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Protective Effect of *Prosopis farcta* Fruit Aqueous Extract against Oxidative Stress Caused by Ethanol in Albino Rats

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Prosopis farcta **was previously used in folk medicine as a dry fruit to relieve pain before its active biological components that contribute to this were known. This study assessed the effectiveness of a dry fruit extract of P. farcta by measuring the indicators of inflammation in albino rats after they were dosed with ethanol. As such, looking at the antioxidant potential of *P. farcta* fruit aqueous extract (PFFAE) in resistance to ethanol's harm in rats given ethanol showed a notable increase in serum C reactive protein (CRP), malondialdehyde (MDA), CRP/ALB ratio (CAR), and WBC count. At the same time, glutathione peroxidase (GPx) and albumin were markedly reduced. PFFAE diminished ethanol-induced amounts of CRP, MDA, and CAR in plasma; additionally, it strengthened the ethanol-induced decline in GPx activity, and albumin had no apparent effect on the ESR level. Consequently, the current findings demonstrate that PFFAE counteracts the toxicity of ethanol and has a protective impact against the ethanol effect.**

Keywords: Albumin, CAR, glutathione peroxidase, Inflammation, malondialdehyde, *Prosopis farcta*.

Prosopis farcta, or Syrian mesquite, is a flowering herb native to Asia and belongs to the Fabaceae family.[1] *P. farcta* fruits contain various bioactive compounds; for this reason, they have been used in traditional medicine in many Asian countries.[1,2] The fruit extract contains 99.2% of the essential substances and bioactive chemicals, such as gallic and vanillic acids, alkaloid compounds, quinones, phenol compounds, glycosides, tannins, triterpenoids, and phytochemical compounds of natural antioxidants, for use in biomedicine and the food industry.[2,3] The phytochemical composition, C-glycosyl flavone content, is increasingly associated with the observed biological effects. Epidemiological research has proposed an opposite relationship between the expenditure of these phytochemicals and a decreased risk of complications, such as certain disorders or chronic.[2] The dried fruits have been used to treat various ailments, including kidney stones.[4] asthma, calluses, diabetes, diarrhea, scabies, otitis, rheumatism, abdominal pain (ulcer), fever, flu, breastfeeding, liver infection, malaria, conjunctivitis, pancreatic stones, and

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cardiovascular conditions.[2] pregnancy, newborn illnesses, skin wounds, and burns.[5] Furthermore, the therapeutic benefits of diabetic foot ulcers, laryngitis, and dyspnea have been demonstrated. It also has antispasmodic, anti-inflammatory, and pain-relieving properties.[6] Possess fascinating antispasmodic, antipyretic, cancer-fighting, antidiabetic, and wound-healing properties.[7] According to several studies, both in vivo and in vitro, antioxidant, antimicrobial, and anticancer activities were discovered in an experiment.[8] The findings also stated that its high concentration of phenols and flavonoids is directly responsible for its antioxidant properties.[9] The n-butanol, ethyl acetate, and 5-fluorouracil extracts of the aerial parts of *P. farcta* were estimated to have anticancer vitality against many lines of tumor cells in humans.[10]

Alcohol intake, non-steroidal anti-inflammatory drugs, cigarettes, a poor diet, and physical and psychological stress usually lead to stomach ulcers.[11] These factors may cause oxidative stress.[12] Ethanol leads to ulceration of the gastric mucosa through the production of extremely harmful free radicals and their effect as a necrotic agent.[13] Because ethanol interferes with stomach mucus secretion, alters the permeability of endothelial cells (mucosa), and reduces mucus secretion, gastric mucosal cells become more vulnerable to free radicals.[14] Oxidative stress (OS) is the mismatch between pro-oxidant processes brought on by reactive oxygen species (ROS) and an organism's ability to fend off their excessive synthesis or deal with the fallout from them. Numerous studies have demonstrated that elevated ROS generation in gastrointestinal diseases causes inflammation and increases ROS creation.[15,16] The current study might offer a quick and safe way to alleviate the inflammation brought on by large doses of ethanol in rats using three different concentrations of the aqueous extract from the fruits of *P. farcta*.

