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Research Article
Comparing the Therapeutic Potency of Camel Milk and Whey Protein Against Toxicity-Induced by Levofloxacin in Male Albino Rats

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Abstract

Background and Objective: Levofloxacin (LFX) is a wide-spectrum antibiotic that is used to treat many types of infections. Camel milk (CM) and camel whey protein (CWP) are natural antioxidants that work as dietary supplements that enhance immune defenses. The goal of this study was to estimate the therapeutic efficacy of camel whey protein and camel milk, in addition to the toxic effects of the antibiotic levofloxacin. **Materials and Methods:** As 42 male albino rats were divided as follows: G1: Control, G2: CM orally for 15 days, G3: CWP orally for 15 days, G4: LFX orally for 10 days, G5: LFX for 10 days and followed with CM daily for 15 days and G6: LFX for 10 days followed by CWP orally for 15 days. At the end of the study blood sera from all groups were collected for estimation of serum total protein, albumin, globulins and glucose. Sections of the liver and kidney were separated for estimation of GSH, CAT, GSH-PX. All data were statistically analyzed using analysis of variance. **Results:** The LFX treatment induced a decrease in serum levels of proteinogram, glucose, hepatic and renal values of oxidative stress and raising values of serum kidney and liver functions, hepatic and renal MDA. The treatment of LFX-treated rats with CWP led to a more increase in serum proteinogram, glucose, hepatic and renal (GSH, CAT, GSH-PX) a decline in serum values of (urea, ALAT, ASAT, ALP, BIL, T.P, D. BIL, Ind. BIL creatinine), hepatic and renal MDA than the treatment with CWP did. **Conclusion:** The use of CWP after LFX-treatment showed greater therapeutic potency than the use of CM.

Key words: Levofloxacin, camel milk, whey protein, oxidative stress, rats

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Levofloxacin is a fluoroquinolone antibiotic having broad bactericidal action[1-4]. Its use has expanded to the treatment of infections, bronchitis, pneumonia and genitourinary infections including both complex and simple urinary tract infections[1-5].

Many previous studies realized that fluoroquinolone consumption, at different amounts and durations of usage, had a negative both short and long-term effect on hepatic and renal function by depleting the antioxidant defense mechanism, resulting in oxidative stress and subsequent liver and kidney disorder[2,3,6-9]. Camel milk is a potent exogenous antioxidant supplement that can help reduce oxidative stress, which has been associated with a variety of diseases. The main antioxidant components in camel milk consist of physiologically active peptides and whey proteins, casein, lactoferrin, lysozyme, lactoperoxidase, alpha-lactalbumin, immunoglobulin and beta-casein[10,11]. Lactoferrin has anti-inflammatory, anti-microbial and antioxidant effects and when beta-caseins are hydrolyzed, they generate bioactive peptides with antioxidant characteristics[10]. Camel milk also includes immunoglobulin, lysozyme, which has antimicrobial properties and regulates the immune system and bioactive peptides with antioxidant properties[11]. Camel whey protein proteomics' fast progress has highlighted how proteins have evolved from being only a dietary component to a substantial contributor to the control of the body's physiological activities, food-derived proteins provide health advantages by releasing bioactive peptides during gastrointestinal transformation, which is mediated by hydrolysis triggered by digestive enzymes, microbial proteases and fermentative enzymes[12,13]. Camel whey protein is rich in amino acids and bioactive proteins, previous research has shown that it is an excellent scavenger of oxidative radicals, with the capacity to enhance antioxidant levels and restore the balance between oxidants and antioxidants, as well as normal liver and kidney function[14-16].

The current study's major purpose was to investigate the toxic impact of the antibiotic levofloxacin, as well as to investigate the medicinal properties of camel milk and camel whey protein against hepatic and renal toxicities and to compare the therapeutic effect of camel milk and camel whey protein.

MATERIALS AND METHODS

Study area: This study was carried out from February to August, 2022 at a Postgraduate Laboratory in the Department of Biology, College of Science, Qassim University.

Animals: As 42 adult male albino rats with an average weight of (150-180 g) were employed in this study, rats were acquired from the Animal House College of Pharmacy at King Saud University in Riyadh.

Preparation of materials

LFX: Levofloxacin (500 mg), manufactured by Sanofi-Aventis Arabia, was acquired from the drug world pharmacy in Qassim. The tablets were pulverized and the powder was kept in dark bottles until used.

CM: The CM was collected daily from the "Modern breeding farms", in Qassim by hand milking then packed in sterile capped bottles and transferred in cool storage boxes to the laboratory.

Preparation of concentrate camel whey protein (CWP): The CWP was produced as reported by Du *et al.*[15]. Fresh bactrian camel milk (CM) was collected aseptically from Modern breeding farms in Qassim and samples were promptly chilled at 4°C and brought to the laboratory. For degreasing, raw milk was spun at 1400 g at 4°C for 30 min. Defatted CM was heated at 80°C for 20 min before being promptly chilled to 43-45°C for pasteurization. The skimmed CM was centrifuged at 11000 g for 10 min at 4°C after the pH was adjusted to 4.3 with 1 M HCl. After centrifugation, the precipitated casein was removed and the supernatant was used to make the CWP sample. The CWP was then precipitated using an ammonium sulphate assay. In other words, an equivalent volume of saturated ammonium sulphate solution was added to the CWP sample and agitated for 6 hrs with a magnetic stirrer. Finally, for 48 hrs, a dialysis bag with a molecular weight cut-off of 6000-8000 kDa was used (the CWP to dH_2O ratio was 1:20). The dialysate was freeze-dried and kept at 80°C until use[15].

Experimental design

Forty-two adult male albino rats *Rattus norvegicus* were divided into six groups:

- **Group I (seven rats):** The control group was fed a normal rodent diet and water
- **Group II (seven rats):** Received milk camel (5mL/rat/day) orally for 15 successive days in drinking bottles[17]
- **Group III (seven rats):** Treated with concentrated camel whey protein orally by gastric tube at a dose of 200 mg kg^{-1} b.wt., for 15 successive days[15]
- **Group IV (seven rats):** Injected orally by gastric tube with levofloxacin at a therapeutic dose of 100 mg kg^{-1} b.wt.,[18] after converting the dose of humans to rats according to Paget and Barnes[19] once a day for 10 days

- **Group V (seven rats):** Injected orally by gastric tube with a therapeutic dose of levofloxacin 100 mg kg^{-1} b.wt., for 10 days[18] followed with fresh camel milk in drinking bottles (5 mL/rat/day) daily for 15 days[17]
- **Group VI (seven rats):** Treated with levofloxacin at a therapeutic dose of 100 mg kg^{-1} b.wt., orally by gastric tube[18] for ten days then received concentrate camel whey protein at 200 mg kg^{-1} b.wt., orally by gastric tube for 15 days[15]

Blood and tissues sampling: At the end of the trial, rats were fasted for 24 hrs before being sacrificed under anesthesia and blood was drawn from rats of all groups for sera separation and storage at -80°C until biochemical analysis. Samples from the liver and kidney were dissected, cleaned and kept at -80°C until use.

Tissue homogenization: For biochemical investigation, a 10% tissue homogenate of the liver and kidney was produced[20].

Biochemical analysis

Estimation of biochemical parameters in serum: Serum values of ALAT, ASAT, ALP, T.BIL, D.BIL, Ind.BIL, T.P, ALB, Globulin, A/G ratio, urea, creatinine and glucose were estimated spectrophotometrically by using "Human kits" that were purchased from Ejadah Medical Company, for scientific medical materials, chemical, laboratory and hospital equipment, Riyadh according to the researches[21-26].

