Therapeutic Effect of Purple Coneflower (Echinacea purpurea L.) on Rats with Immune Dysfunction

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Abstract:

The goal of this research is to examine how administration of Echinacea affects several blood parameters and immunological functioning in mice. Thirty albino male mice weighing 180±5 g were utilized in this research. The 1st group (n = 6) was fed a basic diet, groups 2-5 were injected with cyclosporine (CsA 50) mg for 21 days. Groups 3-5 were fed echinacea powder at three levels (150, 300, and 450 g/kg diet), respectively. The active components of echinacea powder were estimate. Histopathology of the spleen was performed. The results of the active components of the echinacea plant recorded the presence of many important compounds. The results indicated that groups of mice fed with echinacea had a significant elevation in immune parameters ($P < 0.05$). The average IgM and IgG value of mice fed with echinacea elevated contrasted with the positive control group. Blood measurements were significantly elevated ($P < 0.05$) for the groups assumed echinacea in the diet. However, the white blood cell count decreased significantly. However, a significant increase in BWG, feed quantity, and feed efficiency ratio (FER) was observed for the tested groups contrasted with the control group. The findings also revealed a significant elevation in the levels of RBCs & hemoglobin as opposed to the positive control group. There was an improvement in liver enzymes in the groups fed with echinacea as opposed to the positive control group. It can be deduced that echinacea stimulates the immune system of mice with immune disorders.

Keywords: *Echinacea purpurea* - Immune system - liver enzymes - cyclosporine

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Introduction

The most effective form of preventive medicine is to keep one's immune system in tip-top shape **(Santa-Maria *et al*., 2023).** Defense against foreign pathogens and/or the cancerous cells of an individual is the primary role of the immune system **(Daeron, 2022).** Although the immune system is mostly determined by genes, environmental and dietary influences may also have a role. Due to the immune system is interwoven with the neurological system & the endocrine system **(Godinho-Silva *et al*., 2019),** a healthy lifestyle that includes regular exercise, a positive mental state, supportive relationships, meditation, and nutritious foods is essential **(Swarbrick, 2006).**

Keeping the immune system healthy and operating optimally is crucial for warding off a wide variety of illnesses. Since there appears to be a rise in the incidence of immunological disorders, researchers are concentrating on creating preparations and specific goods that can alter the body's immune response (IR) **(Miroshina and Poznyakovskiy ,2023).** There is a pressing need for novel, highly efficient therapies for many diseases, and researchers are exploring promising new avenues for doing so. Herbal supplements and preventative measures are an effective method with a lot of potential. Italian researchers looked at the phytochemical research challenges and prospective novel agent sourcing strategies related to Echinacea spp. and Curcuma longa's immunomodulatory/anti-inflammatory activities **(Catanzaro *et al*., 2018).**

Immunomodulators are substances with the capability to alter the immune system, either by enhancing immunological defenses to enhance the body's reaction against viral or external damage, or by dampening the abnormal IR that occurs in immune diseases. To further improve the IR, immunoadjuvants can also assist the immune system in its action against no immune targets. Altering the micro biota and inflammatory pathways is another method for influencing the immune system. Due to their potential numerous and pleiotropic effects, certain nutraceuticals derived from plants have been investigated as potential immunomodulating safer than pharmaceuticals, their adjuvant contribution is seen as a promising nutraceutical tactic **(Di Sotto *et al*., 2020).**

Cyclosporine (CsA) is a cyclic undecapeptide with significant immunosuppressive activity **(Patocka *et al*., 2020).** Due to its potency and specificity, CsA is increasingly being utilized to prevent and cure rejection following multiple organ transplantation **(Ziaei *et al.,* 2016)**. Additionally, CsA is utilized to treat the greatest number of autoimmune illnesses, including autoimmune dermatitis, psoriasis, and chronic idiopathic urticaria in dermatology **(Colombo *et al*., 2010; Khattri *et al*., 2014).** CsA's most serious side effect is its acute and chronic nephrotoxicity **(Korolczuk *et al*., 2016).**

Several plants and phytochemicals have been used medicinally for decades because of their proven capacity to influence IR **(Mukherjee *et al*., 2012).** They play a crucial role as immunomodulatory processes, namely as immune system boosters by enhancing both adaptive humoral and innate & cellular immunity. Nevertheless, other mechanisms have been revealed **(Wang *et al*., 2017 & Chen *et al*., 2009),** including Conflict with proinflammatory pathways and alteration of the gut flora. The Asteraceae family includes *Echinacea purpurea (EPL.)* Moench (E. purpurea), more popularly identified as purple coneflower. Species of the Echinacea (Ech) genus can be found all throughout North America, although they were first discovered in the US. There are 9 various species of Echinacea, but only EP, Ech pallida(Nutt.) Nutt & Echinacea angustifolia DC are widely utilized as medicinal herbs with extensive therapeutic applications. **(Burlou-Nagy *et al*., 2022).** Echinacea purpurea's (Ech) immunomodulatory and anti-inflammatory characteristics can influence many immune system pathways **(Manayi *et al*., 2015).** Alkamides, polysaccharides, caffeic acid derivatives & glycoproteins are only a few examples of the plant's secondary metabolites that exhibit immunostimulatory action **(Barnes *et al*., 2005) .**

Among the most well-liked genera of medicinal plants is Echinacea, which is indigenous to North America **(Mehdizadeh *et al*., 2022).** There are 9 distinct species of Echinacea, but only E. angustifolia, E. purpurea, and E.