MATERIALS AND METHODS

Extract preparation

Dried fruits of *Prosopis farcta* were purchased from the Ibn Sina's herbarium, Al Nasr District Street, Kerbela, Iraq. The *P. farcta* fruit aqueous extract (PFFAE) is a standardized water extract from *P. farcta* fruits. The fruits were cleaned, the cores were separated, and a mechanical grinder was used to smash the fruits into a fine powder. The 500-gram powdered fruit sample was disintegrated in 500 mL of purified water and left to stand for 24 hours at room temperature (25 ± 2 °C) before being filtered. After that, the filtrate was put into a stainless-steel plate, where the extract was dried for 12 hours at 30 °C in the oven.[17] The concentrated extract was kept in refrigerators in clearly marked containers until it was required for the study. The final product was the crude extract, diluted with distilled water and given to the rats. Ethanol was purchased from Reflecta Laboratory Supplies, South Africa. All other reagents utilized on the practical side were of analytical grade.

Animals and experimental protocol

Thirty-two male *Rattus norvegicus* with an average weight of 180–200 g were used. The current study obtained animals from the animal house of the College of Pharmacy / University of Karbala. The procedure complies with National Institutes of Health (NIH) requirements, and the local committee approved the research design. The animals were kept in groups of four in cages, with unlimited access to food and water. Following two weeks of acclimation, the animals were split into four equal groups: group I (control) was treated with distillation water; group II (ethanol) was dosed with 35% ethanol for 0.005 ml/g to induce inflammation (Abdel-Kawi et al. 2022),[18] Group III were orally treated with PFFAE (400 mg/kg bw),[19] after one hour of dosing with 35% ethanol at 0.005 ml/g. Group IV was orally treated with PFFAE (300 mg/kg bw),[20] after one hour of dosing with 35% ethanol at 0.005 ml/g. All groups were orally administered for 30 consecutive days.

Experimental parameters

The C-reactive protein (CRP) and albumin were measured using Rat CRP and Albumin Detection Kits from Chondrex (USA), and the CRP/albumin ratio This ratio is called "APRs." It is calculated by dividing the level of CRP by the albumin level,[21] erythrocyte sedimentation rate (ESR), white blood cell (WBC) leucocyte count measured by using BC-3000Plus hematology machines Mindray (India), malondialdehyde (MDA) measured by using Dojindo's MDA Assay

Kit (Japan), and glutathione peroxidase (GPx) measured by using the rat glutathione peroxidase (GPX) ELISA Kit Siga-Aldrich (Germany).

Statistical analysis

The statistical significance among the groups was evaluated using IBM SPSS Statistics (22.0) and a one-way ANOVA table. A P-value of less than 0.05 ($P < 0.05$) was considered significant. The least significant difference was taken to verify the validity of the observed effects.

RESULTS

Table 1 showed significant differences in blood parameter levels, i.e., ethanol group 2. The experiment's blood parameters (CRP, CAR, MDA, GPx, ESR, WBC, and albumin) may be altered by ethanol. While there was a significant increase ($P < 0.05$) between the ethanol group II and the low-concentration treatment group (III) compared to the control group, there were no discernible differences in the levels of CRP between the treatment groups (IV and V) and the group I (control) ($P = 0.05$), which could be explained by Group II's high level of ethanol-induced inflammation.

All study groups had significantly lower albumin levels than the control group ($P > 0.05$), and the II and III groups had lower albumin levels than the IV and V groups. Table 1 indicated no significant differences in the albumin/CRP ratio between Groups IV and V and Group I ($P = 0.05$). There is a significant rise ($P < 0.05$) compared to the control group, in contrast to the II and III groups. Compared to other parameters, the ESR levels showed a significant increase ($P < 0.05$) in groups III, IV, and V compared to group I; however, there were no significant differences ($P = 0.05$) between groups III, IV, and V and group II and the control group on the other hand.

Regarding the WBC count, it was found that all research groups saw a substantial increase ($P > 0.05$), especially in group (I) findings. In contrast, the IV and V groups experienced a significant reduction ($P > 0.05$) compared to the II and III groups. Ultimately, the findings showed that, in comparison to the control group, all research groups had significantly higher MDA rates ($P < 0.05$); however, group II saw a significantly lower MDA rate ($P > 0.05$) in the IV and V groups. All experimental groups, including group II (ethanol),

