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Original article

Anti-Inflammatory Activities of Aqueous Extract of *Phoenix dactylifera* Fruits in Levofloxacin-Induced Inflammation in Wistar Female Rats

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ABSTRACT
Phoenix dactylifera, also known as date palm, from time immemorial has been using both for nutritional and medicinal purposes. The present study aimed to evaluate the pro-inflammatory and antioxidant enzymes/biomarkers activities of aqueous extract of Phoenix dactylifera in Levofloxacin–induced inflammation in female rats. A powdered sample of the edible portion of the plant was extracted using the cold-water extraction method. A total of 30 female rats were divided into 5 groups of 6 rats each and were administered different doses of Phoenix dactylifera aqueous extract, ranging from 100, 200, and 400mg/bodyweight, while the reference group was administered the standard drug diclofenac, and the 5th group was left untreated and uninduced. At the end of the study, the animals were sacrificed, and blood samples were collected for analysis. Determination of pro-inflammatory enzymes and antioxidant enzymes was carried out using standard procedures. Findings from the study indicate that the aqueous extract of Phoenix dactylifera exhibits its action in a dose-dependent manner, also it competes favorably well with the group administered the reference drug. Thus, the finding from the study justifies the use of the plant in the treatment of several inflammatory-related illnesses in folk medicine.
***Keywords**: Phoenix dactylifera, Inflammation, Antioxidant, Diclofenac, Enzymes*

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INTRODUCTION

Functional foods such as fruits and vegetables have been widely explored owing to their health-promoting potential. These foods present exciting properties mostly related to the antioxidant and anti-inflammatory actions of their chemical constituents that may prevent the pathogenesis of different diseases. The beneficial effects of these foods have been credited to their chemical composition, such as phytochemicals, polyphenols, vitamins, minerals, or organic acids (1). The nutritional and health benefits of these plants have led to the search for more bioactive secondary metabolites, their bioactivity, nutraceutical properties, and health benefits by the scientific community (2). Research outcome from numerous studies carried out also linked a decline in death rate of individual who consume vegetables and fruit as part of their daily diet to those who do not (3).

Inflammation is a biological form of defense by living organisms against invasive organisms such as viruses, bacteria, and fungi, or it could occur through physical agents or poor immunity (4,5). Some of the key indicators of inflammation in living cells include: swelling, pain, redness, loss of function of cells, and high temperature (6). Living cells in humans naturally developed protective mechanisms in response to body inflammation due to microbial infection, mechanical injuries,

and burn stimuli (7). Most cases of inflammation result in massive activation and mobilization of phagocytes, production of $^{-}O_2$, ^{-}OH radicals, and hydrogen peroxides (H_2O_2) (8). Inflammation has become a focal point for most scientific research, also since there have been recorded adverse drug reactions in the majority of the anti-inflammatory agents, both steroidal and non-steroidal, presently in circulation (9,10). Therefore, food containing antioxidants or processed fruits and vegetables in the form of supplements may be used to scavenge free radicals that are generated during the inflammation process in the human body, thereby reducing oxidative damage. Several medicinal plants are utilized in the management of reactive oxygen species, and positive results are recorded. his plants are important as they have antioxidant potential due to the presence of dietary antiradical supplements and anti-inflammatory properties.

Phoenix dactylifera, also referred to as date palm, is widely cultivated all over the world. According to a report by the Food and Agriculture Organization (FAO), date palm production covers an area of 1.09 million hectares globally, with a total production exceeding 8.5 million tons per year (11). The importance of the plant in human nutrition comes from its rich composition of bioactive compounds with antioxidant and antimicrobial activities; it is also a valuable source of dietary fiber, carbohydrate, and certain essential vitamins and minerals, which can be extracted and used as a value-added ingredient (12,13). Hence, this study was carried out to evaluate the anti-inflammatory activities of the aqueous extract of Phoenix dactylifera fruits on pro-inflammatory and antioxidant enzymes in levofloxacin-induced inflammation in female rats.

METHODS

Animals

A total of 30 female Wistar rats with an average weight of 120.94 ± 2.66g were used for the study. They were obtained from the animal holding facility of the Department of Biochemistry, University of Ilorin, Ilorin, Kwara State, and were acclimatized for two weeks. The animals were maintained on standard rat pellet feed with clean water before the commencement of the experiment.