pallida have been shown to have any therapeutic effects **(Kilani-Jaziri *et al.*, 2017 & Sharifi-Rad *et al.*, 2018).** E. purpurea has anti-inflammatory & immune-boosting properties **(Maggini *et al.*, 2017).** The species has been shown to have immunomodulatory effects in many investigations , with benefits including enhanced innate and specific immunity as well as anti-inflammatory, antiviral & antibacterial activities **(Rondanelli *et al.*, 2018 & Sultan *et al.*, 2014).**The common cold, sore throats, coughing, and other respiratory disorders have all been treated with this herb for generations.18 Different substances with different effects were reported to come from *E. purpurea* depending on the method of extraction and the solvents utilized (e.g., aqueous, alcoholic, and oily extracts) **(Catanzaro *et al.*, 2018).**

Echinacea includes a broad range of physiologically active chemicals, like phenolic acids, caffeic acid, alkamides, rosmarinic acid, polyacetylenes & others **(Jahanian *et al.*, 2017).** Echination is most frequently utilized to treat and prevent upper respiratory tract infections because of its anti-inflammatory, antioxidant & immunomodulatory characteristics. A number of different classes of physiologically active components work together to give echinacea its pharmacological effects. These include alkamides (lipophilic alkamides), water-soluble phenolic compounds (primarily derivatives of caffeic acid), polysaccharides, and benzalkonium chloride. **Kumar and Ramaiah (2011)** argue that the benefits of echinacea have not been well discussed. Echinacea has been shown to be safe, according to the evidence we currently have. to ascertain the safety profiles of different preparations of echinacea, however, more research and monitoring are required. Concerns about safety include hypersensitivity reactions, dose-dependent effects, and lethal overdose. So, echinacea extracts have been utilized historically to treat wounds, boost the immune system & alleviate the signs of bacterial illnesses in the respiratory system. Moreover, specific antioxidant and antibacterial activity is shown **(Sharifi-Rad *et al.*, 2018).** Consequently, this study's goal is to investigate whether or not Echinacea purpurea has any hematological or immunostimulatory effects on immunosuppressed rats.

Materials and Methods

A-Materials:

1-Drug and plant:

- CsA 50 mg/ml (Sandimmune-Novartis) was acquired from Elgomhoria Company, Egypt. The contents of the capsules were dissolved in glycol & fresh lyprepared for subcutaneous (SC) injection relying on the weight of each animal.

- Echinacea was obtained from Imtenan Health Shop, Obour City, Egypt.

2-Rats:

Thirty albino mature male rats (190 ± 5 g) of the Sprague- Dawley strain were gathered from Helwan Farm of Experimental Animals in Egypt.

3-Chemicals:

Egypt's Elgomhoria Company supplied casein, minerals, vitamins, and cellulose. We bought kits from Gama Trade Company in Dokki, Egypt.

B-Methods:

1-Animal ethics statement :

Regarding the treatment & utilization of animals, every relevant national and institutional protocol was adhered to. All samples were gathered from rodents that participated in investigations that were granted approval by the Institutional Animal Care and Use Committee (ARC-IACUC) of the Animal Ethics Research Center. The reference number for these approvals is ARC/HU/54/23.

2- The Agriculture Research Center performed the identification of Kingdom Plantae S.p**. *(EP L.).***

Rank	**Scientific Name**
Kingdom	*Plantae*
Subkingdom	*Tracheobionta* - Vascular plants
Superdivision	*Spermatophyta* - Seed plants
Division	*Magnoliophyta* - Flowering plants
Class	*Magnoliopsida* – Dicotyledons
Subclass	*Asteridae*
Order	*Asterales*
Family	*Asteraceae* - Aster family
Genus	*Echinacea* Moench - purple coneflower
Species	EP (L.)

3- Determination of active component: Active component of Echinacea purpurea was assessed as the technique of **A.O.A.C. (2005).**

4-Induction of immunosuppression by CsA:

Cyclosporine (CsA) stimulated the suppression of the immune system. In rats, CsA was administered via 21-day injections at a dose of 10 mg/kg, as described in (**Rezzani *et al*., 2001).**

5- Experimental design:

Thirty rats were kept in sterile conditions & fed a baseline diet **(Reeves *et al*., 1993)** for a week to allow them to adjust. Following this week, rats were separated into 5 groups randomly. The 1st group (n=6) was the negative control group and was fed a baseline diet. CsA 50 mg/ml (Sandimmune Novartis) was injected into the 2nd-5ve groups (n = 24) once to cause immune dysfunction.The second group was given a control diet (+ve) of a baseline diet. Ech powder was added to the regular diet at a level of 150, 300 & 450 g/kg diet, respectively) for groups 3-5.

Following an 8-week trial period, blood samples from every rat were taken; one was centrifuged to isolate serum for biochemical examination and the other with EDTA as anticoagulant was utilized for hematological parameter assessment. Each rat had its spleen removed for histological analysis.

6- Biological evaluation:

In accordance with **Chapman *et al*. (1959)**, we estimated feed intake (FI), FER, body weight gain (BWG%) & organs relative weight.

7- Biochemical analysis:

According to **(Thomas, 1998),** we calculated alanine aminotransferase (ALT) and aspartate aminotransferase (AST).Alkaline phosphatase (ALP) in the blood was measured using the method described by **(Roy, 1970)**.Methods for determining serum levels of catalase and malondialdehyde (MDA) were developed after reviewing the work of **(Sinha, (1972) and Draper and Hadly (1990).** The levels of IgM and IgG were assessed using the methods described by **Ziva and Pannall (1984).** Red blood cell count, haemoglobin concentration, mean corpuscular hemoglobin, hematocrit, mean corpuscular hemoglobin concentration, monocyte, white blood cell, eosinophils, platelets, lymphocyte & neutrophils were calculated utilizing standard haematological approach outlined by **Ochei and Kolharktar, (2008).**

8- **Histopathological examination:**

The spleen was removed from the animal, rinsed in cold saline solution, patted dry between filter papers & then weighed at the conclusion of the experiment. Hematoxylin and eosin -stained slices were utilized to examine the microscopic alterations.