Estimation of biochemical parameters in tissues: The values of renal and hepatic MDA, GSH, GSH-PX and CAT were estimated by using "Human kits" that were purchased from Ejadah Medical Company, for scientific medical materials, chemical, laboratory and hospital equipment, Riyadh. All parameters were estimated spectrophotometrically according to the studies[27-30].

Statistical analysis: To compare means, One-way Analysis of Variance (ANOVA) was employed, followed by *post hoc* (Tukey) tests using the Statistics Analysis System's General Linear Model Procedure (SAS 1982). Multiple comparisons test at $p \leq 0.01$ according to study by Waller and Duncan[31]. This was carried out using Statistical Analysis System (SAS) program software version 8, copyright©1998 by SAS Institute Inc., Cary, North Carolina, USA.

Ethical consideration: Ethical Committee of Research Ethics, Deanship of Scientific Research, Qassim University, approved the work under the number (21-21-12-Jun-22).

RESULTS

Serum biochemistry

Serum proteins: The treatment of CWP or CM separately for 15 successive days did not deteriorate ($p \leq 0.01$) level of serum (T. protein, ALB, globulin and A/G ratio) when these groups compared to the control animal group, in contrast, oral administration of LFX for ten days resulted in a more significant ($p \leq 0.01$) decline in the value of serum the above-mentioned parameters in comparison to the control group. Interestingly, the administration of CWP to the LFX-treated rats for 15 successive days induced more significant improvement in level of serum parameters in comparison to the LFX-treated animals group. While the oral treatment with CM to the LFX-treated rats for 15 consecutive days revealed a less significant ($p \leq 0.01$) improvement in the decrease in serum parameters values in comparison to the LFX-treated animals group (Table 1 and Fig. 1-4).

Serum kidney functions: The treatment of CWP or CM separately for 15 successive days did not deteriorate ($p \leq 0.01$) level of serum (urea and creatinine) when these groups compared to the control animal group, in contrast, oral administration of LFX for ten days resulted in a more significant ($p \leq 0.01$) rise in the value of serum the above-mentioned parameters in comparison to control group. Interestingly, the administration of CWP to the LFX-treated rats for 15 successive days induced a more significant improvement in the level of serum parameters in comparison to the LFX-treated animals group. While the oral treatment with CM to the LFX-treated rats for 15 consecutive days revealed a less significant ($p \leq 0.01$) improvement in the increased in serum parameters values in comparison to LFX-treated animals group (Table 2 and Fig. 4, 5).

Serum liver enzymes: The treatment of CWP or CM separately for 15 days did not deteriorate ($p \leq 0.01$) level of serum (ASAT, ALAT, ALP) activities and in (T.BIL, D.BIL, Ind.BIL) when these groups compared to the control animal group, in contrast, oral administration of LFX for ten days resulted in a more significant ($p \leq 0.01$) elevation in the value of serum the above-mentioned parameters in comparison to the control group. Interestingly, the administration of CWP to the LFX-treated rats for 15 successive days induced a more significant improvement in the level of serum parameters in comparison to LFX-treated animals group. While the oral treatment with CM to the LFX-treated rats for 15 consecutive days revealed a less significant ($p \leq 0.01$) improvement in the increased in serum parameters values in comparison to LFX-treated animals group (Table 3 and Fig. 6-11).

Table 1: Effect of oral administration of camel milk and whey protein concentrate on proteinogram (A/G: Albumin/globulin ratio) of levofloxacin-treated groups (M±SE)

		Parameters			
Groups		T. protein (g dL^{-1})	Albumin (g dL^{-1})	Globulins (g dL^{-1})	A/G
Control	M±SE	7.7 ± 0.06^{A}	4.5 ± 0.05^{A}	3.2 ± 0.09^{A}	1.4 ± 0.06^{A}
WP	M±SE	7.8 ± 0.07^{A}	4.5 ± 0.03^{A}	3.3 ± 0.08^{A}	1.4 ± 0.07^{A}
	% Change A	1.3%	0%	3.1%	0%
CM	M±SE	7.7 ± 0.07^{A}	4.6 ± 0.1^{A}	3.1 ± 0.1^{A}	1.5 ± 0.1^{A}
	% Change A	0%	2.2%	-3.1%	7.1%
LFX	M±SE	5.1 ± 0.07^{B}	2.2 ± 0.03^{B}	1.8 ± 0.06^{B}	1.2 ± 0.04^{B}
	% Change A	-33.8%	-44.4%	-43.8%	-14.3%
LFX+WP	M±SE	6.9 ± 0.01^{C}	3.9 ± 0.03^{C}	2.6 ± 0.04^{C}	1.5 ± 0.02^{C}
	% Change B	35.3%	56%	44.4%	25%
LFX+CM	M±SE	6.3 ± 0.09^{D}	3.1 ± 0.06^{D}	2.2 ± 0.08^{D}	1.4 ± 0.04^{D}
	% Change B	23.5%	24%	22.2%	16.7%

Data are presented as mean±standard error of mean, data were subjected to one-way ANOVA followed by Duncan's *post hoc* Test at $p\leq0.01$, within the same column, means with different superscript letters are significantly different, WP: Whey protein concentrate, CM: Camel milk and LFX: Levofloxacin

Table 2: Effect of oral administration of camel milk and whey protein concentrate on serum kidney functions of levofloxacin-treated groups (M±SE).

		Parameters	
Groups		Urea (mg dL^{-1})	Creatinine (mg dL^{-1})
Control	M±SE	35.6 ± 0.5^{A}	0.74 ± 0.01^{A}
WP	M±SE	35.1 ± 0.5^{A}	0.73 ± 0.01^{A}
	% Change A	-1.4%	-1.3%
CM	M±SE	34.9 ± 0.7^{A}	0.75 ± 0.01^{A}
	% Change A	-1.9%	1.4%
LFX	M±SE	54.6 ± 0.5^{B}	1.02 ± 0.02^{B}
	% Change A	53.4%	37.8%
LFX+WP	M±SE	43.2 ± 0.7^{C}	0.83 ± 0.01^{C}
	% Change B	-20.9%	-18.6%
LFX+CM	M±SE	47.6 ± 0.5^{D}	0.91 ± 0.01^{D}
	% Change B	-12.8%	9.6%

Data are presented as mean±standard error of mean, data were subjected to one-way ANOVA followed by Duncan's *post hoc* Test at $p\leq0.01$, within the same column, means with different superscript letters are significantly different, WP: Whey protein concentrate, CM: Camel milk and LFX: Levofloxacin

Table 3: Effect of oral administration of camel milk and whey protein concentrate on serum liver functions

