasma, and for this reason it cannot be completely replaced by inert substances such as dextran. The reason is that albumin has a negative charge at normal blood pH and attracts and retains cations, especially Na^+ in the vascular compartment. This is called the Gibbs-Donnan effect. Albumin also binds a small number of Cl^- ions that increase its negative charge and ability to retain Na^+ ions inside the capillaries. This enhanced osmotic force causes the colloid osmotic pressure to be 50% greater than it would be by protein concentration alone. Albumin serves in the transport of bilirubin, hormones, metals, vitamins, and drugs. It has an important role in fat metabolism by binding fatty acids and keeping them in a soluble form in the plasma. This is one reason why hyperlipemia occurs in clinical situations of hypoalbuminemia.The binding of hormones by albumin regulates the amount of free hormone available at any time. Because of its negative charge, albumin is also able to furnish some of the anions needed to balance the cations of the plasma. Albumin is synthesized in the liver. The rate of synthesis is constant in normal individuals at 150 to 250 mg/kg/day, resulting in the production of 10 to 18 g of albumin daily in a 70-kg man. The primary factors affecting albumin synthesis include protein and amino acid nutrition, colloidal osmotic pressure, the action of certain hormones, and disease status. Fasting or a protein-deficient diet causes a decrease in albumin synthesis as long as the deficiency state is maintained. In the normal individual, the liver increases albumin synthesis in response to the increased availability of amino acids provided by the portal blood following each protein-containing meal.A decrease in extravascular colloidal pressure serves as a stimulus for albumin synthesis and is thought to act within the liver. Thyroid hormone, corticosteroids, growth hormone, and insulin all can increase albumin synthesis. The main site of albumin degradation is not known. Albumin appears to be catabolized in locations that are capable of rapid equilibration with the bloodstream. It is degraded into amino acids that are utilized for energy requirements of the

cell or secreted into the pool of extracellular amino acids. The globulin fraction includes hundreds of serum proteins including carrier proteins, enzymes, complement, and immunoglobulins. Most of these are synthesized in the liver, although the immunoglobulins are synthesized by plasma cells. Globulins are divided into four groups by electrophoresis. The four fractions are α1, α2, β and γ, depending on their migratory pattern between the anode and the cathode. Increases in the globulin fraction usually result from an increase in immunoglobulins, but there can be an increase in other proteins in pathologic status that have characteristic electrophoretic patterns. Malnutrition and congenital immune deficiency can cause a decrease in total globulins due to decreased synthesis, and nephrotic syndrome can cause a decrease due to protein loss through the kidney. Immunoglobulins (i.e., antibodies) migrate mainly in the γ region, but some migrate in the β and α 2 regions as well. Each immunoglobulin molecule is composed of two heavy chains that are of the same class and two light chains that are also alike. Each heavy chain has a variable region (in which amino acid substitutes make each chain different from the next) and a constant region (in which there are very few amino acid differences from the constant region of any other immunoglobulin of that heavy chain type). Light chains are of either λ or κ type and have constant and variable regions. The different kinds of immunoglobulins are named by capital letters that correspond to their heavy chain type: IgG, IgA, IgM, IgE, and IgD. Three-fourths of the immunoglobulin level in normal serum is of the IgG type. Many antibodies to bacteria and viruses are IgG. The normal collection of IgG molecules is made up of minute amounts of different IgG antibodies produced from diverse clones of plasma cells; thus it is polyclonal. If a single clone escapes its normal controls, it can reproduce excessively and synthesize an excess of a monoclonal protein with a single heavy chain class and light chain type.

The only clinical situation that causes an elevation in serum albumin is acute dehydration. A variety of clinical entities result in a decreased albumin level, either from depressed synthesis or increased losses. A decrease in albumin synthesis is caused by end-stage liver disease, intestinal malabsorption syndromes and protein-calorie malnutrition. Examples of albumin loss are nephrotic syndrome and severe burns because the skin is the most important extra storage pool for albumin. The consequence of a decrease in serum albumin is a shift of fluid from the intravascular to the interstitial space, resulting in intravascular volume depletion and edema formation.