Preparation of Aqueous Extract

1000g dried pulverized sample of the edible parts of *Phoenix dactylifera* was measured into a plastic container, and 4 liters of distilled water was added, and then made up to 5 liters. This content was stirred continuously for about 30 minutes and allowed to soak for 72 hours. 2 mL of ethanol was added to the mixture to prevent fermentation. At the end of 72 hours, the soaked content was filtered with muslin cloth and Whatman filter paper to obtain the aqueous extract of *Phoenix dactylifera* fruit which was further concentrated in a water bath at 40℃.

Induction of inflammation

A total of 25 female Wistar rats were induced for inflammation by oral administration of 10mg/kg body weight levofloxacin for two weeks in line with the procedure described by Hadjeret et al., 2021. Inflammation was confirmed by evaluating the concentration of C-reactive protein, determination of superoxide dismutase activity, and catalase activity from Serum collected after three (3) days into the study by retro-orbital sinus puncture (14).

Animal Grouping

Experimental animals used for the study were divided into 5 groups of 6 animals each. Animals in group A comprise non-induced/ normal rats, whereas the other groups, B (Inflamed not treated), C (Inflamed rats treated with reference drug) D (Inflamed rats treated with 100mg/kg body weight of diclofenac), E (inflamed treated with 100mg/kg body weight of aqueous fruit extract of *P. dactylifera*), D (Inflamed rats treated with 200mg/kg body weight of aqueous fruit extract of *Phoenix dactylifera* (AFEPD)) and E (Inflamed rats treated with 400/kg b.w. of aqueous fruit extract of *Phoenix dactylifera* (AFEPD)).

Preparations of animal serum

At the end of the study period, the animals were sacrificed by jugular vein puncture, and the blood was collected into two sets of clean centrifuge tubes with EDTA in one of the tubes. Blood samples with EDTA anticoagulant were left undisturbed at room temperature before being subjected to hematological screening, whereas the other sample was stored in an ice pack and later centrifuged at 4000 rpm for 15 minutes using a Uniscope laboratory centrifuge (Model 5M800B, Surgifriend Medicals, England). The serum where thereafter used to assay for the biochemical analysis within 22 hours of preparation.

Preparation of Tissue (Brain) Supernatant

Preparation of tissue (brain) supernatant was carried out by placing the rat skull in a triangular cracker to collect the brain (15). It was kept in a dry, clean organ bottle, and 5 ml of 10% Buffer Normal Formalin at room temperature and 0.25M cold sucrose solution were added to the bottles for histopathological and biochemical studies, respectively. The tissue, placed in cold 0.25M solution to maintain its integrity of the tissue was homogenized in ice-cold 0.25M sucrose solution. The homogenates were appropriately diluted (1:4w/v) with sucrose, after which they were centrifuged at 1789xg for 10 minutes. The supernatant was aspirated with a Pasteur pipette into sample bottles and frozen at 4^{o}c before being used for the determination of various biochemical parameters.

Determination of Pro-inflammatory enzymes/biomarkers activities

The rat sera were evaluated for the pro-inflammatory enzymes/biomarkers' activities using standard procedures. Acetylcholine esterase (AChE) activity was carried out using the method as stated by Ellman (16). Cyclooxygenase-1 (COX-1) and Cyclooxygenase-2 (COX-2) Activity were determined in line with the procedure as described by Gierse (17). Whereas C. Reactive protein (CRP) concentration was estimated according to the method of Kindmark and Sand (18), Prostaglandin E-$_2$ (PGE-$_2$) Concentration was carried out as described by Victoria and Richard (1985 and Nitric oxide concentration was assayed as stated by Wo (19).

Determination of the activities and concentration of Antioxidant Enzymes

Serum antioxidant enzyme activity was evaluated using standard procedures. Glutathione peroxidase activity was determined according to the method of Hafemann (20). Superoxide Dismutase (SOD) activity was assayed in line with the procedure of Misra and Fridovich (21). Whereas catalase (CAT) activity was determined in line with the procedure of Beer and Sizer (22), and Malonaldehyde concentration was estimated according to the methods as stated by Nelson (23).

Determination of Hematological parameters

The automated hematology analyzer was used to determine the levels of Hgb, RBC, MCH, MCHC, and WBC. This machine automatically gives the readings.

Statistical Analysis

Each data point represents the mean of five replicate± SEM, except for results obtained from nutritional or chemical constituents in the fruit of *Phoenix dactylifera,* which represent the mean of three replicates ±SEM. All results were analysed statistically using one-way analysis of variance (ANOVA) and Duncan multiple range test (DMRT), (24). The Graph Pad software (Graph Pad Prism) was used to analyze statistical and graphical data. Values were considered significant at $p < 0.05$.