		Parameters					
Groups		ASAT (U L^{-1})	ALAT (U L^{-1})	ALP (U L^{-1})	T. Bili (mg dL^{-1})	D. Bili (mg dL^{-1})	Ind.Bili (mg dL^{-1})
Control	M±SE	64.6 ± 0.4^{A}	33.2 ± 0.8^{A}	186 ± 0.9^{A}	1.05 ± 0.01^{A}	0.320 ± 0.01^{A}	0.730 ± 0.02^{A}
WP	M±SE	65 ± 0.8^{A}	33.3 ± 0.6^{A}	185.4 ± 0.8^{A}	1.04 ± 0.01^{A}	0.318 ± 0.01^{A}	0.726 ± 0.02^{A}
	% Change A	0.6%	0.3%	-0.9%	-1%	-0.6%	-0.5%
CM	M±SE	65.2 ± 0.8^{A}	33.4 ± 0.4^{A}	185.6 ± 0.5^{A}	1.04 ± 0.01^{A}	0.321 ± 0.01^{A}	0.724 ± 0.01^{A}
	% Change A	0.93%	0.6%	-0.8%	-1%	0.3%	-0.8%
LFX	M±SE	92 ± 0.7^{B}	54.6 ± 0.7^{B}	252 ± 0.7^{B}	2.64 ± 0.07^{B}	0.814 ± 0.04^{B}	1.816 ± 0.07^{B}
	% Change A	42.4%	64.5%	35.5%	151.4%	154.4%	148.8%
LFX+WP	M±SE	75.8 ± 0.2^{C}	40.4 ± 0.5^{C}	212 ± 0.2^{C}	1.18 ± 0.04^{C}	0.468 ± 0.02^{C}	0.712 ± 0.03^{C}
	% Change B	-17.6%	-26%	-15.9%	-55.3%	-42.5%	-60.8%
LFX+C M	M±SE	85 ± 0.3^{D}	47.2 ± 0.6^{D}	225.6 ± 0.3^{D}	1.76 ± 0.7^{D}	0.586 ± 0.1^{D}	1.17 ± 0.05^{D}
	% Change B	-7.6%	-13.6%	-10.5%	-33.3%	-28%	-35.6%

ASAT: Aspartate transaminase, ALAT: Alanine transaminase, ALP: Alkaline phosphatase, T. Bili: Total bilirubin, D. Bili: Direct bilirubin, Ind. Bili: Indirect bilirubin of levofloxacin-treated groups (M±SE), data are presented as mean±standard error of mean, data were subjected to one-way ANOVA followed by Duncan's *post hoc* Test at $p\leq0.01$, within the same column, means with different superscript letters are significantly different, WP: Whey protein concentrate, CM: Camel milk and LFX: Levofloxacin

Serum glucose: The treatment of CWP or CM separately for 15 successive days did not deteriorate ($p\leq0.01$) level of serum (glucose) when these groups compared to control animal group, in contrast, oral administration of LFX for ten days resulted in a more significant ($p\leq0.01$) decrease in the value of serum the above-mentioned parameter in comparison to control group. And interestingly, the administration of CWP to the LFX-treated rats for 15 successive days induced a more significant increase in level of serum glucose in comparison to LFX-treated animals 'group. While the oral treatment with CM to the LFX-treated rats for 15 consecutive days revealed a less significant ($p\leq0.01$) improvement in the decreased in serum glucose values in comparison to LFX-treated animals group (Table 4 and Fig. 12).

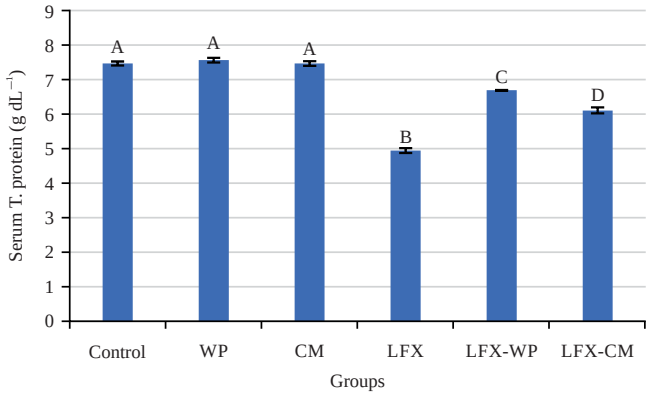

Fig. 1: Means of serum T. protein (g dL^{-1}) of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk, B: Administration of LFX resulted in a significant decline in the serum T. protein when compared with the control groups, C: Treatment with WP resulted in a more significant increase in the serum T. protein when compared with the LFX group and D: Administration of CM resulted in a less significant increase in the serum T. protein when compared with the LFX group

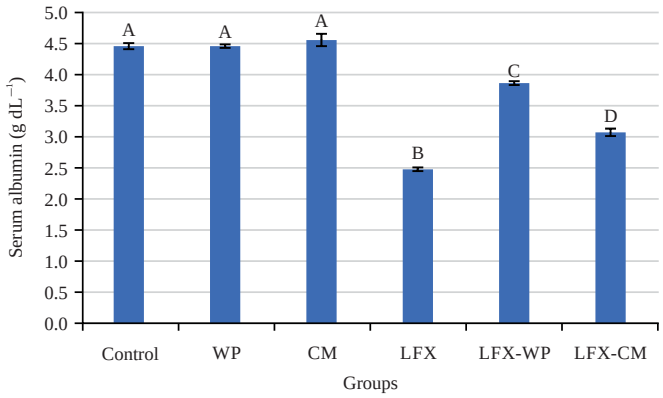

Fig. 2: Means of serum albumin (g dL^{-1}) of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control whey protein and camel milk, B: Administration of LFX resulted in a significant decline in the serum Albumin when compared with the control groups, C: Treatment with WP resulted in a more significant increase in the serum Albumin when compared with the LFX group and D: Administration of CM resulted in a less significant increase in the serum Albumin when compared with the LFX group

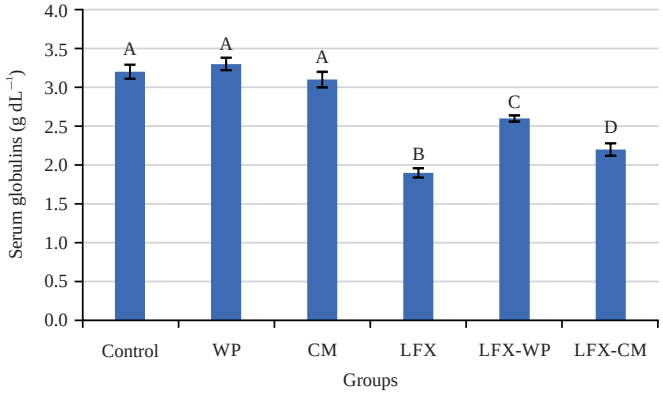

Fig. 3: Means of serum globulins (g dL^{-1}) of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in the levels of serum Globulins, B: Administration of LFX resulted in a significant decline in the serum globulins when compared with the control groups, C: Treatment with WP resulted in a more significant increase in the serum globulins when compared with the LFX group and D: Administration of CM resulted in a less significant increase in the serum globulins when compared with the LFX group

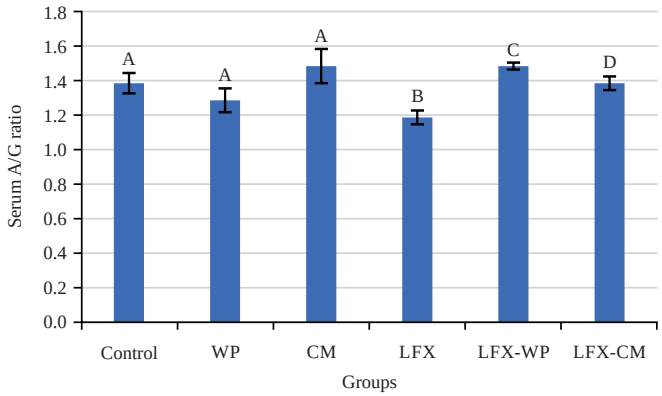

Fig. 4: Means of serum A/G ratio of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk, B: Administration of LFX resulted in a significant decline in the serum A/G ratio when compared with the control groups, C: Treatment with WP resulted in a more significant increase in the serum A/G ratio when compared with the LFX group and D: Administration of CM resulted in a less significant increase in the serum A/G ratio when compared with the LFX group