Table 1. Parameters assessment in various experimental groupings

groups	CRP (mg/dl)	Albumin (mg/dl)	CRP/ALB ratio	ESR mm/hr	MDA (µmol/l)	GPx (IU/l)	WBC (x103/µL)
Group I	0.10 ± 0.00	4.46 ± 0.38	0.21 ± 0.01	2.00 ± 0.00	1.12 ±0.12	47.16 ± 1.40	04.00 ± 0.42
Group II	1.05 ± 0.29C^{a}	2.40 ± 0.38^{a}	0.45 ± 0.15^{a}	2.00 ± 0.00	2.93 ± 0.5^{a}	38.76 ± 0.57^{a}	14.11 ± 0.99^{a}
Group III	0.60 ± 0.33^{ab}	2.70 ± 0.23^{a}	0.23 ± 0.14^{ab}	2.50 ± 0.55^{ab}	3.05 ± 0.40^{ab}	32.41 ± 1.17^{a}	09.58 ± 0.88^{ab}
Group IV	0.17 ± 0.07^{b}	3.77 ± 0.08^{ab}	0.04 ± 0.02^{b}	2.50 ± 0.55^{ab}	1.77 ± 0.15^{ab}	41.75 ± 1.17^{b}	07.56 ± 1.11^{ab}

The values are clearly mean ± SD value, n = 6 in each group, [b]show the difference in statistics. With a control group, [b]statistical disparity according to illness group, ($P < 0.05$).

had lower MDA values than the treatment group with the lowest concentration. All study groups had considerably lower levels ($P > 0.05$) of GPx than the control group, whereas groups IV and V had significantly greater levels ($P > 0.05$) than groups II (ethanol) and III.

DISCUSSION

The effect of ethanol on the Blood parameters levels

We observed a notable rise in the level of C-reactive protein in group II as opposed to other experimental groups, which confirms the role of ethanol in stimulating inflammatory factors, which in turn increase C-reactive protein levels.[22] This is also the case for substances. The levels of malondialdehyde oxidation and the number of red blood cells increased in this second group as opposed to the experimental and control groups. Ethanol stimulates oxidative stress through the production of ROS [23] and plays a crucial role in many diseases, such as gastric ulcers.[24]

The effect of *P. farcta* extract on the CRP level

The CRP levels gradually decreased in the treatment groups (III, IV) that received amounts of 0.15, 0.30, and 0.45 mg/kg of P. farcta extract after receiving 0.005 ml/g of 35% ethanol; this indicates that the aqueous extract lessened the effects of ethanol in these groups relative to group II, and the lower concentration of the aqueous extract in the treatment group III, 0.15 mg/kg, had less effect on the CRP level.

CRP is broadly utilized as an indicator for the diagnosis and control of inflammation and tissue damage involving sepsis, trauma, and malignancies.[25] CRP secondary effects that come after binding share some of the primary characteristics of antibodies, acting as an inflammatory medium and bolstering the host's defense against infection.[26] Rats myocardial infarction has been seen as direct evidence of its role in exacerbating tissue damage as a result of its inflammatory effect,[27] and the fact that levels of CRP are an indicator of the presence of inflammation,[28,29] therefore, its decrease in the groups of 0.30 and 0.45 mg/kg concentration of aqueous extract of *P. farcta* is evidence of its role as an anti-inflammatory,[5] caused by ethanol, which increases the liver's synthesis of CRP.[30] Half of CRP is about 19 hours old in the bloodstream and increases within 6 hours of inflammation or tissue damage. It peaks within 2–3 days of the onset of inflammation but declines rapidly as the state of inflammation disappears.[31] This explains its low level in III, IV, and V groups as opposed to its counterpart in ethanol group II.

The effect of *P. farcta* extract on the Albumin level

Albumin levels considerably dropped in group II due to the ethanol while remaining unaffected in group III, which received the smallest dose of 0.15 mg/kg of the aqueous extract of P. farcta. However, the levels of albumin in the IV and V treatment groups that received doses of 0.30 and 0.45 mg/kg of *P. farcta* extract after receiving 0.005 ml/g of 35% ethanol showed a significant increase, which indicates that the extract's effects are visible in the rise in albumin levels in these two groups.