RESULTS

Confirmation of the induction of inflammation

The result for the concentration/activities of pro-inflammatory biomarkers and antioxidant enzymes after two weeks of induction is shown in Table 1. There was a significant increase at $p<0.05$ in C-reactive protein(C-RP) concentration in the levofloxacin-induced inflamed rats compared to the non-induced rats (normal control). Also, significant decrease was observed at

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p<0.05 in superoxide dismutase (SOD) and catalase (CAT) activity in the levofloxacin induced inflamed rats marched with the normal control rats. The result shows a significant difference between the test and control groups for the stated parameters.

Table 1: Confirmatory test for the induction of inflammation in female Wistar rats

Groups (ng/ml)	SOD (U/I)	CAT (U/I)	C-RP
Normal Control	1.75 ± 0.04[a]	572.73±11.7[a]	0.03±0.00[a]
Test	1.54±0.02[b]	550.88±0.48[b]	0.06±0.01[b]

Values are mean (n=5) ± SEM (value with different superscript are significantly different at p<0.05) C-RP: C-reactive protein; SOD: superoxide dismutase; CAT: catalase

Effect of Aqueous Extract of Phoenix dactylifera Fruit on the Activity/Concentration Of Pro-Inflammatory and Antioxidant Enzymes/Biomarkers

Acetylcholine Esterase (Serum and Brain)

The result of the effect of aqueous extract of Phoenix dactylifera fruit on the activity of serum and brain acetylcholine esterase (AChE) is presented in Figure 1. A significant increase (p<0.05) was noted in the group administered levofloxacin but not treated when compared with the normal control.

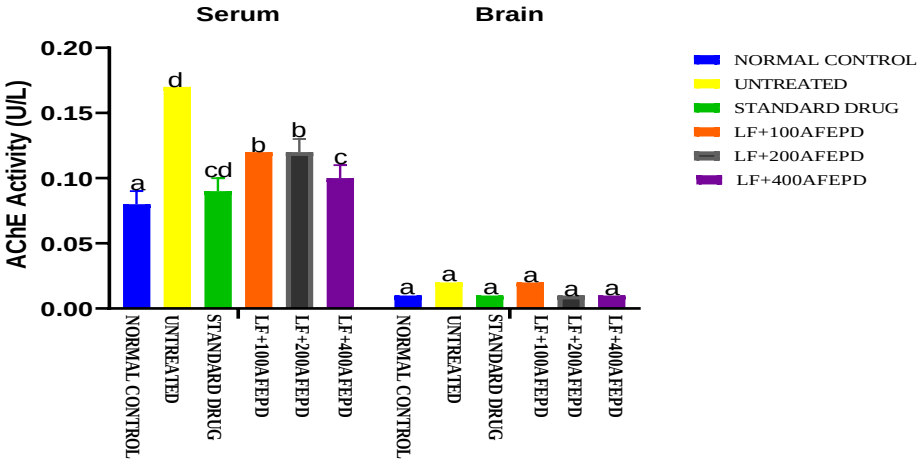

Figure 1: Effect of AFEPD on the activity of AChE in serum and brain of levofloxacin-induced inflamed rats. Values are mean (n=5) ± SEM (bars with different superscript are significantly different at p<0.05). AFEPD: aqueous extract of Phoenix dactylifera fruit, LF: levofloxacin 10mg/kg b.w., Standard Drug: 100mg/kg b.w., diclofenac, Normal control: non-induced rat, AChE: acetylcholine esterase, Untreated: induced but not treated, LF+100AFEPD: levofloxacin-induced and treated with 100mg/kg b.w., of aqueous extract of Phoenix dactylifera fruit, LF+200AFEPD: levofloxacin-induced and treated with 200mg/kg b.w., of aqueous extract of Phoenix dactylifera fruit, LF+400AFEPD: levofloxacin-induced and treated with 400mg/kg b.w., of aqueous extract of Phoenix dactylifera fruit.

Cycloxygenase-1 and 2 (COX-1 and 2)

Findings from the evaluation of aqueous extract of Phoenix dactylifera fruit on the activity of serum Cycloxygenase-1 and 2 are presented in Figure 2. A significant increase (p<0.05) was observed in the group administered levofloxacin but not treated when compared with the normal control.