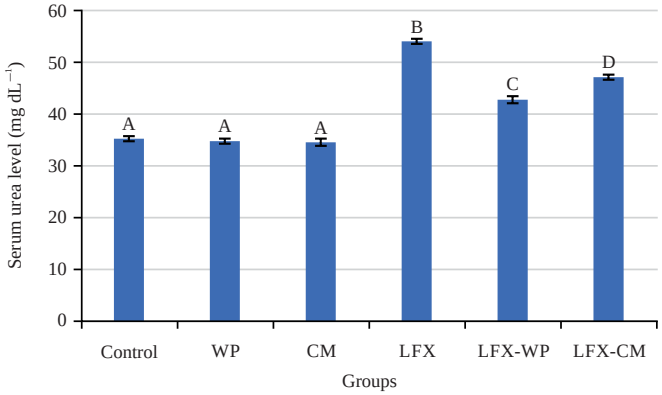

Fig. 5: Means of serum urea level (mg dL^{-1}) of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in the serum urea level, B: Administration of LFX resulted in a significant increase in the serum urea level when compared with the control groups, C: Treatment with WP with resulted in a more significant decrease in the serum urea level when compared with the LFX group and D: Administration of CM resulted in a less significant decrease in the serum urea level when compared with the LFX group

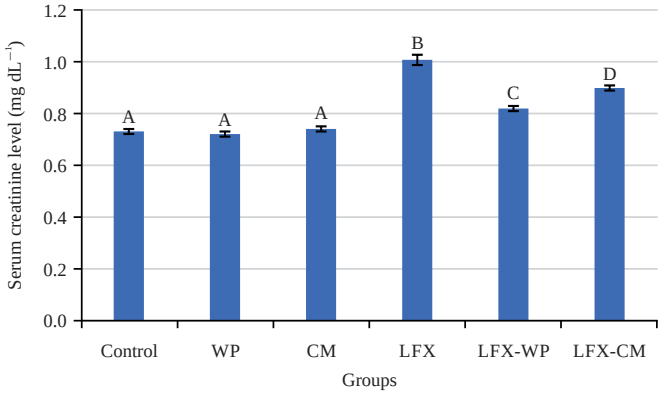

Fig. 6: Means of serum creatinine level (mg dL^{-1}) of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in serum creatinine level, B: Administration of LFX resulted in a significant rise in serum creatinine level when compared with control groups, C: Treatment with WP resulted in a more significant decline in serum creatinine level when compared with LFX group and D: Administration of CM resulted in a less significant decrease in serum creatinine level when compared with LFX group

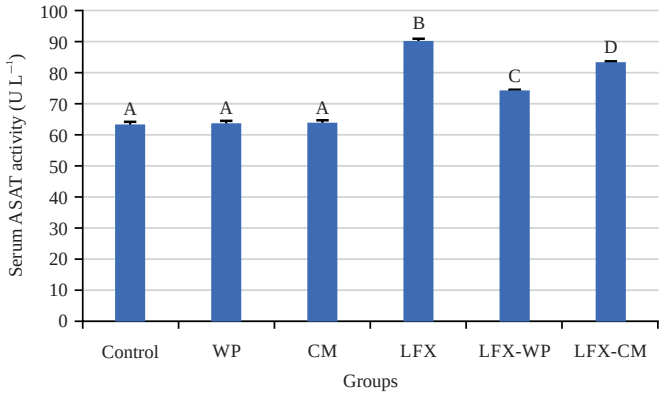

Fig. 7: Means of serum ASAT activity (U L^{-1}) of adult male albino rat *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in the serum ASAT activity, B: administration of LFX resulted in a significant increase in the serum ASAT activity when compared with the control groups, C: Treatment with WP resulted in a more significant decrease in the serum ASAT activity when compared with the LFX group and D: Administration of CM resulted in a less significant decrease in the serum ASAT activity when compared with the LFX group

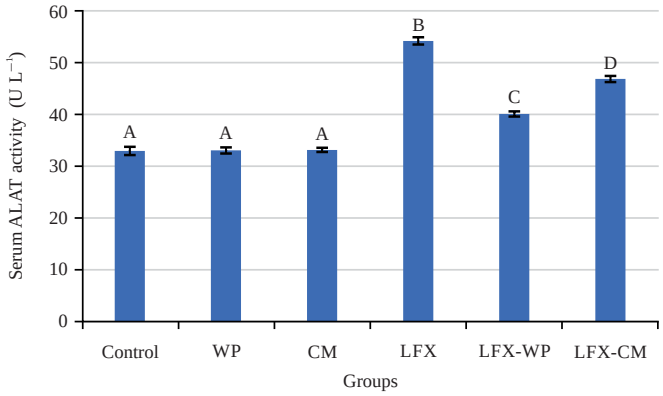

Fig. 8: Means of serum ALAT activity (U L^{-1}) of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in the serum ALAT activity, B: Administration of LFX resulted in a significant increase in the serum in serum ALAT activity when compared with the control groups, C: Treatment with WP resulted in a more significant decrease in the serum ALAT activity when compared with the LFX group and D: Administration of CM resulted in a less significant decrease in the serum ALAT activity when compared with the LFX group

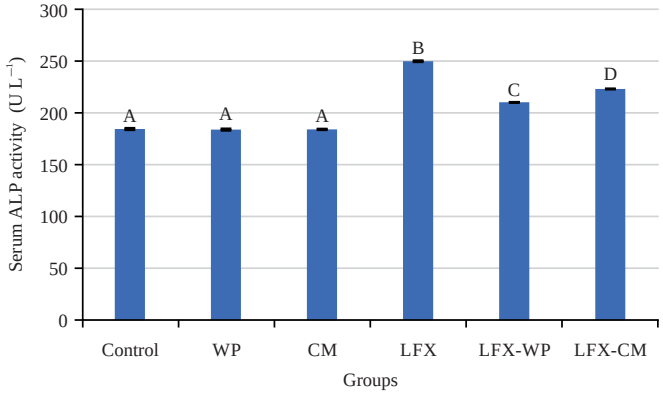

Fig. 9: Means of serum ALP activity (U L^{-1}) of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in the serum ALP activity, B: Administration of LFX resulted in a significant rise in the serum ALP activity when compared with the control groups, C: Treatment with WP resulted in a more significant decrease in the serum ALP activity when compared with the LFX group and D: Administration of CM resulted in a less significant decrease in the serum ALP activity when compared with the LFX group

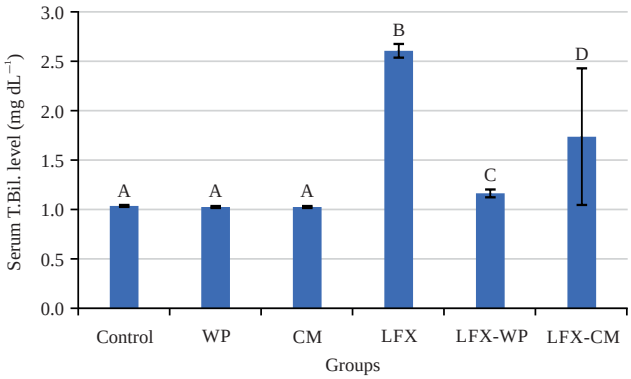

Fig. 10: Means of serum T.Bil. level (mg dL^{-1}) of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in the serum T.Bil. level, B: Administration of LFX resulted in a significant rise in the serum T.Bil. level when compared with the control groups, C: Treatment with WP resulted in a more significant decrease in the serum T.Bil. level when compared with the LFX group and D: Administration of CM resulted in a less significant decrease in the serum T.Bil. level when compared with the LFX group