Any increase or decrease in the globulin fraction should be evaluated byserum electrophoresis. The pattern should be visually inspected for abnormalities in particular regions. The α1 fraction consists mainly of α1 antitrypsin. Significant decreases of this fraction are seen in patients with congenital α1 antitrypsin deficiency; an increase is seen in acute inflammatory disorders because α1 antitrypsin is an acute phase reactant. The major proteins migrating in the α2 region include α2 macroglobulin and haptoglobin. There is an increase in α2 macroglobulin in the nephrotic syndrome when lower molecular weight proteins are lost in the urine. Haptoglobin rises in response to stress, infection, acute inflammation, or tissue necrosis, probably by stimulation of synthesis. Haptoglobin levels decrease after a hemolytic reaction because the haptoglobin complexes with free hemoglobin and is cleared from the circulation. The major β globulin is transferrin. Elevations occur in severe iron deficiency. Complement components C3, C4, and C5 also migrate in the β region. The most frequent abnormalities in the γ region are a broad-based polyclonal increase or a narrow monoclonal spike. Polyclonal increases are seen in chronic infections, connective tissue diseasesand liver disease.Monoclonal spikes suggest multiple myeloma,Wald Enstrom's macro-globulinemia,primary amyloidosis, lymphoma, or monoclonal gammopathy. Any abnormality in the γ region suggesting a monoclonal spike should be further evaluated by immunoelectrophoresis. Hypogammaglobinemia is characterized by a decrease in the γ component. It is seen in congenital immune deficiency syndromes or in association with diseases such as nephrotic syndrome, chronic lymphocytic leukemia, and corticosteroid treatment. **(Busher JT *et al.*, 1990).** The persent investiagtion was carried out to examine the effect of *Echincea purpera*, *orginum vulgaris* and mixing of both extract as immunostimulant on serum total protein, albumin and gloubin in rats.

MATERIAL AND METHODS

Extract application:

The herbs were purchased from a local herbal company (Organic Company). Each extract was soluted in water before administration to experimental animal groups.

Animal groups:

A total of eighty mature male mice (5 week of age) 150gm and purchased from Shabramant farm all rats were housed in cages plastic tube 26- 5x7x12 with stealing steel, wool shaving scratted in floor. Rats were kept under hygenic conditions, fed on balanced ration and water

adlibtium with water change every day. Rats were divided into 4 groups 20 rats each

1st group: control untreated rats.

2nd group: *Echinacea* extract in drinking water 300mg/rat/day.

3rd group: *Origunium* extract in drinking 200mg /rat/day.

4th group:Mix of both extracts by half dose in drinking water (Organium 100 mg /day and echinacea extracts 150 mg/day) for 2 weeks.

Blood Sampling:

Blood samples were taken from the eye median eye cansus vein of rats .Blood samples were collected at respectively days 1, 3, and 5,7,9,12,15 after spending the experimental animals group one week as rest. The blood samples were centrifuged at speed of 3000 rpm for 15 mins. Serum was kept at 6 c until helated. Estimation of Serum total protein.Albumin and globulin. Total protiens were measured using colorimetric standard method. Serum total protein was measured according to the Biuret method as modified by Hutsonetal using bovine serum albumin as standard. Serum albumins were assayed by Bromcresol.**(Peters T, Jr, Biamonte, GT, Doumas, BT. E. Faulkner, E and Meites, S. Eds *at el.*, 1982).** And serum gloubin was calculated by subtraction of total protein and gloubin.

Statistical analysis:

Data were expressed as mean ± SD (standard deviation). The normality of residuals and heteroscedasticity of variances were calculated using the Shapiro-Wilk and Levene's tests. Statistical comparison between the mean of the different groups (Gp. 1,Gp. 2,Gp.3 and Gp. 4) was made by one-way analysis of variance (ANOVA) and multiple comparison between groups (post hoc) using least significant difference (LSD).Values of $p \leq 0.05$ were considered statistically significant. All statistical analyses were performed on SPSS version 26 software (SPSS Inc., Chicago, IL, USA).

RESULTS

After one day post treatment, there was no statistically significant difference in serum total protein (g/dl) among the experimental groups (F (3, 8) =2.413, p= .142) (Table 1), Fig. (1).

Table (1): Total protein (g/dl) of different experimental groups post treatment.