9- Statistical Analysis: SPSS was utilized to do the analysis of the data. The ANOVA test was done to evaluate the significance of the distinctions among the groups **(SPSS, 1986).**

Results and discussion

Table (1): Active component of *Echinacea purpurea*.

Active Component	Outcomes of the Tests
Caftaric acid	+
Rosmarinic acid	+
Echinacoside acid	+
Cichoric acid	+
Polyacetylenes	+
Polysaccharides	+
Flavonoids	+
Terpenoid	+

Echinacea has a wide variety of active chemicals, including alkylamides, caftaric acid, rosmarinic acid, caffeic acid derivatives, echinacoside & cichoric acid, polysaccharides, polyacetylenes, flavonoids, and Terpenoid compounds. Polysaccharide components (63%) were found to be more abundant than soluble sugars (2%), which accounted for a maximum of 5 percent of total carbs, corresponding to the analysis of compositional data. Fructose was the main soluble sugar, subsequently glucose as well as sucrose. As stated in Table 1, the most prevalent polysaccharide in the root is cellulose (32%), a component of main cell walls, while the 2nd most abundant is uronic acids (17%), which make up an acidic polysaccharide like pectin. The total fructan content of echinacea roots was found to be 16% **(Petrova *et al*., 2023)** and was the highest of any plant studied.

E. purpurea's primary chemical components have been extensively described, and several different biological processes related to them have been identified **(Bauer, 1998).** Certain groups of phenolic compounds and alkamides have been found to exhibit antiviral and antifungal properties **(Merali *et al.,* 2003)**. Additionally, the polysaccharide fraction has been observed to enhance macrophage activity and multiple additional purposes associated with the generation of cytokines **(Goel *et al.,* 2002a; Randolph *et al.,* 2003).** Polysaccharides, polyacetylenes, caffeic acid esters (cichoric acid), alkamides, & cichoric acid are all observed in E. purpurea **(Chen *et al*., 2005).**

The roots of Echinacea purpurea exhibited the highest concentrations of caffeic acid derivatives and cichoric acid, with values reaching 2.27% **(Pellati *et al.*, 2005)**. The presence of cichoric acid and verbascoside was found to be more abundant in the extracts derived from the roots of Echinacea purpurea (**Sloley *et al.*, 2001**). In a free radical scavenging experiment and a lipid peroxidation assay, extracts of the roots and leaves were discovered to exhibit the antioxidant characteristics **(Pellati *et al*., 2004).** Echinacea is thought to exert its immunomodulatory impacts thanks to a number of different physiologically active ingredients, including alkamides, essential oils, caffeic acid derivatives (cichoric acid), and polysaccharides **(Burlou-Nagy, *et al*., 2022; Murray, 2020).** However, researchers have not settled on a single leading candidate for the principal active ingredient. Instead, they have hypothesized that the preparations' many components work together to provide a synergistic effect **(Dalby-Brown *et al*., 2005).**

Echinacea extracts' capability to scavenge free radicals was linked to the amount of cichoric acid they contained, while alkamides had no effect on free radicals **(Orhan *et al.*, 2009; Thygesen *et al*., 2007).** The phenolic contents & cichoric acid in the plant have been correlated with the plant's antioxidant activity **(Hu and kitts, 2000; Tsai *et al*., 2012),** but some studies have found that the extract of the plant has no such property. The radical scavenging activity of cichoric acid against 2,2'-diphenyl-1-picrylhydrazyl (DPPH) is equivalent to that of flavonoids & rosmarinic acid. Even though alkamides have not been displayed to have antioxidant properties, they can boost cichoric acid's activity in two ways: (a) by increasing the acid's surface activity, so it can better access lipophilic emulsion droplets, and (b) by regenerating cichoric acid by transferring allylic hydrogen to the one-electron oxidized form of the acid. Both of these processes are necessary for cichoric acid to be able to effectively inhibit lipid oxidation **(Thygesen *et al*., 2007& Becker *et al*., 2004).**

Table (2): Effect of *Echinacea purpurea* powder on BWG, FI, and FER on rats with immunodeficient.

Parameters / Groups	BWG (%)	Feed intake (g/day)	FER
G1: Control(-Ve)	218.60±22.50[a]	26.50±2.63[a]	0.82±0.004[b]
G2: Control(+Ve)	170.00±27.08[e]	18.42±3.92[c]	0.62±0.004[d]
G3: (CsA) +150 g Ech.	214.40±17.08[b]	24.67±2.10[b]	0.87±0.006[a]
G4: (CsA) +300 g Ech.	206.00±27.85[c]	24.48±3.41[b]	0.80±0.005[c]
G5: (CsA) +450 g Ech.	202.20±25.17[d]	24.37±2.88[b]	0.83±0.037[b]

*Values are expressed as means ±SE.

*Values at the same column with different letters are significant at P<0.05.

According to the findings provided in table (2), the (+ve) control group had a statistically significant reduction in body weight growth percentage contrasted with the negative control group (170.00±27.08 VS 218.60±22.50%), When in contrast to the positive control group, BWG% was shown to be significantly higher in those fed meals supplemented with *E. purpurea*. When contrasting the BWG of groups fed a meal supplemented with varying concentrations of *E. purpurea*, our positive control group, which produced immunological suppression, considerably lagged behind.