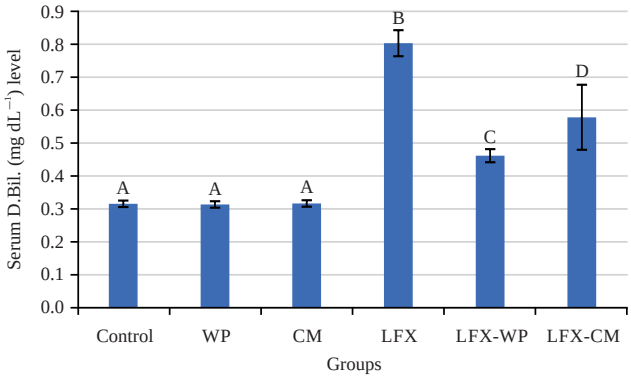

Fig. 11: Means of serum D.Bil. (mg dL^{-1}) level of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in the serum D.Bil. level, B: Administration of LFX resulted in a significant decrease in the serum D.Bil. level when compared with the control groups, C: Treatment with WP resulted in a more significant decrease in the serum D.Bil. level when compared with the LFX group and D: Administration of CM resulted in a less significant decrease in the serum D.Bil. level when compared with the LFX group

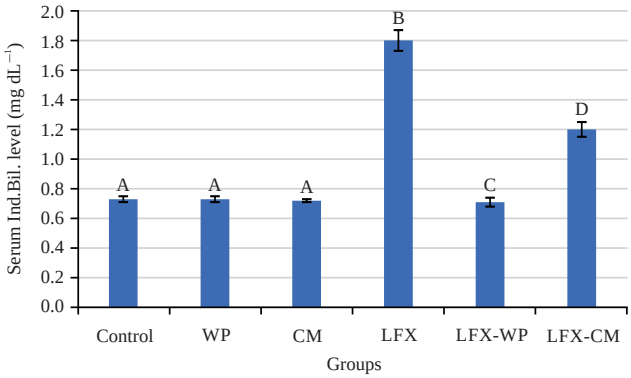

Fig. 12: Means of serum Ind.Bil. (mg dL^{-1}) level of adult male albino rat *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in the serum Ind.Bil. level, B: Administration of LFX resulted in a significant rise in the serum Ind.Bil. level when compared with the control groups, C: Treatment with WP resulted in a more significant decrease in the serum Ind.Bil.level when compared with the LFX group and D: Administration of CM resulted in a less significant decrease in the serum Ind.Bil. level when compared with the LFX group

Tissues antioxidant markers

Hepatic antioxidant markers: The treatment of CWP or CM separately for 15 successive days did not deteriorate ($p \leq 0.01$) level of liver (MDA) and in (GSH, CAT and GSH-PX) activities when these groups compared to the control animal group, in contrast, oral administration of LFX for ten days resulted in a more significant ($p \leq 0.01$) increase in the value of liver (MDA) while it's resulted in a more significant decrease in the (GSH, CAT and GSH-PX) activities in comparison to control group. Interestingly, the administration of CWP to the LFX-treated rats for 15 successive days induced a more significant decrease in the level of liver (MDA) while, it's resulted in a more significant rise in the (GSH, CAT and GSH-PX) activities in comparison to LFX-treated animals 'group. The oral treatment with CM to the LFX-treated rats for 15 consecutive days revealed a less significant ($p \leq 0.01$) improvement in the increased value of liver (MDA) and a less significant ($p \leq 0.01$) improvement in the decreased value of liver (GSH, CAT and GSH-PX) activities in comparison to LFX-treated animals group (Table 5 and Fig. 13-16).

Renal antioxidant markers: The treatment of CWP or CM separately for 15 successive days did not deteriorate ($p \leq 0.01$) level of kidney (MDA) and in (GSH, CAT and GSH-PX) activities when these groups compared to the control animal group, in contrast, oral administration of LFX for ten days resulted in a more significant ($p \leq 0.01$) increase in the value of kidney (MDA) while it's resulted in a more significant decrease in the (GSH, CAT and GSH-PX) activities in comparison to control group. Interestingly, the administration of CWP to the LFX-treated rats for 15 successive days induced more significant decrease in level of kidney (MDA) while, it's resulted in a more significant rise in the (GSH, CAT and GSH-PX) activities in comparison to LFX-treated animals group. While, the oral treatment with CM to the LFX-treated rats for 15 consecutive days revealed a less significant ($p \leq 0.01$) improvement in the increased value of kidney (MDA) and revealed a less significant ($p \leq 0.01$) improvement in the decreased value of kidney (GSH, CAT and GSH-PX) activities in comparison to LFX-treated animals group (Table 6 and Fig. 17-21).

Table 4: Effect of oral administration of camel milk and whey protein concentrate on serum glucose level of levofloxacin-treated groups (M±SE)

		Parameter
Groups		Serum glucose (mg dL^{-1})
Control	M±SE	105.2 ± 0.9^{A}
WP	M±SE	104.6 ± 0.8^{A}
	% Change A	-0.6%
CM	M±SE	105 ± 0.7^{A}
	% Change A	-0.2%
LFX	M±SE	74.8 ± 1.1^{B}
	% Change A	-28.9%
LFX+WP	M±SE	95 ± 0.7^{C}
	% Change B	27%
LFX+CM	M±SE	88 ± 0.7^{D}
	% Change B	17.7%

Data are presented as mean±standard error of mean, data were subjected to One-way ANOVA followed by Duncan's *post hoc* Test at $p \leq 0.01$, within the same column, means with different superscript letters are significantly different, WP: Whey protein concentrate, CM: Camel milk and LFX: Levofloxacin

Table 5: Effect of oral administration of camel milk and whey protein concentrate on liver oxidative stress of levofloxacin-treated groups (M±SE)

		Parameters			
Groups		MDA (nmol mg^{-1} prot)	GSH (mg GSH g^{-1} prot)	CAT (U mL^{-1})	GSH-Px (U mg^{-1} prot)
Control	M±SE	12.6 ± 0.1^{A}	93.2 ± 0.8^{A}	0.71 ± 0.01^{A}	19.8 ± 0.2^{A}
WP	M±SE	12.5 ± 0.1^{A}	93.6 ± 0.6^{A}	0.73 ± 0.01^{A}	19.9 ± 0.06^{A}
	% Change A	-0.8%	0.4%	2.8%	0.5%
CM	M±SE	12.5 ± 0.1^{A}	93.8 ± 1.3^{A}	0.72 ± 0.03^{A}	19.7 ± 0.09^{A}
	% Change A	-0.8%	0.6%	1.4%	-0.5%
LFX	M±SE	25.1 ± 0.4^{B}	55.2 ± 1.1^{B}	0.42 ± 0.01^{B}	9.3 ± 0.09^{B}
	% Change A	99.2%	-40.8%	-40.8%	-53%
LFX+WP	M±SE	16.2 ± 0.2^{C}	85.6 ± 0.03^{C}	0.62 ± 0.01^{C}	13.5 ± 0.1^{C}
	% Change B	-35.5%	55.1%	47.6%	45.2%
LFX+CM	M±SE	19.5 ± 0.3^{D}	67.2 ± 0.9^{D}	0.50 ± 0.01^{D}	11.7 ± 0.2^{D}
	% Change B	-22.3%	21.7%	19%	25.8%

