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Research Article

L-CARNITINE AND CO-ENZYME Q10 AMELIORATE CIPROFLOXACIN-INDUCED REPRODUCTIVE TOXICITY IN MALE RATS: REGULATION OF INFLAMMATION AND EXPRESSION OF STEROIDOGENIC GENES

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ABSTRACT

This study was conducted to evaluate Ciprofloxacin (CPX) reproductive toxicity in 30 days and the protective effect of L-Carnitine (LC) and /or Co-Enzyme Q10 (Co-Q_{10}) against reproductive toxicity induced by CPX and the molecular changes that related to their effects. Animals were divided into 5 groups (12 rats/group). Group 1, was kept as a control. Group 2, was administered CPX (90 mg/kg/day, p.o) and kept as a positive control. Group 3, was co-administered CPX with LC (94.5 mg/kg/day p.o). Group 4, was co-administered CPX with Co-Q10 (8.1 mg/kg/day p.o). Group 5, was concurrently administered CPX with Co-Q10 + LC orally for 30 days. After thirty days, body and genital sex organ weights (testes, prostate glands, and seminal vesicles) and semen analysis (sperm count, motility and morphology), were assayed. Gene expression of StAR, SR-B1, and 3βHSD were assayed by using real-time PCR. Hormonal assay (Testosterone, LH, and FSH), biomarkers of inflammatory mediators (TNF-α) and anti-inflammatory mediators (IL-10) were assayed by using ELISA. MDA, GSH, and TAC were investigated by a spectrophotometer. Results: The thirty-day administration of CPX to adult male rats promotes reproductive toxicity in rats by generating oxidative damage. It induces an adverse effect on reproductive organs weights, sperm parameters, reduction of gene coordination (StAR, SR-B1, and 3 βHSD) and reproductive hormones. Also, increases TNF-α and decreases IL-10 Notably, LC and Co-Q10 co-administration overcame all of these side effects. Conclusion: concurrent administration of both LC and Co-Q10 with CPX ameliorating reproductive toxicity induced by CPX in thirty days administration.

Keywords: L-Carnitine, Co-EnzymeQ10, Ciprofloxacin, Male infertility, Steroidogenic acute regulatory protein and Scavenger receptor class.

INTRODUCTION

Infertility is one of the problems of both human and animal society. According to the WHO, 15-20% of couples have experienced some forms of infertility problems. About 40% of these problems are due to male factor[1]. Drug treatment and chemotherapy can have a harmful effect on spermatogenesis and sperm normal production[2]. Ciprofloxacin (CPX) is antibiotic which belongs to the family of fluoroquinolones with a very broad spectrum against many microbial pathogens[3]. It is widely used as an oral synthetic chemotherapeutic antimicrobial agent with broad-spectrum activity against infections caused by both Gram-positive and Gram-negative bacteria[4]. However, there is recent evidence assured that it can directly lower sperm quality, testes weight, and testosterone levels, that are dose and time-dependent[5]. Levo-carnitine (L-carnitine) is a biologically active water-soluble antioxidant molecule[6]. It is present in all mammals localized on the inner mitochondrial membrane and facilitates the transport of long chain fatty acids (LCFAs) through the mitochondrial membrane for utilization in energy production (β-Oxidation) [7]. The major exogenous dietary sources of LC are milk, fish, and meat. It shows a broad range of biological activities including; anti-inflammatory, cardioprotective, gastroprotective, and neuroprotective properties[8]. Furthermore, LC plays an important part in sperm metabolism by providing readily available energy for employ by spermatozoa that positively impacts sperm maturation, motility, and the spermatogenic process[9]. Co-enzymeQ10 (Co-Q10), a vitamin-like substance, is essential for the body and presents in a small amount in a wide variety of foods. It is a component of the mitochondrial respiratory chain; playing a role in energy metabolism so acting as an antioxidant for cell membranes and lipoproteins[10]. Co-Q10 biosynthesis is markedly active in testis, and spermatozoa. Co-Q10 level decreased in seminal plasma and spermatozoa of infertile men[11]. Moreover, the exogenous administration of Co-Q10 has been reported to improve sperm motility[12]. This study was conducted to evaluate CPX reproductive toxicity in 30 days and the protective effects of LC and/or Co-Q10 against reproductive toxicity induced by CPX and the molecular changes that related to their effects.