Across all tested supplementation levels, animals with access to the tested feed consumed more of it. FI was lowered in the positive control group in contrast to the negative control group considerably (18.42±3.92 VS 26.50±2.63). The (+ve) control group had a lower mean FER (0.62±0.004) contrasted with the (-ve) control group (0.82±0.004), which is a statistically significant distinction (P<0.05). There were no significant variations in FER among the control group and the groups given any of the studied items.

In a study contrasting groups exposed to 7, 12-dimethylbenz (α) anthracene (DMBA) and those exposed to DMBA plus aqueous extracts of Artemisia annua (Art) and Echinacea pupurea (Ech), we found that the DMBA-treated group gained less weight than the Art+ Ech group. Consistent Outcomes were found by **Sarhadi *et al.*, 2020** and **El-Sherbiny**

***et al*., 2021**, who both concluded that Art aided in weight growth and improved total body mass. Rats that had CsA injected into them had their ultimate BWG% and FI significantly reduced after receiving EPR, as compared to the control group. Previous authors **(Nematalla *et al*., 2011)** were not supported by the findings. One possible explanation for these findings is that the toxicity of CsA combined with the anorexia produced by EPR significantly reduced the FI. Studies have shown that taking Echinacea for 4 weeks might increase BW, which is consistent with our findings. Study parameters, such as dosage and length of experiment, may account for the discrepancy **(Ali, 2008).**

Table (3): The impact of *Echinacea purpurea* powder on the relative organ weight of rats exhibiting immune dysfunction.

Parameters / Groups	Heart	Kidney	Liver	Spleen
	(%)			
G1: Control(-Ve)	0.36±0.01[a]	0.77± 0.04[d]	3.11±0.31[a]	0.32±0.05[c]
G2: Control(+Ve)	0.30±0.03[c]	0.74±0.11[e]	3.00±0.29[a]	0.39±0.09[a]
G3: (CsA) +150 g Ech.	0.35±0.02[a]	0.84±0.09[b]	3.21±0.46[a]	0.39±0.05[a]
G4: (CsA) +300 g Ech.	0.34±0.01[b]	0.88±0.05[a]	3.10±0.33[a]	0.39±0.05[a]
G5: (CsA) +450g Ech	0.35±0.05[a]	0.80±0.06[c]	3.03±0.26[a]	0.34±0.04[b]

The impact on the relative weight of the organs is illustrated in Table (3). Heart and liver weights were significantly lower in the (+ve) group of rats with induced immune deficit contrasted with the (-ve) group. When contrasted with the (+ve) control, the mean relative weight of the heart, liver, and kidneys increased when *E. purpurea* introduced into the diet. In contrast to the positive control group, there was a significant elevation in the relative weight of the spleen of the rats compared to the (-ve) group.

Table (4): Effect of *Echinacea purpurea* powder on monocyte, lymphocyte and WBcs of rats with immune dysfunction.

Groups \ parameters	Monocyte	Lymphocyte	WBC
	($\times 10^3$/ul)		
G1: Control(-Ve)	5.00±1.00[a]	43.80±2.68[a]	64.60±3.50[c]
G2: Control(+Ve)	2.60±0.54[c]	38.80±4.55[c]	94.80±3.34[a]
G3: (CsA) +150g Ech.	2.80±0.83[c]	41.60±6.14[b]	40.80±2.16[d]
G4: (CsA) +300g Ech.	2.95±0.83[c]	44.00±1.22[a]	77.80±6.22[b]
G5: (CsA) +450g Ech.	3.40±0.54[b]	40.80±3.27[b]	76.20±8.16[b]

Results illustrated in Table (4) revealed the effect of diet supplemented with *Ech. Purpurea* on monocyte, lymphocyte and WBC in rats with induced immune dysfunction. The positive control group had significant decrease (P<0.05) in the mean value of monocyte and lymphocyte, compared with the control negative group and the groups fed on supplemented diet. Rats fed on different levels of *Ech. Purpurea* had significant decreased in the mean value of WBC compared to the positive control group. On the other hand, the positive control group had significant increase (P<0.05) in the mean value of WBC compared with the control negative group.

The present drop of the total WBCs and differential lymphocytic counts coupled with a decline in RBCs count and Hb concentrate were compatible with the findings of **(Lekhooa, 2015).** This drop was attributed to less erythropoietin being produced, which in turn led to less erythropoiesis being stimulated in the bone marrow **(Nielsen *et al.*, 2008).** On contrary, when EPR was given to CsA-injected rats, A statistically significant improvement was observed across the board for the hematological parameters, with the low-dose group significantly outperforming the high-dose group. These results matched those found by other researchers **(Ezz *et al.*, 2011 & Dehkordi and Fallah, 2011).** According to a previous research **(Goel *et al.*, 2002b),** the cichoric acid & echinacin found in *E. purpurea* are responsible for the beneficial effects on bone marrow & hematopoietic stem cells.

Table (5): The impact of *Echinacea purpurea* powder on RBC parameters in immunocompromised rats.