MDA: Malondialdehyde, GSH: Reduced glutathione, CAT: Catalase, GSH-Px: Glutathione peroxidase, data are presented as mean±standard error of mean, data were subjected to one-way ANOVA followed by Duncan's *post hoc* Test at $p \leq 0.01$, within the same column, means with different superscript letters are significantly different, WP: Whey protein concentrate, CM: Camel milk and LFX: Levofloxacin

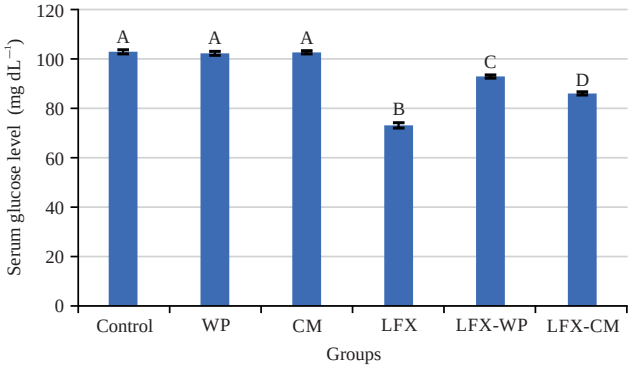

Fig. 13: Means of serum glucose (mg dL^{-1}) of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in the serum glucose level, B: Administration of LFX resulted in a significant decline in the serum glucose level when compared with the control groups, C: Treatment with WP resulted in a more significant increase in the serum glucose level when compared with the LFX group and D: Administration of CM resulted in a less significant increase in the serum glucose level when compared with the LFX group

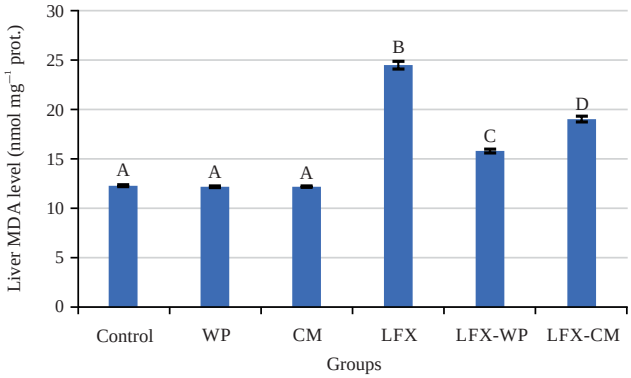

Fig. 14: Means of liver MDA level (nmol mg^{-1} prot) of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in liver MDA level, B: Administration of LFX resulted in a significant rise in liver MDA level when compared with control groups, C: Treatment with WP resulted in a more significant decrease in liver MDA level when compared with LFX group and D: Administration of CM resulted in a less significant decrease in liver MDA level when compared with LFX group

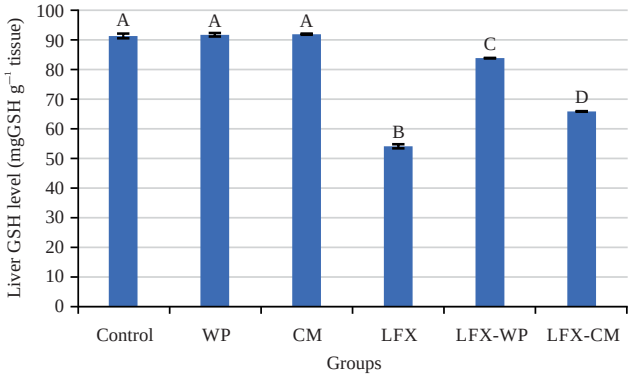

Fig. 15: Means of liver GSH level (mg GSH g^{-1} tissue) of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in liver GSH level, B: Administration of LFX resulted in a significant decline in liver GSH level Albumin when compared with control groups, C: Treatment with WP resulted in a more significant increase in liver GSH level when compared with LFX group and D: Administration of CM resulted in a less significant increase in liver GSH level when compared with LFX group

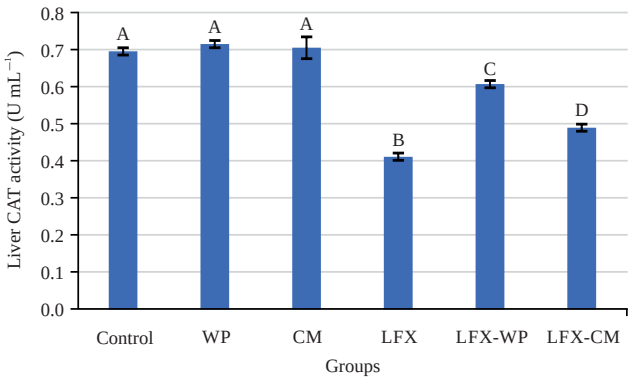

Fig. 16: Means of liver CAT activity (U mL^{-1}) of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in liver CAT activity, B: Administration of LFX resulted in a significant decline in liver CAT activity when compared with control groups, C: Treatment with WP resulted in a more significant increase in liver CAT activity when compared with LFX group and D: Administration of CM resulted in a less significant increase in liver CAT activity when compared with LFX group

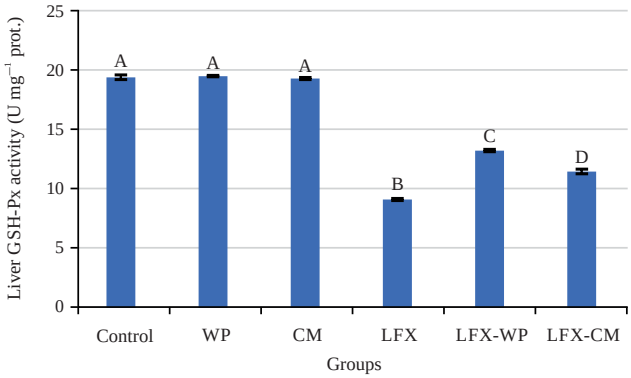

Fig. 17: Means of liver GSH-Px activity (U mg^{-1} prot.) of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in liver GSH-Px activity, B: Administration of LFX resulted in a significant decline in liver GSH-Px activity when compared with control groups, C: Treatment with WP resulted in a more significant increase in liver GSH-Px activity when compared with LFX group and D: Administration of CM resulted in a less significant increase in liver GSH-Px activity when compared with LFX group

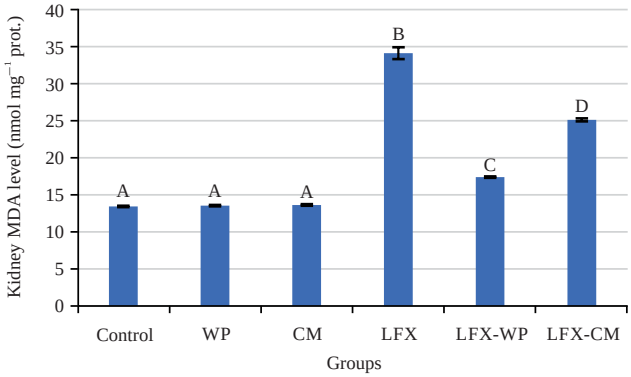

Fig. 18: Means of kidney MDA (nmol mg^{-1} prot.) of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in kidney MDA level, B: Administration of LFX (100 mg kg^{-1} b.wt.) resulted in a significant rise in kidney MDA level when compared with control groups, C: Treatment with WP with 200 mg kg^{-1} b.wt., resulted in a more significant decrease in kidney MDA level when compared with LFX group and D: Administration of CM at a dose 5 mL/rat/day resulted in a less significant decrease in kidney MDA level when compared with LFX group