Groups	1st day Post treatment	3rd day post treament	5th day post treament	7th day post treament	9th day post treament	12th day post treament	15th post treatment
G1	5.30+_0.173	6.23+_0.252	6.17+_0.208	6.23+_0.321	6.17+_0.306	6.23+_0.252	5.90+_0.1005
G2	5.13+_0.115	6.07+_0.153	6.13+_0.058	6.30+_0.200	6.10+_0.100	6.23+_0.208	6.00+_0.100
G3	5.07+_0.058	6.07+_0.115	6.30+_0.200	6.10+_0.100	6.10+_0.265	6.13+_0.115	6.17+_0.289
G4	5.03+_0.153	6.17+_0.153	6.07+_0.208	6.03+_0.208	6.20+_0.100	6.10+_0.173	6.20+_0.200
F(3,8)	2.413	0.694	0.889	0.904	0.164	0.378	1.674
P value	0.142	0.606	0.487	0.481	0.918	0.772	0.249

Data represented as mean ± SD (standard deviation). Gp. 1: control group; Gp. 2: group treated by *Echinca* extract; Gp. 3: group treated by *Orignuim* extract; Gp. 4: group treated by *Echinca* and *Orignuim* extracts. Column with different superscript was statistically significant at $p \leq 0.05$.

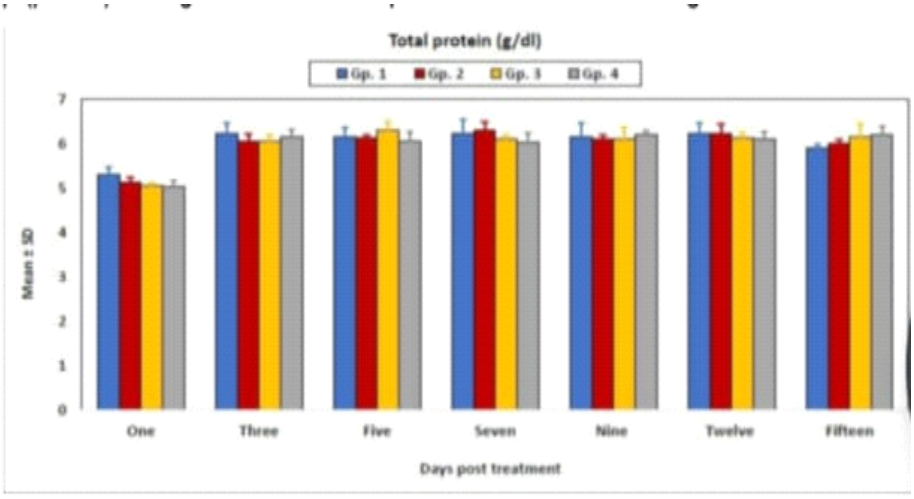

Fig. (1): Column chart showing total protein (g/dl) of different experimental groups post treatment Column chart represented as mean ± SD (standard deviation). Gp. 1: control group; Gp. 2: group treated by echinca extract; Gp. 3: group treated by orignuim extract; Gp. 4: group treated by echinca and orignuim extracts.

Rats treated by extract of *Echinacea*, extract of *Echinacea* combined with *Orignuim* extract and *Orignuim* extract for fifteen days produced more effective enhancement in serum Albumin and globulin levels compared with control rats As summarized in (Table 2) ,Fig.(2) . Albumin levels in serum of rats treated by *Echinacea* extract (Gp 2) were significantly increased compared with rats treated by *Orignuim* extract (Gp 3).

Table (2): Albumin (g/DI) OF different experimental groups post treatment.

Groups	1st day post treament	3rd day post treament	5th day post treament	7th day post treament	9th day post treament	12th day post treatment	15th day post treament
G1	2.93+_0.252	2.90+_0.256	2.97+_0.153	3.03+_0.153	3.00+_0.100	2.97+_0.058	2.97+_0.058
G2	3.07+_0.451	2.93+_0.153	2.90+_0.100	3.47+_0.462	3.20+_0.265	2.97+_0.153	2.93+_0.058
G3	3.17+_0.208	3.00+_0.361	2.97+_0.153	2.93+_0.058	2.93+_0.231	3.03+_0.058	2.77+_0.058
G4	3.20+_0.361	3.20+_0.400	2.97+_0.503	2.90+_0.100	2.87+_0.351	2.93+_0.153	2.83+_0.058
F(3,8)	0.391	0.565	0.043	3.29	0.97	0.39	7.58
P value	0.763	0.653	0.987	0.079	0.453	0.76	0.01

Data represented as mean ± SD (standard deviation). Gp. 1: control group; Gp. 2: group treated by echinca extract; Gp. 3: group treated by orignuim extract; Gp. 4: group treated by echinca and orignuim extracts. Column with different superscript was statistically significant at $p \leq 0.05$.