MATERIAL AND METHODS

Drugs

Ciprofloxacin: Each extended release film coated tablet contains 1164 mg of CPX-HCl equivalent to 1 gram of CPX. Manufactured by Mash for pharmaceutical industries (Mash Premiere)- Bader City - Egypt

L-Carnitine: Each capsule contains 350 mg of LC (as tartrate). Produced by Arab Company for Pharmaceuticals & Medicinal Plants Mepaco-Medifood (Enshas – Sharkeye – Egypt)

Co-Enzyme Q10: Each hard gelatin capsule containing 30 mg of Co- Q10. Produced by Arab Company for Pharmaceuticals & Medicinal Plants Mepaco-Medifood (Enshas- Sharkeye – Egypt).

Animals

Adult male Wistar rats weighing (275 ± 25g) were obtained from the animal house of the National Organization for Drug Control and Research (NODCAR), Giza, Egypt. They were allowed two weeks for accommodation to the new environment before starting the experiment. The rats were housed at 23 ± 2^0 C and 55 ± 5% humidity with 12 h light/dark cycle and were given standard rodent chow and drinking water ad libitum. All animal´s procedure and the current investigation conform to the standard ethical procedures and policies approved by Ethical Committee for Animal Experimentation at Faculty of Pharmacy, Al-Azhar University and were approved by the Guide for the Care and Use of Laboratory Animals (Code No. 92).

Experimental Design

Induction of Reproductive toxicity
Reproductive toxicity was induced in rats by orally administration of CPX at a dose of (90 mg/kg) once daily for 30 days that equivalent to human recommended dose (1000 mg/kg)[13].

Experimental group
Rats were divided into 5 groups each the group contained 12 rats and treated as follows:

Group (1) was given distilled water orally and kept as a control.

Group (2) administered only CPX served as positive control.

Group (3) simultaneous administered CPX and LC orally at a dose of (94.5 mg/kg) once daily for 30 days that equivalent to human recommended dose (1050 mg/kg).

Group (4) simultaneous administered CPX and Co-Q10 orally at a dose of (8.1 mg/kg) once daily for 30 days that equivalent to human recommended dose (90 mg/kg).

Group (5) simultaneous administered CPX and both of Co-Q10 and LC orally for 30 days.

Collection and Preparation of Samples

Blood samples
Blood samples were collected from the retro-orbital sinus, under mild ether anesthesia and serum was separated, aliquoted and stored at -20°C till the determination the levels of (testosterone, LH, FSH, TNF-α and IL-10) by enzyme-linked immunosorbent assay (ELISA) and determination the level of TAC by spectrophotometer.

Tissue specimens and semen analysis:
After blood collection, the rats were immediately decapitated. Pairs of testes and epididymides, seminal vesicles (without coagulation and full of secretion) and prostate gland were removed, cleared from adhering tissue, washed in ice-cold 1.15% KCL then blot dried and weighed. The right epididymis was used for estimating sperm count while the left one was used for assessing sperm motility. The right testis was kept in 10% formalin saline for gene expression for (StAR, SR-B1, and 3βHSD). While the left testis was homogenized in ice-cold 1.15% KCL to make 10% (w/v) homogenate with Glass-Col motor-driven homogenizer (USA) and the homogenate was used for measuring (MDA& GSH).

METHODS

Body weight: At the end of the experimental period, the body weight of each individual rat was measured.

Reproductive organ indices

Reproductive organs weight
Rats were sacrificed after the last day of treatment and reproductive organs; testes, prostate glands, and seminal vesicles were weighed.

Sperm functions analysis
Sperm count: The pipette of counting erythrocytes by haemocytometer was used. The epididymal content was withdrawn up to the mark 0.1 then the pipette was filled up to the mark 101 by 0.9% sodium citrate solutions. The content of the pipette was mixed and shacked well then a cover slide was placed over the counting chamber and a drop of diluted epididymal content was spread between the haemocytometer chamber and the cover slide. The sperms in five large squares (80 small squares) were counted using the high power objective lens (x400). The total number in five small squares was multiplied by million[14].

Mass motility: A small droplet of epididymal content was added to one drop of 2.9% sodium citrate solution on a clear glass slide then the slide was gently warmed. Several fields were quickly examined under the microscope (x100) and the progressive motility of sperms was estimated as a percentage[14].

Epididymal sperm abnormalities: A drop from the epididymal content of each rat was immediately taken and mixed with an equal drop of Eosin-Nigrosin stain for detection of dead and malformed sperm. The semen was carefully mixed with the stain, then films were examined at random per slide under x 200 and the type (live and dead) and percentage of abnormal sperms[15].