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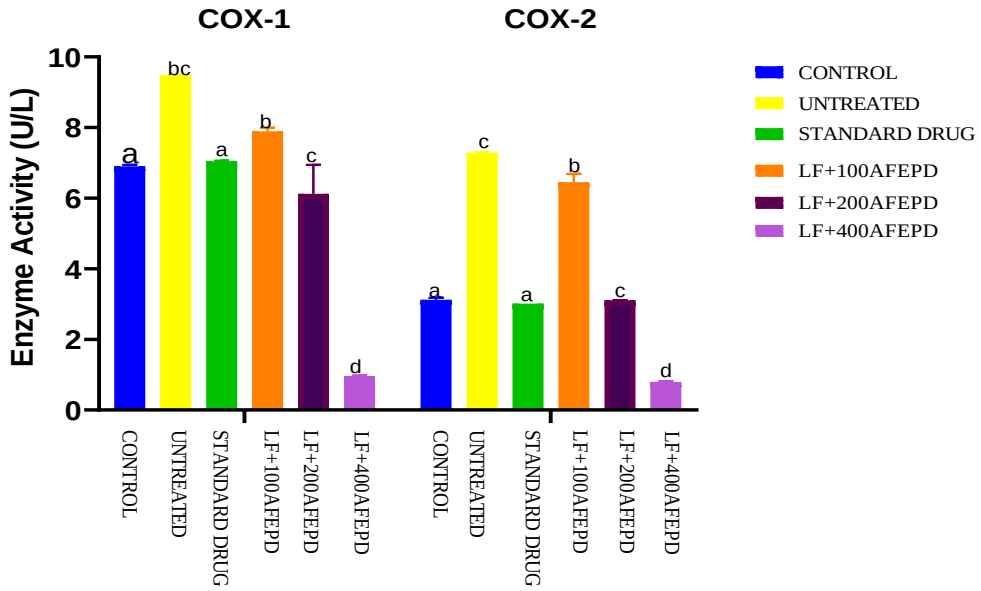

Figure 2: Effect of AFEPD on the activity of COX-1 and COX-2 in serum of levofloxacin-induced inflamed rats. Values are mean (n=5) ± SEM (bars with different superscript are significantly different at p<0.05). AFEPD: aqueous extract of Phoenix dactylifera fruit, LF: levofloxacin 10mg/kg b.w., , Standard Drug: 100mg/kg b.w., diclofenac, Control: non-induced rat, COX-1: cyclooxygenase-1, COX-2: cyclooxygenase, Untreated: induced but not treated, LF+100AFEPD: levofloxacin-induced and treated with 100mg/kg b.w., of aqueous extract of Phoenix dactylifera fruit, LF+200AFEPD: levofloxacin-induced and treated with 200mg/kg b.w., of aqueous extract of Phoenix dactylifera fruit, LF+400AFEPD: levofloxacin-induced and treated with 400mg/kg b.w., of aqueous extract of Phoenix dactylifera fruit.

Pro-inflammatory biomarker

C-Reactive protein and Prostaglandin E_2

The result of the effect of aqueous extract of Phoenix dactylifera fruit on the concentration of serum C-reactive protein (C-RP) in presented in table 2. A significant increase ($p<0.05$) was observed in the group administered levofloxacin but not treated when compared with the normal control. Whereas there was a significant increase ($p<0.05$) in Prostaglandin E_2 concentration in the group administered levofloxacin but not treated when compared with the normal control.

Table 2: Effect of aqueous extract of Phoenix dactylifera fruit in serum of levofloxacin induced-inflamed rat

Group	PGE-2 (Pg/ml)	C-RP (ng/ml)
Normal control	518.60±1.27^{a}	0.04±0.00^{a}
Levofloxacin induced not treated	669.44±0.33^{d}	0.06±0.00^{a}
Levofloxacin induced treated with diclofenac	453.84±0.27^{e}	0.03±0.00^{b}
levofloxacin induced +100AFED	631.11±0.96^{c}	0.06±0.01^{c}
levofloxacin induced +200AFED	590.92±0.00^{b}	0.04±0.00^{a}
levofloxacin induced +400AFED	522.18±0.16^{f}	0.03±0.00^{b}

Values are mean (n=5) ± SEM (value with different superscript are significantly different at p<0.05) AFEPD: aqueous fruit extract of Phoenix dactylifera, LF: levofloxacin 10mg/kg bdwt, DF: 100mg/kg bdwt diclofenac, NC: normal control,PG E_2: Prostaglandin E_2, C-RP: C Reactive protein100,200 and 400: 100mg/kgbdwt, 200mg/kgbdwt and 400mg/kgbdwt

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Nitric Oxide (Serum and Brain)

The effect of aqueous extract of Phoenix dactylifera fruit on the concentration of serum and brain nitric oxide (NO) is presented in figure 3. A significant increase ($p<0.05$) was observed in the group administered levofloxacin but not treated when compared with the normal control.