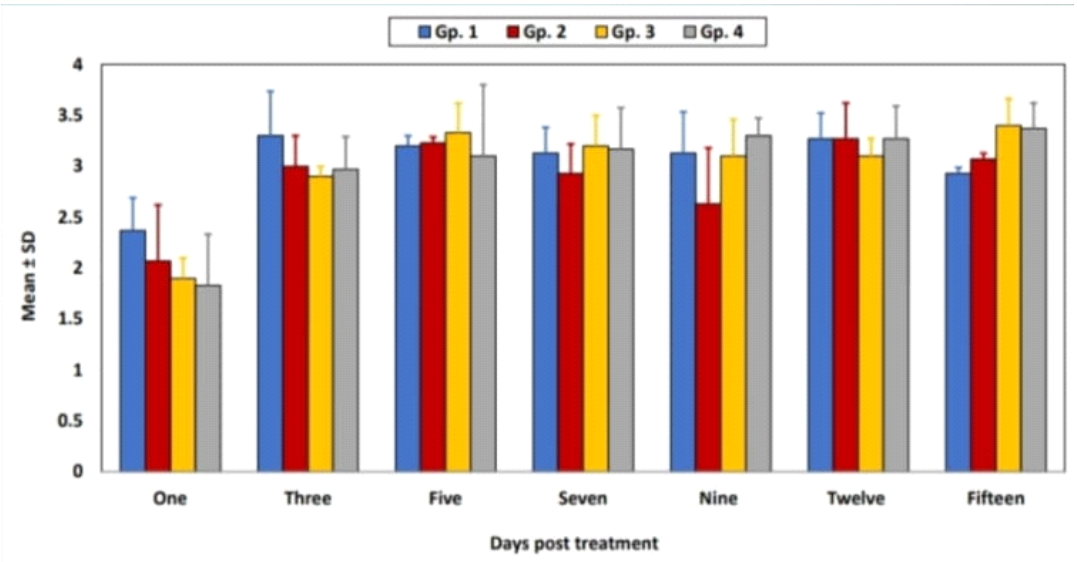

Fig. (2): Column chart showing albumin (g/dl) of different group post treatment Column chart represented as mean ± SD (standard deviation). Gp. 1: control group; Gp. 2: group treated by echinca extract; Gp. 3: group treated by orignuim extract; Gp. 4: group treated by echinca and orignuim extracts.

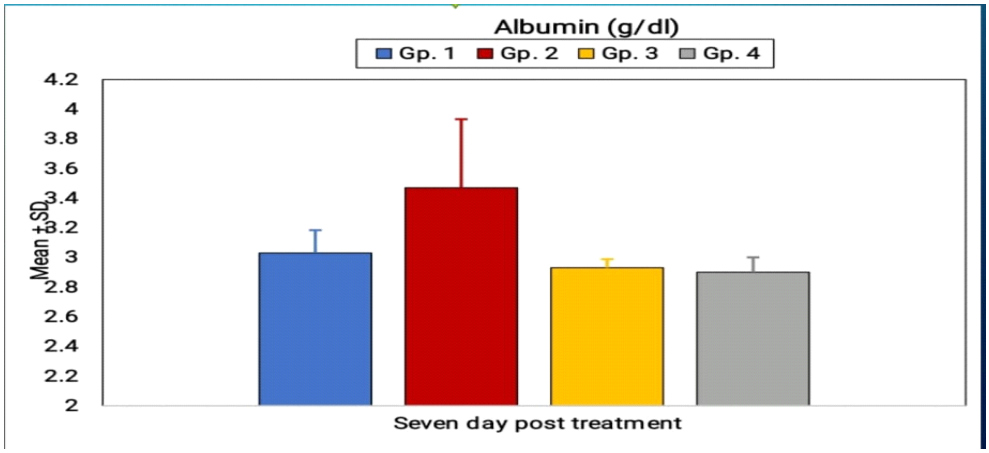

Fig. (3): Column chart showing albumin (g/dl) of different group nine post treatment Column chart represented as mean ± SD (standard deviation). Gp.1: control group; Gp. 2: group treated by echinca extract; Gp. 3: group treated by orignuim extract; Gp. 4: group treated by echinca and orignuim extracts.