Biochemical analysis

Serum analysis
Hormonal assay for Testosterone, luteinizing hormone (LH), and follicle stimulating hormone (FSH) was performed using enzyme-linked immunosorbent assay (ELISA). Biochemical analysis of inflammatory and anti-inflammatory marker; tumor necrosis factor alpha (TNF-α) and Interleukin-10 (IL-10) estimated using immunoassay CUSABIO ELISA kit®. Furthermore, the serum level of TAC (Total antioxidant capacity) was determined by Bio-Diagnostic kit.

Tissue Homogenate
The right testis was kept in 10% neutral buffered formalin for Gene expression using real-time PCR (StAR, SR-B1, and 3βHSD). While the left testis was homogenized in ice-cold 1.15% KCL to make 10% (w/v) homogenate with Glass-Col motor-driven homogenizer (USA) and the homogenate was used for measuring (MDA& GSH).

Gene expression using RT-PCR
Detection of (StAR, SR-B1, and 3βHSD) gene expression by real-time quantitative reverse transcription PCR: Total RNA was extracted from frozen samples using TRIzol® reagent (Invitrogen, USA) according to a standard protocol. The isolated total RNA was turned into complementary DNA (cDNA) utilizes the Moloney murine leukemia virus (M-MLV) reverse transcriptase (Promega, USA). Real-time PCR was proceeded

using an ABI 7500 Real-Time PCR System (Applied Biosystems, USA) and an SYBR® Green PCR Master Mix (Applied Biosystems) in a final volume of 10˚µL together with the following thermic cycling conditions: 95˚C for 10min, followed by 40 cycles of 95˚C for 15s and 60˚C for 1min [16].The sequences of PCR primer pairs employed for each gene are displayed in (Table 1)**.** Finally, all values were normalized to the β-actin genes as an invariant endogenous control (reference gene**)**.

Statistical analysis

The results were expressed as the mean ± standard error (SE). Differences between groups were assessed by one-way analysis of variance (ANOVA). Subsequent multiple comparisons between the different groups were analyzed by Tukey (compare all pairs of columns) tests. Data were statistically analyzed using the (GraphPad Prism version 5® (GraphPad Prism software). Values at $P < 0.05$ were considered significant[17]**.**

RESULTS

Effect of different treatment on body and genital organ weights

All weights are shown in (Table 2) administration of CPX caused a significant decrease in body weight by 27.75 % in comparison with the control group. However, administration of LC and Co-Q10 is significantly ameliorated this decreasing in body weight. In addition, CPX induced a significant decrease in the weights of testes (37.93%), prostate gland (50%) and seminal vesicles (44.23%) as compared to the control group. These reductions were significantly improved by co-administration of LC and Co-Q10.

Effect of different treatment on semen analysis

Data of the epididymal sperm motility, sperm count, and viability % are shown in (Table 3)**,** a marked reduction in sperm motility, sperm count and viability% was recorded in CPX treated group (64.64% and 63.43%, 58.12% respectively) when compared with the control group. Co-administration of LC or Co-Q10 with CPX attenuates the decrease in sperm count, motility and improves sperm viability % in comparison to the control group. Moreover, administration of both LC and Co-Q10 with CPX caused the significant increase in the motility, number, and viability of sperm in compared to the positive group.

Effect of different treatment on StAR, SR-B1 and 3βHSD

(Figure 1) was shown that the administration of CPX caused a significant decrease in StAR (80%), SR-B1 (81%), and 3βHSD (83%) relative quantification as compared to the control group. Co-administration of LC or Co-Q10 with CPX attenuates the decrease in StAR, SR-B1, and 3βHSD incomparable to the positive group. On the other hand, concurrent administration of LC and Co-Q10 with CPX increase StAR, SR-B1 and 3βHSD relative quantification compared to the positive group.

Effect of different treatment on Testosterone, LH and FSH

The values obtained for serum sex hormones level are shown in (Figure 2). Administration of CPX was associated with a significant reduction in testosterone (70.55%), LH (50%) and FSH (61.90%) as compared to the control rats. Co-administration of LC or Co-Q10 with CPX ameliorates the decrease in testosterone, LH and FSH. On the other hand, concurrent administration of both LC and Co-Q10 with CPX increase testosterone, LH and FSH serum levels but not reaching the values of control rats.