Groups \ Parameters	HB	RBCS	Platalet
G1: Control(-Ve)	12.82±0.63[b]	7.05±0.19[a]	796.80±56.42[a]
G2: Control(+Ve)	9.34±0.53[c]	5.04±0.66[b]	586.60±93.15[e]
G3: (CsA) +150g Ech.	13.12±0.16 [a]	7.56±0.29[a]	616.80±82.11[c]
G4: (CsA) +300g Ech.	12.98±0.20[b]	7.51±0.16[a]	608.60±58.07[d]
G5: (CsA) +450g Ech.	13.76±0.50[a]	7.61±0.28[a]	681.40±42.33[b]

In contrast to the healthy control group, the mean values of Hb, RBC, and PLT in the positive control group reduced significantly. Conversely, contrasted with the positive control group, the mean levels of HB parameters in rats fed diets supplemented with *E. purpurea* elevated significantly.

Table (6): The impact of *Echinacea purpurea* powder on leucocytic count of rats with immunodeficiency.

Groups \ Parameters	Esonophilis	Mesophilis	Basophilis
	($\times 10^3$/ul)		
G1: Control(-Ve)	2.40±0.54[b]	47.60±2.88[c]	0.60±0.54[a]
G2: Control(+Ve)	3.20±0.83[a, b]	52.00±4.58[a]	0.20±0.44[c]
G3: (CsA) +150g Ech.	3.18±0.83[a, b]	51.40±5.50[a, b]	0.20±0.44[c]
G4: (CsA) +300g Ech.	2.80±0.44[b]	49.00±1.87[b]	0.39±0.54[b]
G5: (CsA) +450g Ech.	4.20±0.83[a]	51.40±2.88[a, b]	0.40±0.54[b]

Comparatively, the mean levels of eosinophilis and mesophilis in the positive control group increased significantly over those in the negative control group. Furthermore, in comparison to the negative control group, the mean value of basophilis decreased significantly in the positive control community.

The total number of leucocytic cells in rats that had undergone induced immune suppression was determined using Echinacea, as shown in Table 6. The average value of mesophilis in rats that were provided with varying concentrations of Echinacea was considerably reduced in comparison to the untreated group.

(Agnew *et al.*, 2008) found a comparable elevation in the leukocyte count in additional research. The capability of echinacin and cichoric acid to stimulate bone marrow & activate macrophages, as well as the capacity of polysaccharides and echinacocide to augment leukocyte count, may account for this result. Furthermore, alterations in the proportion of lymphocyte subpopulations induced by Echinacea suggest that Echinacea could potentially regulate both innate and adaptive immune cellular processes **(Zhai, 2008)**.

Table (7): The impact of *Echinacea purpurea* powder on the levels of serum malondialdehyde and catalase in rats exhibiting immune dysfunction.

Parameters / Groups	MDA (ng/ml)	Catalase (U/L)
G1: Control(-Ve)	1.18±0.05[b]	2.21±0.17[a]
G2: Control(+Ve)	2.94±0.02[a]	1.01±0.22[d]
G3: (CsA) +150g Ech.	1.15±0.05[b]	1.11±0.04[c]
G4: (CsA) +300g Ech.	1.2±0.07[b]	1.08±0.03[c]
G5: (CsA) +450g Ech.	1.6±0.06[b]	1.82±0.05[b]

The mean value of MDA activity decreased markedly ($P<0.05$) when immune deficient rats were fed echinacea, with compared to the positive control group. The catalase activity of rats was elevated when they were fed varying concentrations of echinacea, contrary to the positive control group. The three concentrations of echinacea that were evaluated exhibited beneficial impacts on both MDA levels and catalase activity.

The natural agent, purified polysaccharide extracted from E. purpurea, induced an immunostimulatory response in immune cells **(Wills *et al.*, 2000).** Numerous investigations involving both animals and humans have documented that E. purpurea induces phagocytic functions in macrophages and neutrophils **(Cundell *et al.*, 2003)**. The elevated levels of SOD activity in the bloodstream were attributed to the existence of antioxidant compounds in E. purpurea, including echinacocide and caffeine acid, which eliminate superoxide through the scavenging of free radicals **(Mishima *et al*., 2004).**In addition, an examination of extracts from E. purpurea revealed the existence of a variety of bioactive compounds, such as polyphenolics, caffeic acid (involving glycosylated flavonoids, cichoric acid & polysaccharides), and caffeic acid. These compounds are accountable for specific antioxidant and anti-inflammatory properties **(Turner *et al*., 2005).**

When contrasted with an antibiotic (flavofosfolipol), the desiccated aerial part powder of Echinacea purpurea (EP) significantly increases the total antioxidant activity (AOA) in the serum of broiler chickens. It was discovered that 10 g EP/kg diet increased the antioxidant activity of broiler chickens' serum. Therefore, the plant possesses considerable potential for conducting an assay to determine its AOA, which can be further analyzed in terms of its ability to scavenge free radicals and prevent oxidation **(Gholamreza *et al*., 2011).**

Table (8): Effect of Echinacea *purpurea* powder on serum IgG and IgM of rats with immune dysfunction.

Parameters / Groups	IgG	IgM
	(g/L)	
G1: Control(-Ve)	3.47±0.39[c, d]	27.86±2.90[d]
G2: Control(+Ve)	1.84±0.36[d,e]	19.86±1.17[e]
G3: (CsA) +150g Ech.	3.53±0.34[c]	39.76±2.03[c]
G4: (CsA) +300g Ech.	4.18±0.26[b]	42.18±5.90[b]
G5: (CsA) +450g Ech.	4.40±0.65[a]	43.68±2.73[a]

The results of E. purpurea at various concentrations on the serum immunoglobulins (IgG and IgM) of suppressed rats are shown in Table (8). Injecting into rats to generate immunological dysfunctions led to a substantial drop in the mean value of IgG and IgM in contrast to the control negative group. The average levels of IgG and IgM in the supplemented E. purpurea diet group were greater than in the control positive group ($P<0.05$). The third-level E. purpurea-feeding group also had the greatest levels of IgG and IgM, with mean values of 4.40±0.65 (g/L), 43.68±2.73 (g/L), respectively.