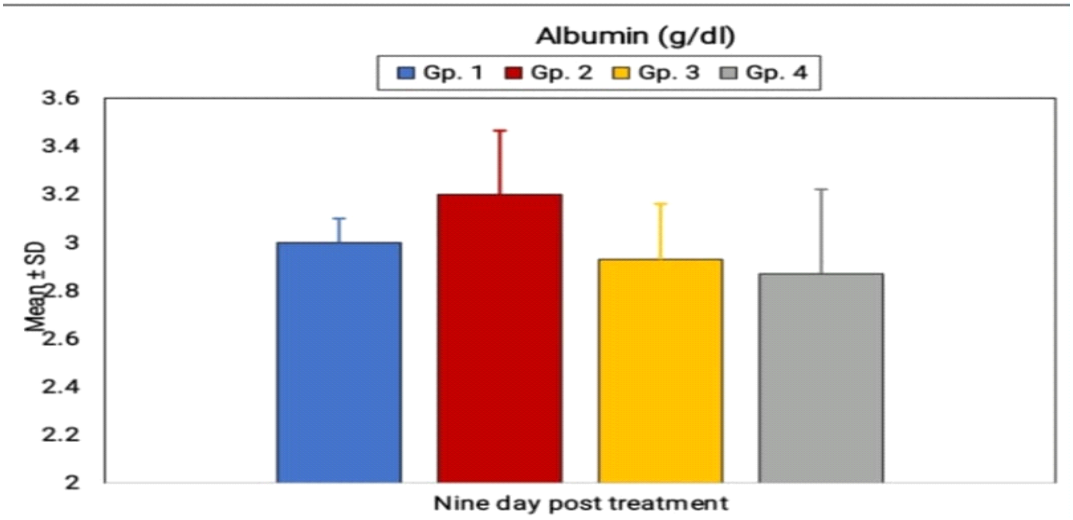

Fig.(4): Column chart showing globulin (g/dl) of different experimental groups post treatment Column chart represented as mean ± SD (standard deviation). Gp. 1: control group; Gp. 2: group treated by echinca extract; Gp. 3: group treated by orignuim extract; Gp. 4: group treated by echinca and orignuim extracts. Fifteen-day post administering rats with *Orignuim* extract (Gp.3) and a mixture of *Echincae* and *Orignuim* extracts caused a statistically significant increase in globulin levels compared with control rats, where as The serum globulin levels of rats treated by *Echinacea* extract (Gp.2) were not statistically significant compared with control rats. Rats treated by *Orignuim* extract (Gp.3) and rats treated by a mixture of *Echinacea* and *Orignuim* extracts (Gp.4) (F (3, 8) =4.468, p=.04) (Table3), Fig. (5, 6).

Table (3): Globulin (g/dl) of different experimental groups post treatment.

Group	1st day post treatment	3rd day post treatment	5th day post treatment	7th day post treatment	9th day post treatment	12th day post treatment	15th day post treatment
Gp. 1	2.37 ± 0.321[a]	3.30 ± 0.436[a]	3.20 ± 0.100[a]	3.13 ± 0.252[a]	3.13 ± 0.404[a]	3.27 ± 0.252[a]	2.93 ± 0.058[a]
Gp. 2	2.07 ± 0.551[a]	3.00 ± 0.300[a]	3.23 ± 0.058[a]	2.93 ± 0.289[a]	2.63 ± 0.551[a]	3.27 ± 0.351[a]	3.07 ± 0.058[ab]
Gp. 3	1.90 ± 0.200[a]	2.90 ± 0.100[a]	3.33 ± 0.289[a]	3.20 ± 0.300[a]	3.10 ± 0.361[a]	3.10 ± 0.173[a]	3.40 ± 0.265[b]
Gp. 4	1.83 ± 0.503[a]	2.97 ± 0.321[a]	3.10 ± 0.700[a]	3.17 ± 0.404[a]	3.30 ± 0.173[a]	3.27 ± 0.321[a]	3.37 ± 0.252[b]
***F* (3, 8)**	0.97	0.958	0.189	0.431	1.566	0.26	4.468
***P* value**	0.453	0.458	0.901	0.737	0.272	0.852	0.04

Data represented as mean ± SD (standard deviation). Gp. 1: control group; Gp. 2: group treated by echinca extract; Gp. 3: group treated by orignuim extract; Gp. 4: group treated by echinca and orignuim extracts. Column with different superscript was statistically significant at $p \leq 0.05$.