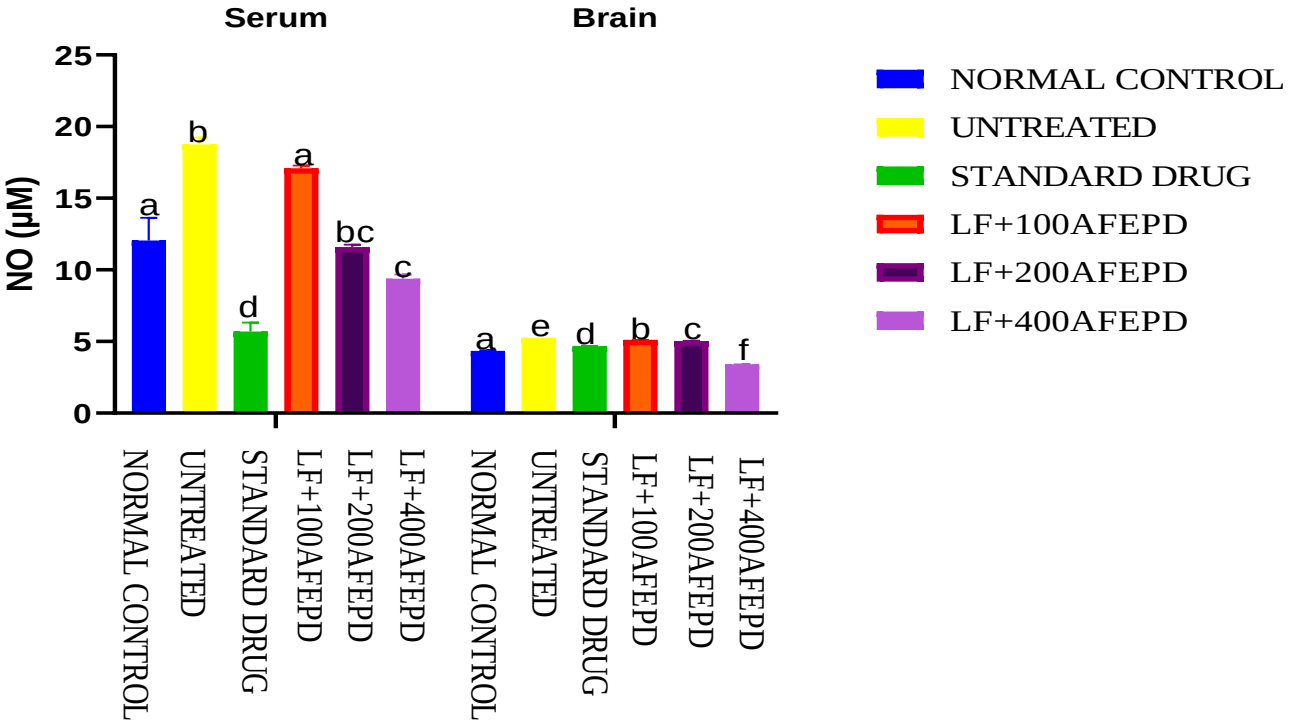

Figure 3: Effect of AFEPD on nitric oxide concentration in serum and brain of levofloxacin-induced inflamed rats. Values are mean (n=5) ± SEM (bars with different superscript are significantly different at p<0.05). AFEPD: aqueous extract of Phoenix dactylifera fruit, LF: levofloxacin 10mg/kg b.w., , Standard Drug: 100mg/kg b.w., diclofenac, Normal control: non-induced rat, NO: nitric oxide, Untreated: induced but not treated, LF+100AFEPD: levofloxacin-induced and treated with 100mg/kg b.w., of aqueous extract of Phoenix dactylifera fruit, LF+200AEPDF: levofloxacin-induced and treated with 200mg/kg b.w., of aqueous extract of Phoenix dactylifera fruit, , LF+400AFEPD: levofloxacin-induced and treated with 400mg/kg b.w., of aqueous extract of Phoenix dactylifera fruit.

Serum antioxidant enzymes and biomarkers

The effect of aqueous extract of Phoenix dactylifera fruit on the activity of serum antioxidant enzymes and biomarkers is presented in Table 3. A significant increase in Glutathione peroxidase and a decrease in Catalase and Superoxide dismutase ($p<0.05$) were observed in the group administered levofloxacin but not treated when compared with the normal control.