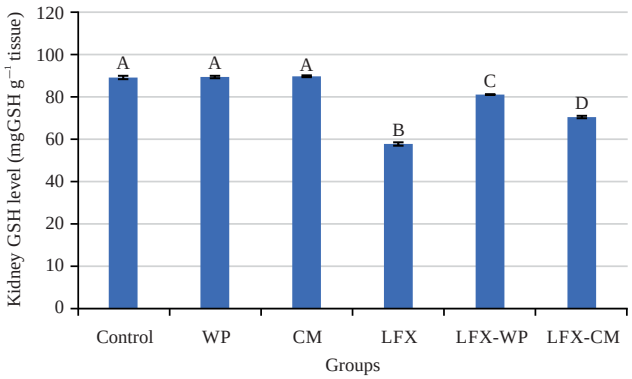

Fig. 19: Means of kidney GSH level (mgGSH g^{-1} tissue) of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in levels of kidney GSH, B: Administration of LFX resulted in a significant decline in levels of kidney GSH when compared with control groups, C: Treatment with WP resulted in a more significant increase in levels of kidney GSH when compared with LFX group and D: Administration of CM at a dose 5 mL/rat/day resulted in a less significant increase in levels of kidney GSH when compared with LFX group

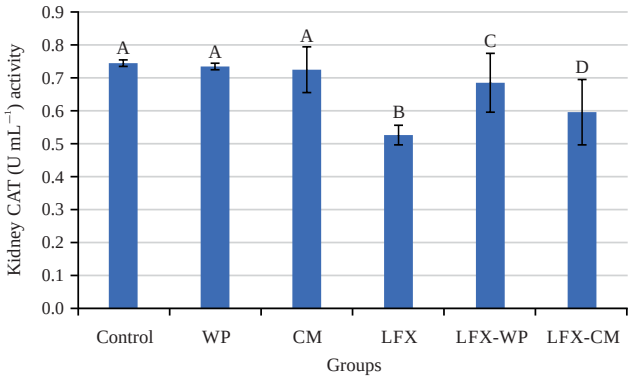

Fig. 20: Means of kidney CAT activity (U mL^{-1}) of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in kidney CAT activity, B: Administration of LFX resulted in a significant decline in kidney CAT activity when compared with control groups, C: Treatment with WP resulted in a more significant increase in kidney CAT activity when compared with LFX group D: Administration of CM resulted in a less significant increase in kidney CAT activity when compared with LFX group

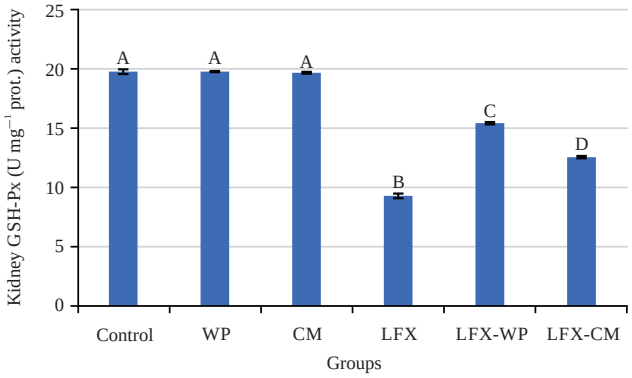

Fig. 21: Means of kidney GSH-Px (U mg^{-1} prot.) activity of adult male albino rats *Rattus norvegicus*

A: There is no significant difference between control, whey protein and camel milk in kidney GSH-Px activity, B: Administration of LFX resulted in a significant decline in kidney GSH-Px activity when compared with control groups, C: Treatment with WP resulted in a more significant increase in kidney GSH-Px activity when compared with LFX group and D: The administration of CM resulted in a less significant increase in kidney GSH-Px activity when compared with LFX group

Table 6: Effect of oral administration of camel milk and whey protein concentrate on kidney oxidative stress

		Parameters			
Groups		MDA (nmol mg^{-1} prot)	GSH (mg GSH g^{-1} prot)	CAT (U mL^{-1})	GSH-Px (U mg^{-1} prot)
Control	M±SE	13.6±0.09^{A}	94.6±0.7^{A}	0.75±0.01^{A}	20±0.2^{A}
WP	M±SE	13.7±0.1^{A}	94.8±0.5^{A}	0.74±0.01^{A}	20±0.05^{A}
	% Change A	0.7%	0.25%	-1.3%	0%
CM	M±SE	13.8±0.1^{A}	95.1±0.4^{A}	0.73±0.07^{A}	19.9±0.08^{A}
	% Change A	1.5%	0.5%	-2.7%	-0.5%
LFX	M±SE	34.5±0.8^{B}	67.4±0.7^{B}	0.53±0.03^{B}	10.2±0.2^{B}
	% Change A	153.7%	-28.8%	-29.3%	-49%
LFX +WP	M±SE	17.6±0.1^{C}	87.6±0.03^{C}	0.69±0.09^{C}	15.6±0.1^{C}
	% Change B	-48.9%	29.9%	30.2%	52.9%
LFX+CM	M±SE	25.4±0.2^{D}	78.4±0.5^{D}	0.60±0.1^{D}	12.7±0.1^{D}
	% Change B	-26.4%	16.3%	13.2%	24.5%

MDA: Malondialdehyde, GSH: Reduced glutathione, CAT: Catalase, GSH-Px: Glutathione peroxidase of levofloxacin-treated groups (M±SE), data are presented as mean±standard error of mean, data were subjected to one-way ANOVA followed by Duncan's *post hoc* Test at $p \leq 0.01$, within the same column, means with different superscript letters are significantly different, WP: Whey protein concentrate, CM: Camel milk and LFX: Levofloxacin

DISCUSSION

The following study found that levofloxacin consumption decreased T.P possibly due to liver damage caused by the medication and led to a significant drop in albumin, globulin and A/G ratio parameters which was in line with findings from other studies, which may be due to reduced liver synthesis or increased albumin loss from damaged kidneys[2,3,6,7].

The study found that camel milk has improved therapeutic effects on rats treated with LFX, resulting in improved (T.P, ALB, globulin and A/G ratio) parameters and stabilization of serum metabolites, our results are consistent with[32-34.] This was due to the high zinc and vitamin content, lactoferrin and exosomes in camel milk[33-37]. Findings showed the significant improvement of CWP in (T.P, ALB, globulin and A/G ratio) levels, the chemical makeup of CWP, which is rich in amino acids, vitamins and minerals with antioxidant activity[14,16,35] is responsible for its beneficial action.

Taking LFX orally for 10 days raised urea and creatinine levels, which was consistent with earlier research indicating a rise in the levels of the aforementioned parameters[2,3,6]. Drug toxicity, the third leading cause of kidney damage, is responsible for high urea and creatinine levels, which are a marker of abnormal kidney function[6]. Oral delivery of camel milk significantly lowered urea and creatinine levels[36,37], supporting the theory that antioxidants in camel milk may prevent kidney damage by scavenging free radicals[37]. The capacity of CWP to restore normal renal function is proven by a drop in urea and creatinine levels following a considerable increase induced by levofloxacin poisoning, ordinarily, an increase in urea and creatinine levels indicates aberrant renal function[38].