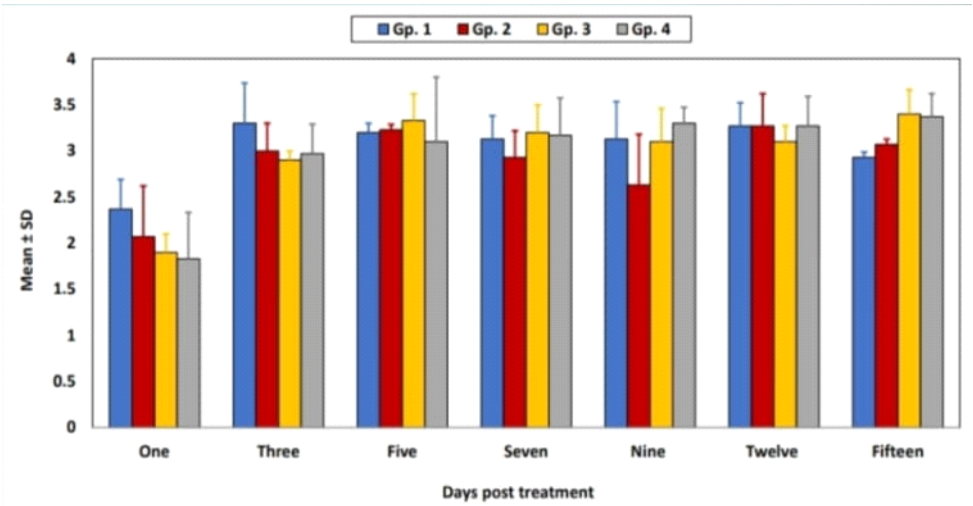

Fig. (5): Column chart showing gloubin (g/dl) of different experimental groups post treatment Column chart represented as mean ± SD (standard deviation). Gp. 1: control group; Gp. 2: group treated by echinca extract; Gp. 3: group treated by orignuim extract; Gp. 4: group treated by echinca and orguinum vulgaris extracts.