Table 3: Effect of aqueous extract of Phoenix dactylifera fruit on antioxidant enzymes and oxidative stress markers in the serum of levofloxacin-induced inflamed rat

Groups	GPX(U/L)	SOD(u/ml)	CAT(u/ml)	MDA (µM)	GSH (mM)
Normal Control	1.13± 0.00^{a}	2.87±0.03^{a}	584.59±0.58^{a}	2.59±0.31^{a}	0.66±0.01^{a}
Levofloxacin Untreated	6.79±0.11^{d}	0.63±0.48^{c}	434.62±67.04^{b}	3.95±0.53^{c}	0.63±0.02^{a}
Levofloxacin +Diclofenac	4.43±0.42^{c}	2.13±0.08^{ab}	597.84±6.18^{a}	2.39±0.01^{a}	0.81±0.01^{ab}
Levofloxacin +100AFEPD	4.33±0.17^{c}	2.00±0.08^{b}	563.89±2.78^{a}	2.28±0.02^{ab}	0.73±0.00^{ab}
Levofloxacin +200AFEPD	2.58±0.01^{b}	2.14±0.05^{ab}	593.24±3.96^{a}	2.12±0.01^{ab}	0.93±0.03^{b}
Levofloxacin +400AFEPD	0.36±0.20^{a}	2.21±0.20^{bc}	599.88±1.23^{a}	1.46±0.03^{b}	1.62±0.62^{c}

Values are mean (n=5) ± SEM (value with different superscript are significantly different at p<0.05) AFEPD: aqueous fruit extract of Phoenix dactylifera, LF: levofloxacin 10mg/kg b.w., , DF: 100mg/kg b.w., diclofenac,NC: normal control, SOD: superoxide dismutase;

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GPX: Glutathion peroxidase, MDA: Malonyldialdehyde CAT: catalase; GSH: reduced glutathione, 100,200 and 400: 100mg/kgbdwt, 200mg/kgbdwt and 400mg/kgbdwt

Brain antioxidant enzymes and biomarkers

The effect of aqueous extract of Phoenix dactylifera fruit on the activity of brain antioxidant enzymes and biomarkers is presented in Table 4. A significant increase in Glutathione peroxidase and a decrease in Catalase and Superoxide dismutase ($p<0.05$) were observed in the group administered levofloxacin but not treated when compared with the normal control.

Table 4: Effect of aqueous extract of Phoenix dactylifera fruit on antioxidant enzymes and oxidative stress markers in the brain of levofloxacin-induced inflamed rat

Groups	GPX(U/L)	SOD(u/ml)	CAT(u/ml)	MDA (µM)	GSH (mM)
Normal Control	2.13±0.01^{a}	1.64±0.03^{a}	24.19±0.01^{a}	4.36±0.58^{a}	0.35±0.00^{a}
Levofloxacin Untreated	4.04±0.02^{f}	1.36±0.15^{a}	20.83±0.82^{a}	6.20±0.08^{d}	0.26±0.04^{a}
Levofloxacin +Diclofenac	2.17±0.02^{a}	1.82±0.03^{c}	24.73±0.14^{d}	3.68±0.27^{a}	0.37±0.01^{c}
Levofloxacin +100AFEPD	3.73±0.02^{e}	1.51±0.01^{ab}	21.72±0.01^{ab}	5.89±0.13^{cd}	0.31±0.01^{ab}
Levofloxacin +200AFEPD	3.02±0.02^{d}	1.54±0.01^{d}	22.59±0.29^{bc}	5.68±0.28^{cd}	0.34±0.00^{bc}
Levofloxacin +400AFEPD	2.46±0.01^{c}	1.60±0.02^{ab}	23.26±0.53^{c}	5.05±0.10^{bc}	0.39±0. 01^{c}

Values are mean (n=5) ± SEM (value with different superscript are significantly different at $p<0.05$) AFEPD: aqueous fruit extract of Phoenix dactylifera, LF: levofloxacin 10mg/kg b.w., DF: 100mg/kg b.w., diclofenac,NC: normal control, SOD: superoxide dismutase; GPX: Glutathione peroxidase, MDA: Malonyldialdehyde CAT: catalase; GSH: reduced glutathione, 100, 200 and 400: 100mg/kg b.w., , 200mg/kg b.w., and 400mg/kg b.w.,