The immunostimulant action of EP and the anti-inflammatory properties of E. angustifolia may be attributed to the polysaccharides present in the tissue cells, which serve as a protective barrier against pathogenic invasion **(Ghaemi *et al.,* 2009).** The anti-inflammatory, anti-oxidative, and anti-proliferative activities of both Echinacea purpurea and Echinacea angustifolia were observed in in vitro tests done by **Aarland *et al.,* (2017).**

Geneva, (1999) demonstrated that, the immunostimulant action of E. purpurea is generated by 3 mechanisms: fibroblast stimulation, Phagocytosis activation, and an improvement of respiratory activity that leads in augmentation of leukocyte mobility. In addition, many in vivo studies have revealed that *E. purpurea* has immunomodulatory and anti-inflammatory effects, which strengthen the immune system against pathogenic infections by activating macrophages, neutrophils & NK cells, polymorphonuclear leukocytes **(Barnes *et al.,* 2005)**.

The first clinical experiment investigating EP for its immunomodulatory properties included female subjects. Following treatment for four weeks, levels of complement properdin were found to have risen. Cases treated with either *E. purpurea/ E. angustifolia* or *E. purpurea/ E. angustifolia* with larch arabinogalactan **(Linda *et al.,* 2002).**

Some of the phytoconstituents found in E. purpurea include caffeic acid derivatives, alkamides, essential oils, flavonoids, and polyacetylenes, all of which are identified to stimulate the synthesis and the process of leukocyte, monocyte, lymphocyte & cytokine activation, which are key components of the non-specific cellular and humoral IR. These factors also regulate the IR by influencing macrophage phagocytosis, B cell response enhancement, pro-inflammatory cytokine production, T cell proliferation, NK cell activation, and T cell cytokine production **(Thygesen *et al.,* 2007)**.

The immune system is boosted by E. purpurea, and the duration and intensity of common colds, flu, fever, sore throats, coughs, and infections are all diminished when utilizing the plant **(Nichols *et al.*, 2008; Ruuskanen *et al.*, 2011)**.

Table (9): The impact of *Echinacea purpurea* powder on serum liver function in rats exhibiting immune dysfunction.

Parameters / Groups	AST	ALT	ALP
	(mg/dl)		
G1: Control(-Ve)	26.60±1.67[d]	14.40±2.40[d]	76.40±5.50[d]
G2: Control(+Ve)	50.16±1.51[a]	45.60±2.07[a]	171.40±9.71[a]
G3: (CsA) +150g Ech.	32.60±4.33[b]	21.60±2.40[b]	138.40±3.20[b]
G4: (CsA) +300g Ech.	28.80±1.09[c]	21.20±2.58[b]	128.80±7.66[c]
G5: (CsA) +450g Ech.	32.60±2.51[b]	18.60±2.40[c]	127.40±6.76[c]

When contrasting the normal group to the immune-suppressed group, the serum liver function activities were significantly greater in the (+ ve) group ($P<0.05$) (Table 9). EP supplementation resulted in a substantial ($P<0.05$) reduction in serum AST, ALT and ALP levels in the immune deficiency group contrasted to the (+ ve) group.

Improvements in hepatocellular structure, as well as a decrease in collagen fibers and hepatic stellate cells (HSCs) proliferation, were seen in hepatic sections of rats given echinacea **(Rezaie *et al.*, 2013).** Protective against toxicity, phenolic diterpenes, polyphenolic components such phenolic acids, flavonoids, and caffeoyl derivatives may be accountable for Ech's antioxidant qualities **(Stanisavljevic *et al.*, 2009).** Ech produced a small decrease in hepatocytes degradation and minor elevation in protein & glycogen staining **(Abdel-Salam *et al.*, 2012).**

The hepatic hypermetabolic state **(Zhi *et al.*, 2001)** and preventing bilirubin and bile salts from crossing the canalicular membranes of hepatocytes via ATP-dependent transport **(Bohme *et al.*, 1994)** are two ways by which CsA causes liver damage. Evidence shows that oxidative stress is involved in the hepatotoxic process when it is treated with antioxidants in experimental rats exposed to CsA **(Akbulut *et al.*, 2015; Kwak and Mun, 2000).**

The liver is negatively impacted by immunosuppressive medication that is kept up for an extended period of time. Loss of appetite, weight loss, jaundice, weariness, and irritability can all be signs of CsA-induced hepatotoxicity, which can progress all the way to death in extreme situations **(Kassianides *et al.,* 1990).** Additionally, elevated levels of BIL, LDH, ALT, and AKP were detected. Total protein, albumin, and globulin all saw a drop in their respective ratio coefficients. First-stage hepatotoxicity caused by CsA is characterized by vacuolar degeneration, turbidity, edema, necrosis, and nuclear disintegration in hepatocytes. Lymphocytes and neutrophils were seen infiltrating the vascular region with the deterioration of the central lobule's underlying structure and the disappearance of cord-like structures. By the end of CsA-induced hepatotoxicity, cholestasis had set in, and Kupffer cells and fibroblasts had multiplied **(Mostafavi-Pour *et al*., 2008).**

Hepatotoxicity caused by CsA involves a number of inter connected processes, including the production of free radicals in the liver, an imbalance in mitochondrial biology, and an elevation in intracellular calcium **(Qi *et al.,* 2018). Korolczuk *et al*., (2016)** discovered that in rats, CsA therapy led to oxidative stress and a redox imbalance in hepatocytes, damaging liver function. Further evidence that mitochondrial damage and the associated alteration of oxidative stress indicators play a significant role in the development of CsA-induced hepatotoxicity was found when mitochondrial activity was damaged in liver cells. Toxic effects of CsA on the liver were demonstrated by **Kayah *et al*. (2008),** who discovered that ROS production was a contributing factor. CsA produced ROS buildup in liver cells, resulting in an increasein hydrogen peroxide and a reduction in SOD activity in vivo, which further culminated in the incidence of liver damage.