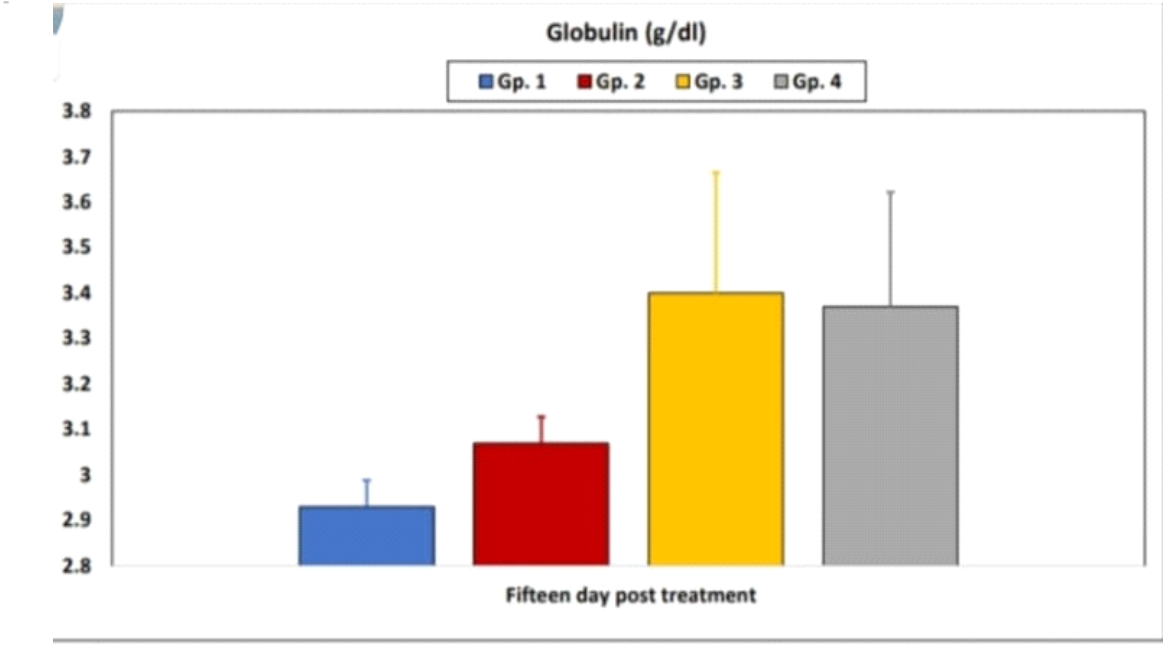

Fig. (6): Column chart showing globulin (g/dl) of different experimental groups fifteen-day post treatment Column chart represented as mean ±SD (standard deviation). Gp. 1: control group; Gp. 2: group treated by echinca extract; Gp.3: group treated by orignuim extract; Gp. 4: group treated by echinca and orignuim extracts.

DISSCUION

The immunomodulating effects of natural constituents are studied extensively with great interest due to the growing awareness on immune system modulation and to attain the essential goals on disease hindrance **(Badr*et al.*2011;Neamat-Allah *et al.* 2019b).**

Numerous plant medications well branded in conventional medicine possess anti-infective character not only by directly affecting on pathogen alone, but also by stimulating nature and adaptive shield mechanism of the host **(Ortuño-Sahagún *et al.* 2017).**

The immunostimulation of immulant may be linked to its polysaccharide fraction which has been found to stimulate the activity of macrophage and several other functions linked to cytokine production. Various phenolic compounds and alkamides were found to exhibit antiviral and antifungal properties **(Chen *et al;* 2005).** Immulant contains alkamides, caffeic acid esters, polysaccharide, and polyacetylenes **(Merali *et al;* 2005).** Several animal and human studies reported stimulation of neutrophil and macrophage phagocytic functions by E. *Purpurea* **(Cundell *et al;* 2003).** *Echinacea purpurea (EP)* is one of these plants, which has an antibacterial **(Chiellini *et al;* 2017),** immunomodulation effects **(Seckin *et al;* 2018).**

EP contains a variety of active substances like glycoproteins, phenolic complexes, alkamides, and flavonoids **(Erenler *et al.* 2015)** which have and immunomodulation effect that increases the resistance of chickens against infection leading to decrease of the severity of the infection and improve the body weights **(Rahimi *et al.* 2010 and Hashem *et al.*, (2020).** Moreover, EP stimulate T-lymphocytes proifration (**Cowell 2004).** The using of EP as prophylactic showed anti-inflammatory and antibacterial effects **(Manayi *et al.* 2015).**

Origanum vulgare (OV) L. Ssp. Hirtum (Greek oregano) is a native plant rich in phenolic and ester compounds, especially in rosmarinic acid **(Yang and Shetty (1998).** This plant has been used as an antiseptic and for stomach and respiratory ailments **(Eddouks *et al;* 2002).** The main medicinal activities of *Oregano* are anti-bacterial **(Burt and Reinders *et al;* 2003)** antioxidant **(Zhang *et al;* (2014).** The strong antioxidant activity of the extract is mainly attributed to its key phenolic compounds such as rosmarinic acid, salvianolic acid B-lithospermic acid B and caffeic acid that exhibit high radical-scavenging capacity **(Chen *et al.* 2013 and Zhang *et al.* 2014).** It has been shown that caffeic acid dynamically and synergistically interacts with ascorbic acid and α-tocopherol and amplifies their antioxidant potential and the protection of cells along mitotic phases **(Laranjinha and Cadenas 1999).** Also, salvianolic acid B inhibits lipid peroxidation as well as rosmarinic acid which is considered one of the major componants of (OV) and as active phytochemical of (OV). Asactingas an antioxidant,immunomodulator and as an anti-apoptotic manner,that importantly, preserves β-cells. Finally, it exhibits only partial protection from diabetes induction. In vitro studies have revealed that rosmarinic acid affected both macrophages and lymphocytes. It inhibited macrophage function judging by reduced NO production and IL-1β secretions). However, rosmarinic acid stimulates T lymphocyte proliferation **(Vujicic *et al.*, 2015).** The therapeutic properties of ethyl extract of *Origanum vulgare* in rat and its role in preservation of the pancreatic islets morphology lowering of proinflammatory macrophage levels were reported.