Albumin plays an essential role in physiology by distributing body fluids, regulating basal acid balance, inhibiting the functioning of platelets and vascular permeability, maintaining osmosis pressure[32], and binding essential ingredients in the bloodstream.[33] Furthermore, a result of being prescribed properties as an antioxidant by trapping free radicals,[34] compared to the CRP that rises in inflammation, and because the half-life of albumin is 19 days,[35] it gradually decreases from the moment inflammation begins, especially in hepatocytes, whose levels may indicate a wide range of conditions and diseases, including kidney disease, liver disease, malnutrition, inflammation, and cancer[36]; therefore, doctors may use it to evaluate the nutrition of patients and follow up on infections that cause a significant decrease in its concentration,[37] a decrease in serum albumin (< 3.5 g/dL) is often due to the death of hepatocellular cells resulting from chronic liver disease and impaired albumin synthesis; a decrease in its level in inflammatory cases is expected; and it has been proposed that this product plays a crucial role in reducing production during inflammation.[38,39] The decreased albumin level in the ethanol group II indicates hepatocyte damage. In contrast, the beginning of its gradual rise in the therapeutic groups of 0.30 and 0.45 mg/kg concentration of aqueous extract of *P. farcta*

indicates an improvement in the physiological condition of these groups due to the effect of this extract.

The effect of *P. farcta* extract on the CAR level

In the current investigation, the albumin/CRP ratio was determined to corroborate the findings that the levels of albumin and CRP are inversely correlated. Recent works have focused on the interactions between albumin and CRP. For example, the ratio of albumin to CRP, i.e., CAR, is considered a new biomarker of clinical conditions.[40] More recently, CAR was examined in patients with several types of malignant tumors,[41] and in the context of cardiovascular disease,[42] by linking the adjusted early warning index (MEWS) with the CAR ratio for rapid diagnosis of these critically ill patients.[43] The CAR is commonly used as a factor to measure the activity of inflammatory cases and determine the degree and activity of inflammatory disease with a consistent recording system, which is a more useful indicator of inflammatory cases than the measurement of CRP or albumin in isolation.[44] Its elevation was found in acute pancreatitis patients; the CAR was calculated in the current study to support the results of the level of CRP and albumin, which are inversely proportional.[45] As a result, the *P. farcta* extract's impact on the CAR is still obvious because it follows from its impact on CRP and albumin.

The effect of *P. farcta* extract on the ESR level

Because of ESR's slow reaction to inflammation due to its poor sensitivity to simple inflammation, the initial rise starts within 24–28 hours and drops once inflammation resolves. It cannot diagnose disease due to its slow response to inflammation.[46] ESR is known to be impacted by an extensive array of physiological and pathological factors that include not only changes in the concentration of fibrinogen in plasma but also changes in the size, shape, and number of aqueous chloride, as well as the presence of acute-phase reaction proteins (such as immunoglobulin).[47] and for the speed at which it is affected by the factors caused by the disease (inflammation), so it is expected that there will be a variation between its rates in all experimental groups; in other words, it is a non-specific indicator of diseases, and since our current study did not include inducing a specific disease in itself but rather an inflammatory response produced by the high and repeated concentration of ethanol, Therefore, when designing the experiment, several considerations were considered. The most important was the selection of male laboratory animals for the sensitivity of ESR to physiological factors between females and males on the one hand, between pregnant females, the period of menstruation, and natural females on the other hand.[48] Success in treating many diseases depends on early recognition of the patient's condition. The ESR is a valuable test for this purpose.[49] In addition, the induction of a pathological condition in healthy and medium-life laboratory rats with alcohol may not be sufficient to stimulate severe inflammatory conditions that raise ESR levels, especially since this is a biomarker that is often used to assess and follow up on specific conditions such as rheumatic arthritis.[50] Finally, due to the presence of more sensitive and specific inflammatory biomarkers, ESR is often not recommended as an examination test.[51] There was no clear effect of *P. farcta* on the ESR level in the present study; ESR was not affected by the high doses of ethanol.

The effect of *P. farcta* extract on the WBC count

The increasing count of WBC in the ethanol group II was gradually reduced when they received amounts of 0.15, 0.30, and 0.45 mg/kg of aqueous extract *of P. farcta* after receiving 0.005 ml/g of 35% ethanol, to the point where there was a considerable decrease in it compared to the ethanol group II, to be the highest in the treatment group III (0.15 mg/kg concentration) among the three treatment groups. These results are consistent with the study by Shakeri and Boskabady, 2017.[52]

Because of their immunological importance, leukocytes (WBC) are highly affected by inflammation and are more than usual in pathological cases.[53] Therefore, a rising count of WBCs in ethanol group II was gradually decreased when they were treated in groups of 0.15, 0.30, and 0.45 mg/kg concentration of aqueous extract of *P. farcta*, which indicated two main factors: factors that have aided in the rise in the incidence of inflammation in the blood of experimental rats (ethanol), as seen in all experimental groups, Other factors have contributed to some extent to the reduction of the incidence of ethanol-induced inflammation in groups III, IV, and V, which have been an aqueous extract of *P. farcta* .[54] This shows the WBC count in this group is closer to that in group I.