<u>Histopathological examination of the spleen:</u>

Histological analysis of the white pulp lymphoid follicles in the spleens of rats in the first group revealed a typical organization **Photo (1).** Instead, the spleens of group 2 rats showed signs of lymphocytic necrosis and lymphoid follicle depletion, as well as the development of visible macrophages **Photo (2).** Meanwhile, spleen of rats from group 3 demonstrated no histological changes **Photo (3).**While group 4 sections showed mild lymphocytic necrosis and depletion **Photo (4).** Additionally, there were no histopathological changes found in any of the Group 5 sections that were analyzed histopathology **Photo (5)**.

Corresponding to the observations of **Abdel-monem *et al.*, (2015),** who observed that addressing Ech against oxidative stress reduced inflammation in cardiac tissues, the present study's results support this hypothesis. Since Ech is inexpensive and has no known adverse effects, **Abdel-monem *et al.*, (2015)** concluded that it is an appropriate therapeutic agent for fostering cardiac stem cell proliferation, differentiation, and survival. Further, **Sloley *et al.*, 2001** stated that Ech extract's preference in reducing histopathological alterations was because of its antioxidant capabilities and components such flavonoids and polyphenolic complexes.

It has been suggested that the Ech root extract's free radical scavenging and transition metal chelating abilities are responsible for its protective benefits in the current investigation **(Izzo and Ernst, 2001).**

Reducing overall levels of oxidative stress helps repair tissue damage caused by oxidative stress. Antioxidants prevent illness by scavenging free radicals and mitigating the adverse effects resulting from lipid peroxidation and other free radical-mediated processes **(Marsoul *et al.*, 2016).** Keeping antioxidant capacity high to shield tissues from oxidative stress is crucial to the protective impact of EPR seen here. The AOA of EPR, which includes scavenging free radicals and chelating transition metals, may be responsible for this beneficial effect **(Hu and Kitts, 2000).**

EPR was shown to reduce the severity of the hematological alterations, concluding the present investigation. Microscopic alterations in the rat spleen caused by CsA were partially restored. From a biological perspective, CsA may be a BW-reducing agent, which offers hope to medicinal pharmacists in pursuit of novel drugs.

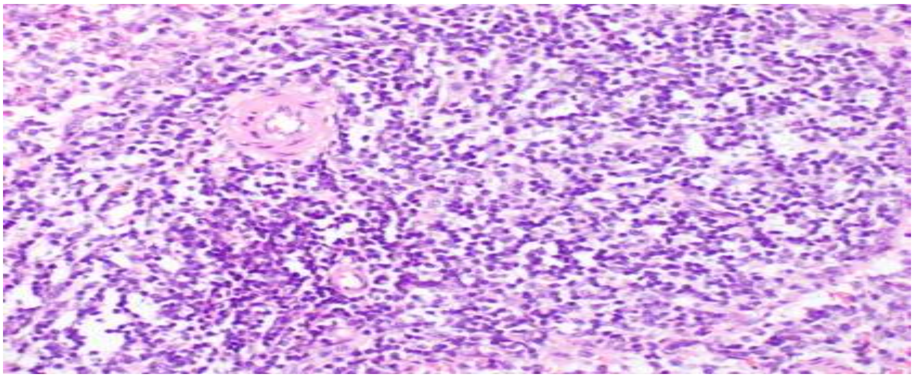

Photo (1): Spleen section of rat from group 1 displaying the normal histological architecture of white pulp (H & E, X 400)

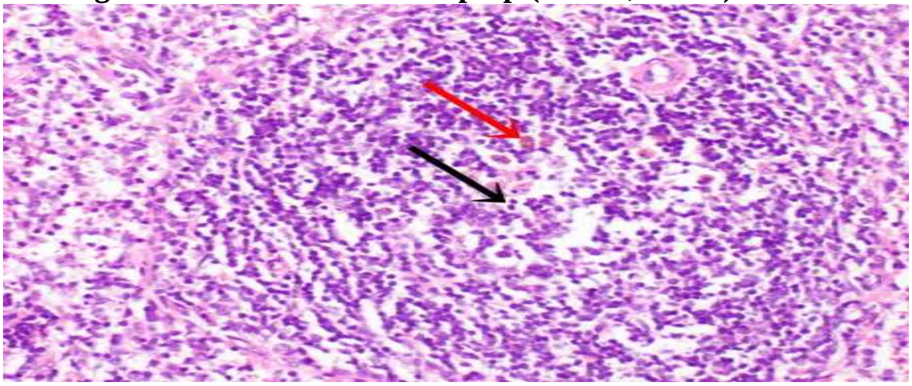

Photo (2): A spleen section from a rat in group 2 exhibited lymphocytic necrosis and depletion (black arrow), accompanied by the presence of tangible macrophages (red arrow) (H&E, X 400).