Recent studies on the toxicity of LFX show a significant increase in ASAT, ALAT and ALP activities. This increase is consistent with the previous studies[6,8,37]. When an organ, such as the liver, is injured, ASAT, ALAT and ALP are released into the bloodstream. Because these enzymes are released in response to tissue damage caused by blood cells-such as leukocytes, liver cells, red blood cells and other types of cells-LFX may increase the activities of these enzymes[8]. The findings also support the causal relationship between liver dysfunction and LFX toxicity, with elevated ALP associated with biliary hepatitis[3,7].

The studies by some researchers[32,34,39] corroborate the findings of the research regarding the beneficial effects of camel milk oral administration in LFX-treated rats on decreasing (ASAT, ALAT and ALP activities).

The following camel milk qualities might explain the results: Camel milk's primary antioxidant-rich components are casein, LAB, active peptides and whey proteins, notably lactoferrin, whose antioxidant qualities lower the oxidative stress associated with numerous disorders[11,32,34].

Findings showed a significant improvement of CWP in (ALAT, ASAT and ALP) activities in animals treated with LFX and the data showed homeostasis of parameter values in the serum in the whey group, consistent with current results[35].

The LFX actions in markedly raising (T.BIL, D.BIL, Ind.BIL) levels are consistent with[3,6] and this might be because of hepatic problems including necrosis, gallbladder enlargement, nucleus hypertrophy and impaired hepatocyte drug absorption because of inflammation or hepatic cirrhosis[3,40] due to this, both instances of metabolic malfunction and excessive bilirubin production have been seen. An increase in serum unconjugated bilirubin is caused by problems with liver storage, excretion and absorption[41].

Studies have validated the report that camel milk oral administration lowered (BIL, D.BIL and Ind.BIL). This is what happened in the animals treated with LFX in this study and preserved parametric values in the camel milk group. An increase in liver function, decreased levels of toxicity and tight

control of the parameters in both groups may be due to CM containing higher quantities of vitamins C, B2 and E[32]. Normally, water-insoluble and unconjugated bilirubin travels through the bloodstream to the liver where it is converted to a water-soluble conjugated form by (Uridine diphosphate glucuronyl transferase) (UDGT) and then excreted into bile so toxicity in the (UDGT) system leads to elevated serum levels of unconjugated bilirubin so hypersecretion bilirubin is the result of a decrease in the enzyme (UDGT). The significant decrease in bilirubin levels as a result of oral administration (CWP), may be attributed to its effect in restoring the enzyme activity (UGT) to its normal levels after the toxicity caused by levofloxacin[42].

This investigation confirms previous studies showing LFX's significant glucose-lowering impact[43,44]. However, hypoglycemia is an uncommon adverse effect (0.1%)[44]. The effect of LFX on glucose deficiency may be due to blocking ATP-sensitive potassium channels in pancreatic beta cells, causing calcium-dependent channels to open[40,44,45]. While hyperglycemia is more common. Factors like stress and steroid use also contribute to increased levels[5].

The study's findings suggest that elevating glucose parameters following the administration of camel milk has a substantial effect on LFX-treated rats when compared to the LFX group, inconsistent with the results[36,37,43]. Giving camel milk to diabetics reduces the amount of insulin needed to regulate blood sugar levels[46,47].

One probable explanation is that the amino acid is present in some proteins of camel milk and the existence of insulin-like molecules in camel milk, as well as the number of intracellular immunoglobulins, may be the cause of these results. This sequence contains a high homocysteine content and is akin to insulin family peptides[48].

On the other hand, one study examined the effect of digestive enzymes on insulin activity in camel milk. Insulin in camel milk is not involved in antidiabetic effects as it is very susceptible to breakdown by digestive enzymes, the results of our current study trace back to what was shown in one of the previous studies that differences in climatic conditions, lactation stages and food types influence the formation of the carbohydrate content in camel milk[37,49].

The current study's findings suggest that concentrating whey protein may significantly improve low glucose indices due to LFX-induced toxicity, which is in line with earlier research, supplementation of treated animals with camel whey protein led to an increase in glucose levels after a decrease because of STZ induction, restoration of glucose levels is linked to the down-regulation of phosphatidylinositol triphosphate (PIP3), which is important in the regulation of insulin pathways, so increased phosphorylation is linked to increased glucose metabolism[35].

Research shows a significant increase in MDA markers in liver and kidney tissue due to LFX toxicity compared to the control group[7,8]. Because enzymatic and non-enzymatic antioxidants found in liver cells play an important role in preventing injury from oxygen-based reactive species and free radicals, it is possible that liver damage causes free radical formation, mitochondrial degeneration, lipid peroxidation and changes in redox states. This prolonged exposure of the cell to lipid peroxidation eventually causes oxidative stress in liver cells[3].

The findings of the current indications show improvement in the parameters (MDA) following oral administration of milk in the LFX-treated group of rats compared to the LFX-treated group, as the parameter values were maintained to within a few degrees of control in the CM group. It agrees with the findings of other investigations[32,33]. Active free radical intermediates with proteins, lipids and carbohydrates cause hepatic cell damage, antioxidants are produced to develop the antioxidant defense system, lactoferrin, casein, exosomes and other active peptides in camel milk increase antioxidant levels and immunological response and lipid peroxidation is thus neutralized[33].

In this study, LFX had a significant effect in reducing GSH, CAT and GSH-PX indicators in liver and kidney tissues, which is consistent with previous studies in which LFX caused a significant decrease in tissues after different times of treatment[6,8].

Free radical removers and chain reaction termination enzymes are just two of the defense mechanisms that cells must use to protect themselves from the damaging effects of ROS. Because of the buildup of superoxide and hydrogen ions peroxide, inhibiting or lowering the activity of these defense systems would make cells more vulnerable to cellular damage caused by free radicals[6].

Camel milk showed a less significant effect (GSH, CAT and GSH-PX activities) on boosting antioxidant markers and decreasing oxidative stress, which is consistent with prior research[33,37].

Camel milk has various health benefits because of the element zinc, which is essential for the functioning of many enzymes, plays a vital role in DNA, transcription and protein synthesis and can influence cells to avoid or limit cell damage through antioxidant activity[32].

The results demonstrated a considerable improvement in elevating (GSH, CAT and GSH-PX) markers because of whey protein therapy in LFX-treated mice, which is consistent with some studies[16,35].

This might be attributable to the white phosphorus in whey, which is regarded as a major antioxidant agent because it provides cysteine, which promotes antioxidant production in numerous tissues and hence detoxification[35].

CONCLUSION

According to the current study's findings, levofloxacin depleted the antioxidant defense system and caused oxidative stress after 10 days and ingestion of camel milk and concentrated whey protein for 15 days after triggering levofloxacin toxicity had a beneficial capacity in minimizing peroxidation of lipids and enhancing the antioxidant system of defense in biochemical indicators. Compared to camel milk, concentrated whey protein has a higher proportion of therapeutic effectiveness for serum, liver and kidney tissues. Vitamins, magnesium, zinc and bioactive peptides may all play a role in the reduction process. In terms of lowering the toxicity of antibiotics like levofloxacin, this data suggested that camel milk and concentrated whey in the diet have advantages.

SIGNIFICANCE STATEMENT

This article is done to investigate the therapeutic potency of CWP and CM against LFX-toxicity. The article discovered that the use of Camel whey protein as a therapy showed potential modulatory effects against oxidative stress and changes in the values of hormones. Although concentrated camel whey protein was helpful in reducing medication toxicity additional research is required to identify the main ingredients contributing to the therapeutic effectiveness.

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