The effect of *P. farcta* extract on the GPx and MDA levels

In the current investigation, oxidants and antioxidants were among the most crucial characteristics that were compared since they are impacted by several physiological aspects brought on by the action of ethanol and the impact of *P. farcta*. The treatment group with the lowest concentration displayed the highest MDA value compared to all experimental groups, including group II (ethanol). Specifically, the 0.30 and 0.45 mg/kg of aqueous extract of *P. farcta* after receiving 0.005 ml/g of 35% ethanol had a noticeable effect in that it lowered the level of MDA to the lowest level in the IV and V groups.[55] The low percentage of MDA in the 0.30 and 0.45 mg/kg of aqueous extract of *P. farcta* after receiving 0.005 ml/g of 35% ethanol is explained by oxidants being inversely related to GPx levels.

Oxidants and antioxidants are among the most critical parameters that were compared in the current study because they are affected by the different physiological factors resulting from the action of ethanol and the effect of *P. farcta.* MDA is produced as a by-product that has the role of head of the oxidative reaction and is one of the vital signs of oxidative stress,[56] which occurs due to the accumulation of free radicals that increase lipid oxidation as a result of the imbalance between oxidizing substances and antioxidants, which leads to cell damage such as liver cells.[57,58] Therefore, its accumulation in the blood leads to excess free fatty acids and then hyperlipidemia, which can cause the overproduction of reactive oxygen species (ROS), thereby damaging the mitochondrial DNA.[59] MDA from lipid peroxide is associated with an intense contributory link due to the presence of two groups of carbonyl within the molecule, affecting its function.[60] So the low level of antioxidants such as SOD, GPx, glucose, or excessive output of ROS such as (OH-), superior (O2"), and (H2O2) will both cause an increase in oxidative stress, thereby increasing the level of MDA.[61] The major inflammatory factors are increased oxidative substances, oxidative stress, and ROS levels.[62] Increased levels of ROS lead to the oxidation of polyunsaturated fatty acids (PUFA) found abundantly in cell membranes to form MDA. Hence the low production of SOD, GPx, and Catlaz. Under oxidative stress conditions, this MDA might be utilized as a biomarker of the cell damage caused by free radicals,[63] Accordingly, it can be argued that the cellular machinery for reducing oxidative stress is done by increasing antioxidants that interact with oxidants (free radicals and their types),[64] but this mechanism occurs within the low limits of fat oxidation by-products and cannot treat the large quantities that occur to accumulate and cause cell aging and some pathological conditions.[65,66]

Since the oxidants are inversely proportional to the levels of GPx, and this explains the low percentage of MDA in the groups treated with the aqueous extract of *P. farcta*, the effect of the GPx is attributed to the presence of the flavonoids,[9] which are polyphenols that prevent the oxidation reactions by giving free radicals one electron in exchange for a non-double electron, therefore lowering their quantity.[67] Therefore, to maintain normal metabolism in the body, GPx is an essential antioxidant. Some recent studies suggest that glutathione types are associated with the occurrence, development, and treatment of different types of tumors.[68] and prevention. In addition to being an antioxidant, GPx is an antioxidant, and it is vital to human health, reducing the generation of free radicals through their unique chemical reaction [69] and neutralizing free radicals from their original form [57]. For this reason, there are opposite results between MDA and GPx levels.[70]

CONCLUSIONS

It was found that the aqueous extract of the P. Farcta fruits had an apparent effect on reducing the inflammatory markers that were measured in laboratory albino rats, which included CRP, albumin, GPx, MDA, and WBC because it contains antioxidants such as gallic acids and vanillic acids and reduces inflammation such as apigenin, quercetin, and luteolin.[71,72] Many types of flavonoids are anti-inflammatory agents that reduce CRP levels.[73] There was no apparent effect on the ESR level in the treatment groups fed high concentrations of the aqueous extract of *P. farcta*, which reduced the percentage of MDA.

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Author contributions

MM and TJ contributed equally to this work; conceptualization and methodology; resources; data project administration; MA and TJ; funding acquisition; MM and MA. All authors have read and agreed to the published version of the manuscript.

Conflict of interest

The authors declare that the research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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