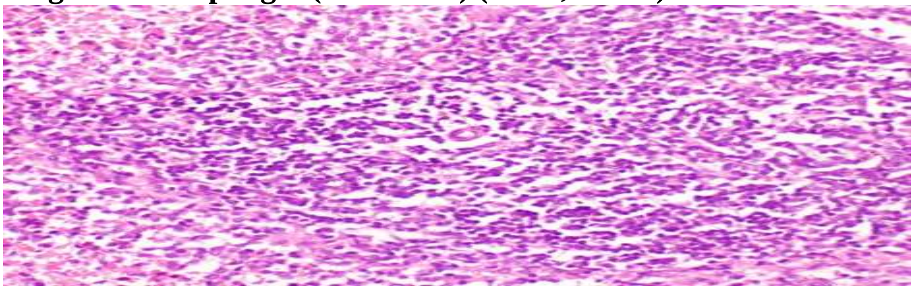

Photo (3): A section of the rat spleen from group 3 demonstrated no histopathological changes (H&E, X 400).

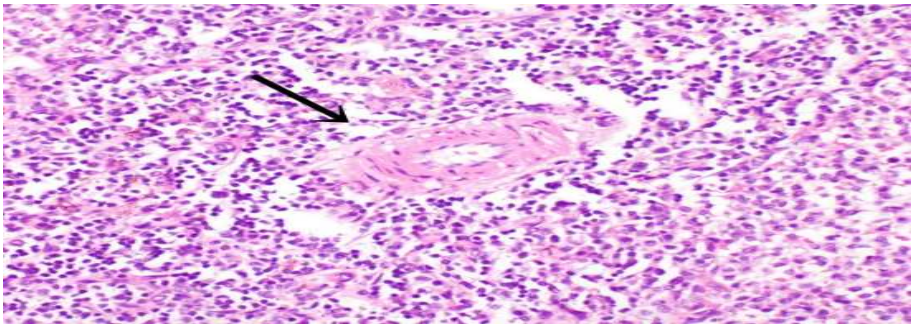

Photo (4): A rat spleen section from group 4 exhibits slight lymphocytic necrosis and depletion, as indicated by the black arrow (H&E, X 400).

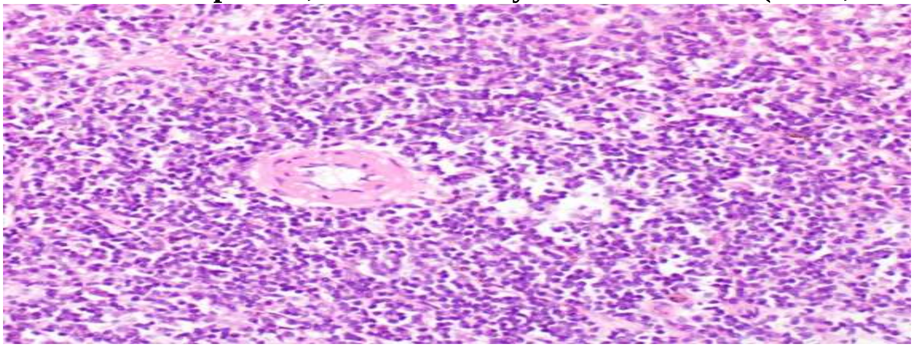

Photo (5): Spleen section of rat from group 5 displaying no histopathological alterations (H & E, X 400).

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التأثير العلاجي للاخنسيا على الفئران المصابة بخلل في المناعة

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الملخص العربي:

الهدف من هذا العمل هو دراسة تأثير التدعيم بالاخنسيا على مقاييس الدم والوظائف المناعية في الفئران. تم استخدام ثلاثين فأر من ذكور ألبينو وزنها ١٨٠±٥ جم في هذه الدراسة. المجموعة الأولى (ن = ٦) تم إطعامها على النظام الغذائي الأساسي، المجموعات من ٢- ٥ تم حقنها سيكلوسبورين (50 CsA) مجم لمدة ٢١ يوم. المجموعات من ٣- ٥ تم تغذيتها على مسحوق الاخنسيا بثلاثة مستويات (٣٠٠ و١٥٠ و٤٥٠ جم/كجم دايت) على التوالي. تم تقدير المكونات الفعالة لمسحوق الاخنسيا. تم عمل هستوباثولوجي للطحال. سجلت نتائج المكونات الفعالة لنبات الاخنسيا وجود العديد من المركبات الهامة. أشارت النتائج إلى أن مجموعات الفئران التي تتغذى على الاخنسيا قد زادت بنسبة معنوية من مقاييس المناعة ($P < 0.05$). زاد متوسط قيمة IgM وIgG للفئران التي تتغذى على الاخنسيا مقارنة بالمجموعة الضابطة الموجبة. تمت زيادة القياسات الدموية معنويا ($P<0.05$) للمجموعات التي أعطيت الاخنسيا في النظام الغذائي. ومع ذلك، انخفض عدد خلايا الدم البيضاء بشكل ملحوظ. ومع ذلك، لوحظت زيادة معنوية في زيادة وزن الجسم والمأخوذ من الطعام ونسبة كفاءة التغذية للمجموعات المختبرة مقارنة بالمجموعة الضابطة. كما أظهرت النتائج زيادة معنوية في مستويات كرات الدم الحمراء والهيموجلوبين مقارنة بالمجموعة الضابطة الموجبة. كان هناك تحسن في إنزيمات الكبد للمجموعات التي تغذت على الاخنسيا مقارنة بالمجموعة الضابطة الموجبة. يمكن أن نستنتج أن الأخنسيا تحفز الجهاز المناعي للفئران المصابة بخلل المناعة.

الكلمات المفتاحية: الإخناسيا بوربوريا، الجهاز المناعي، إنزيمات الكبد، السيكلوسبورين

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