The metobolic profile of total protein ,albumin and gloubin in rats as a marker of immune stimulantion for echinca ,orignium and mixing of both extracts **(Rasecktel ,2008)** also the synthetic product of the body like albumin and protien can be used as markers for assessment the functional capities of the organs **(Jesso , 1989).** In this study one way ANOVA was conducted to compare the effect of different treatments on the level of serum total protein (g/ dl) of different rats of the expermintal groups .and it was found that after one day post

treatment , there was no statistically significant difference in serum total protein(g/dl) a mong the experimental groups (F(3, 8) =2. 413, p=. 142) . At the fifteen day post treament there was no statistically significant difference in serum total protein(g/ dl) among the experimental groups(F(3, 8) =1.674, p=.249) (Table1).This means good general health with higher immune functional capilites of the organs

These results indicate improvements in hepatic functions because of hepato-protective effect of EP owing to the antioxidant effect of its higher contents of phytophenolic compounds **(Gharieb and Youssef 2014). Hashem *et al.*, (2020).***Orignum* protect B cells by intefering with apoptosis induced by cytokines regulation. The serum level of total protein of rats treated by *Echinacea* extract (Gp. 2) ,*Orignuim* extract(Gp. 3) and a mixture of *Echinacea* and *Orignuim* extracts (Gp. 4) showed no statistically significant difference in comparison with control rats (Gp. 1) during the course of experiment (Table1) .

Moreover, at fifteen day post treatment, the increase in serum total protein levels rats treated with Echinacea extract or *Orignuim* extract or a mixture of two extracts were not statistically significant as compared with control rats. Treatment with *Echinacea* extract, Orignuim extract and a mixture of two extracts, bring the levels of total serum protein near normal level with no significant difference from the control group (p>. 05) during the course of experiments. Similar to our results, **(Hussein *et al;* 2014)** also reported a significant increase in total protein and globulin in rabbits given Echinacea. Moreover, **Radwan *et al.* (2019)** reported that oral administration of Echinacea with dexamethasone resulted in a great normalization in the levels of liver's protein. Similarly, **(Ibrahim *et al.*,2020)** induced a significant increase in total protein level and ameliorated the dexamethasone -induced decrease in serum total protein, albumin, and albumin/globulin ratio in rabbits on the other hand this result doesn't agree with **(AKrami *et al* 2015).**

Serum albumin and globulin are summarized in (Table 2). Albumin levels in serum of rats treated by Echinacea extract (Gp. 2) were significantly increased compared with rats treated by Orignuim extract (Gp. 3) whereas the serum albumin levels of rats treated by Orignuim extract (Gp.3) were significantly decreased compared with control rats (Gp. 1) and rats treated by *Echinacea* extract (Gp. 2) at fifteen day post treatment (F(3, 8) =7. 58, p=. 01). The significant increase in the level of Albumin at 7th and 9th day post treament by *echinca* extract is an indication of good liver function .The reduction in

the level of albumin at 200mg/day/rat on 15 day post treatment with the *O.vulgris* extract may be an indication of adminstration as synthetic function of liver resulting from heptocelluer damage, this result agree with **(Woodman, 1996).** The same values of serum albumin at 15th day post treament for echincae purparea and mix of *Echincae purparea* and *Orguinum vulgaris* extracts indicate good liver function with long period treament without heptocellureal damage obtianed with *oragiumn vulgaris* alone.

Also the elevated level of gloubins suggests dose spcefic effect of the extract on liver parameters. At Fifteen day post administering *Orguinum vulgaris* extract (Gp.3) and a mixture of *Echinacea* and *Orignuim* extracts caused a statisticaly significant increase in globulin levels as compared with control rats. Our result suggest supplementation of 200mg /day /rat for 15 days of *Orgnuim vulgarsis* extract enhanced the cellular immunitiy (non- specific immunity) of rats by increasing serum gloubin level .

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