Discussion

Confirmation of the induction of inflammation

The anti-inflammatory activities of aqueous extract of *Phonenix dactylifera* fruits on pro-inflammatory and antioxidant/biomarkers in Levofloxacin-induced inflammation in female rats were evaluated in this study. The findings from the confirmatory induction of inflammation in the experimental rats show a significant increase at $p<0.05$ in C-reactive protein (C-RP) concentration in the Levofloxacin-induced inflamed rats when compared to the non-induced rats (Normal Control). Whereas for the antioxidant enzymes assayed, the recorded activity for superoxide dismutase and catalase was lower when compared to the normal control group. Thus, the outcome of the study indicates a significant difference between the extracts administered group and the normal control group for the stated parameter. This finding is in line with that of Chandrashekar (25), where they affirmed that an elevated C-reactive protein level after the administration of Levofloxacin is an indication of the animal's state of inflammation. Also, the degradation of the C-RP yields small bioactive peptides that inhibit many pro-inflammatory and tissue-destructive potentials of neutrophils. These peptides play a key role in signal transduction, leading to the activation of neutrophils, which in humans are known to activate the synthesis of IL-1α, IL-1β, TNF-α, and IL-6 in the peripheral blood mononuclear cells and alveolar macrophages. On the other hand, the decrease SOD and catalase activity recorded following the administration of levofloxacin indicates an oxidative damage process in the experimental animals. The outcome from the study supports the report of Gurbay (26) where their assessment of the liver after the administration of levofloxacin results in the formation of free radicals and lipid peroxidation of the membrane.

Acetylcholine Esterase

Acetylcholinesterase (AChE, EC 3.1.1.7) is a key component of cholinergic brain synapses and neuromuscular junctions. The major biological role of the enzyme is the termination of impulse transmission by rapid hydrolysis of the cationic neurotransmitter acetylcholine (27).

Administration of aqueous extract of *Phoenix dactylifera* fruit at different concentration shows a reduce activity in a dose dependent manner with the group administer 100mg/kgbody weight having a significant increase in enzymes activity when compared with the normal control, likewise the groups administered 200mg/kg and 400mg/kg body weight compete favorable well at p>0.05 with the group administered the standard drug. Findings from the study correlate with the report of Yingjie et al (28) where the ACh-induced suppression of inflammation was abolished in AChE overexpressed cells, but did not show a significant change in AChE mutant (enzymatic activity knockout) transfected cells. Thus, the outcome of the study results indicate that the neuroinflammation-regulated function of AChE may be mediated by controlling the ACh level in the brain system.

Cycloxygenase-1 and 2 (COX-1 and 2)

COX-2 (E.C. 1.14.99.1) is a predominantly inducible enzyme, considered to be mainly responsible for the production of proteinoids in inflammation (29). Although COX-2 has a major role, COX-1 also contributes in the initial stage of inflammation (One of the main stimuli for COX-2 induction is cytokines (such as interleukin-1, IL-1, and tumor necrosis factor-α, TNF-α) (30). In this study, administration of aqueous extract of *Phoenix dactylifera* fruit significantly lowered COX-1 and COX-2 at P<0.05, which was observed to be high in levofloxacin-induced untreated rats. Among the doses used, 400mg/kg b.w., shown to be very effective in restoring the AChE activity to normal in serum. The result of this finding correlates with various reports on anti-inflammatory activities of *Phoenix dactylifera*. The study of Saryono et al. (31) reveals that the expression of IL-1b, TGF-b, COX-1, and COX-2 decreased after the administration of date palm seeds to middle-aged women. The anti-inflammatory activity of the aqueous extract of date palm seeds is related to components of polyphenols such as caffeoyl hexoside, 5-O-caffeoyl shikimic ac isomers, hydrocaffeic acid, and isorhamnetin (32).

C-Reactive protein and Prostaglandin E_2

Also, the activity of C-reactive protein and Prostaglandin E_2 was significantly lowered at p<0.05 when experimental groups were administered with different doses of the aqueous extract of *phoenix dactylifera* when compared with the group induced with levofloxacin and untreated. From the choice of doses, 400mg/kgbdwt shows to be very effective in decreasing the PGE-2, C-RP concentration to normal in serum. The outcome from the study correlates with various report on anti-inflammatory activities of *Phoenix dactylifra.* In the study of (33), comparing the results of different groups treated with formalin induces edema over time to the control group, it shows that *P. dactylifera* extracts significantly decreased the C-RP levels and the volume of edema began to decrease gradually over time as the immune system naturally degraded the rate of inflammation which is attributed to the bioactive constituents present in the plants.

There was a decrease in activity in a dose-dependent manner in the concentration of nitric oxides in the groups administered aqueous extracts of *Phoenix dactylifera,* and there was a significant difference at P<0.05 when compared to the group administered the standard drug and that of the normal control. Findings from the study correlate with various report on anti-inflammatory activities of *Phoenix dactylifra.* The anti-inflammatory activity could also be associated with the phenolic acid contents of *Phoenix dactylifera*, which can inhibit the production of nitric oxide, Tumor Necrosis Factor-α, and Interleukin-6 (34). The possible explanation is that *P. dactylifera* extract exhibits an anti-inflammatory effect by inhibiting the filtration of immune cells to the inflammation site (35).

Antioxidant enzymes and biomarkers

The administration of aqueous extract of *Phoenix dactylifera* fruit at different concentration shows an increase activity of Glutathione Peroxidase (GPx), SOD and CAT enzymes, in a dose dependent manner, compared to the group administered levofloxacin but not treated. Similar studies show an increase in antioxidant enzymes in as reported by Huang et al. (36). The increase in the antioxidant enzymes is attributed to the rich source of phytochemicals present in the fruit, specifically the phenolics, which are known for their protective potential against most chronic diseases.

Antioxidant enzymes and oxidative stress markers in brain of levofloxacin stress markers in brain of levofloxacin-induced-inflamed rat were evaluated. Administration of aqueous extract of *Phoenix dactylifera* fruit (AFEPD significantly increased catalase and superoxide dismutase activity and red. glutathione concentration at $P<0.05$, which was observed to be low, and decreased glutathione peroxidase activity and malondialdehyde concentration at $p<0.05$, that was observed to be high in levofloxacin-induced untreated rats. Among the chosen doses, 400mg/kg bdwt of AFEPD shown to be very effective in elevating catalase and superoxide dismutase activity as well as red. glutathione concentration to normal in serum and brain. Similarly, this dose also shows to be highly effective in reducing glutathione peroxidase activity and malondialdehyde concentration to normal in serum and brain. Secondary plant metabolite analysis of aqueous extract of *Phoenix dactylifera* fruit shows that the presence of flavonoids, glycosides, alkaloids, saponins, terpenoids, coumarins, and steroids is responsible for the antioxidant activities. The result of this study is supported by various findings on date antioxidant properties. It is reported that flavonoids such as catechin and rutin were observed in thirteen varieties of Saudi Arabian dates. The presence of flavonoids in dates further confirms their ability to function as antioxidants (36).

Conclusion

It is established in this study that aqueous extract of *Phoenix dactylifera* fruit possesses anti-inflammatory activity as evident from the reduction in the activity of pro-inflammatory enzymes; acetylcholine esterase, cyclooxygenase-1, cyclooxygenase-2, as well as a decrease in the concentration of pro-inflammatory markers; nitric oxide, prostaglandin E-2, and C-reactive protein. It possesses antioxidant properties associated with its anti-inflammatory effect, which is evident in the presence of phytochemical constituents such as saponins, phenolics, flavonoids, alkaloids, fatty acids, and steroids known to have antioxidant potentials, regulating the effect of antioxidant enzymes/biomarkers. Thus, *Phoenix dactylifera* possesses anti-inflammatory and antioxidant properties and thus supports its usage as an anti-inflammatory agent in folklore medicine in Nigeria.

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

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الملخص

استُخدمت نخيل التمر، المعروف أيضًا باسم فينيكس داكتيليفيرا، منذ القدم لأغراض غذائية وعلاجية. هدفت هذه الدراسة إلى تقييم نشاط الإنزيمات/المؤشرات الحيوية المُحفّزة للالتهابات ومضادات الأكسدة للمستخلص المائي لنخيل التمر في الالتهاب المُحفّز بالليفوفلوكساسين لدى إناث الجرذان. استُخلصت عينة مسحوقة من الجزء الصالح للأكل من النبات باستخدام طريقة الاستخلاص بالماء البارد. قُسّم 30 جرذًا أنثى إلى 5 مجموعات، كل مجموعة تضم 6 جرذان، وأُعطيت جرعات مختلفة من المستخلص المائي لنخيل التمر، تراوحت بين 100 و200 و400 ملغ/وزن الجسم، بينما أُعطيت المجموعة المرجعية دواء ديكلوفيناك القياسي، وتُركت المجموعة الخامسة دون علاج أو تحريض. في نهاية الدراسة، قُدّمت الحيوانات، وجُمعت عينات دم لتحليلها. وتم تحديد الإنزيمات المُحفّزة للالتهابات والإنزيمات المُضادة للأكسدة باستخدام الإجراءات القياسية. تشير نتائج الدراسة إلى أن المستخلص المائي لنبات فينيكس داكتيليفيرا يُظهر تأثيره بناءً على الجرعة، كما أنه يُنافس بشكل إيجابي المجموعة التي تناولت الدواء المرجعي. وبالتالي، تُبرر نتائج الدراسة استخدام هذا النبات في علاج العديد من الأمراض الالتهابية في الطب الشعبي.