Effect of different treatment on TNF-α and IL-10

The values obtained for TNF-α and IL-10 levels are shown in (Figure 3). Administration of CPX was associated with a significant increase in inflammatory marker (TNF-α) and a significant decrease in anti-inflammatory marker (IL-10) compared to the control group. Co-administration of LC and/ or Co-Q10 with CPX improved inflammation as TNF-α level was decreased and IL-10 level was increased incomparably to CPX group.

Oxidative stress markers

The Data represented in (Table 4) were revealed a significant increase in the mean values of MDA and a significant decrease in GSH and TAC activity in CPX treated rats versus the control group. Concurrent administration of CPX with LC and/or Co-Q10 were caused a significant decrease in lipid peroxidation were caused a remarkable increase in the GSH and TAC level compared with the CPX treated rats.

Table 1: Primers Sequences of studied gene

Studied gene	Primer sequence
StAR	Forward primer :5'- GGGCATACTCAACAACCAG -3- Anti – sense :5′- ACCTCCAGTCGGAACACC -3-
SR-B1	Forward primer :5'-ACAGGTCCCAGGGCTCAG-3- Reverse primer:5′-CGTGCGGTTCATAAAGG-3-
3-βHSD	Forward primer :5'- TGTGCCAGCCTTCATCTAC -3- Reverse primer:5′- CTTCTCGGCCATCCTTT-3-

Table 2: Effect of different treatment on body and genital organ weights

Groups \ Variables	Final body (g)	Testes (g)	Prostate gland (g)	Seminal vesicles (g)
Control	279.2 ± 6.38	2.61 ± 0.08	0.44 ± 0.02	0.52 ± 0.02
CPX	201.7 ± 7.03^{a}	1.62 ± 0.10^{a}	0.22 ± 0.02^{a}	0.29 ±0.02^{a}
CPX + LC	235 ± 4.83^{abc}	2.09 ± 0.11^{abc}	0.34 ± 0.02^{abc}	0.42 ± 0.02^{abc}
CPX + Co-Q10	222.5 ± 7.042^{abc}	1.95 ± 0.09^{ac}	0.32 ± 0.02^{abc}	0.41 ± 0.01^{abc}
CPX + LC + Co-Q10	260.8 ± 3.27^{b}	2.54 ± 0.09^{b}	0.43 ± 0.02^{b}	0.50 ± 0.02^{b}

The data are presented as mean ± SE (n=12 rats/group). The symbols **a**: significant difference from control values; **b**: significant difference from CPX values; **c**: significant difference from CPX +LC+ Co-Q10 values. The values at $p < 0.05$ were considered significant

Table 3: Effect of different treatment on semen analysis

Groups	Variables		
	Motility %	**Sperm count ×10^6/ml**	**Sperm Viability %**
Control	85.33 ± 2.89	82.15 ± 2.64	85.17 ± 2.94
CPX	30.17 ± 2.52^a	30.17 ± 2.52^a	35.67 ± 2.96^a
CPX + LC	72.00 ± 3.65^{abc}	67.17 ± 3.88^{abc}	62.83 ± 4.04^{abc}
CPX + Co-Q10	62.5 ± 3.35^{abc}	57.50 ± 3.79^{abc}	57 ± 4.83^{abc}
CPX + LC + Co-Q10	83.83 ± 2.76^b	81.27 ± 3.37^b	78.83 ±3.32^b
The data are presented as mean ± SE (n=12 rats/group). The symbols **a**: significant difference from control values; **b**: significant difference from CPX values; **c**: significant difference from CPX +LC+ Co-Q10 values. The values at $p < 0.05$ were considered significant			

Table 4: Effect of different treatment on oxidative stress markers

Groups	Variables		
	MDA (nmol/g.tissue)	**GSH (mmol/gm)**	**TAC (mM/L)**
Control	3.103 ± 0.31	1.34 ± 0.09	2.28 ± 0.13
CPX	9.09 ± 0.67^a	0.57 ± 0.04^a	0.55 ± 0.08^a
CPX + LC	6.25 ± 0.32^{abc}	0.85 ± 0.04^{abc}	1.34 ± 0.09^{abc}
CPX + Co-Q10	6.71 ± 0.28^{abc}	0.79 ± 0.04^{abc}	1.25 ± 0.07^{abc}
CPX + LC + Co-Q10	4.08 ± 0.32^b	1.15 ± 0.01^b	2.03 ± 0.09^b
The data are presented as mean ± SE (n=12 rats/group). The symbols **a**: significant difference from control values; **b**: significant difference from CPX values; **c**: significant difference from CPX +LC+ Co-Q10 values. The values at $p < 0.05$ were considered significant			

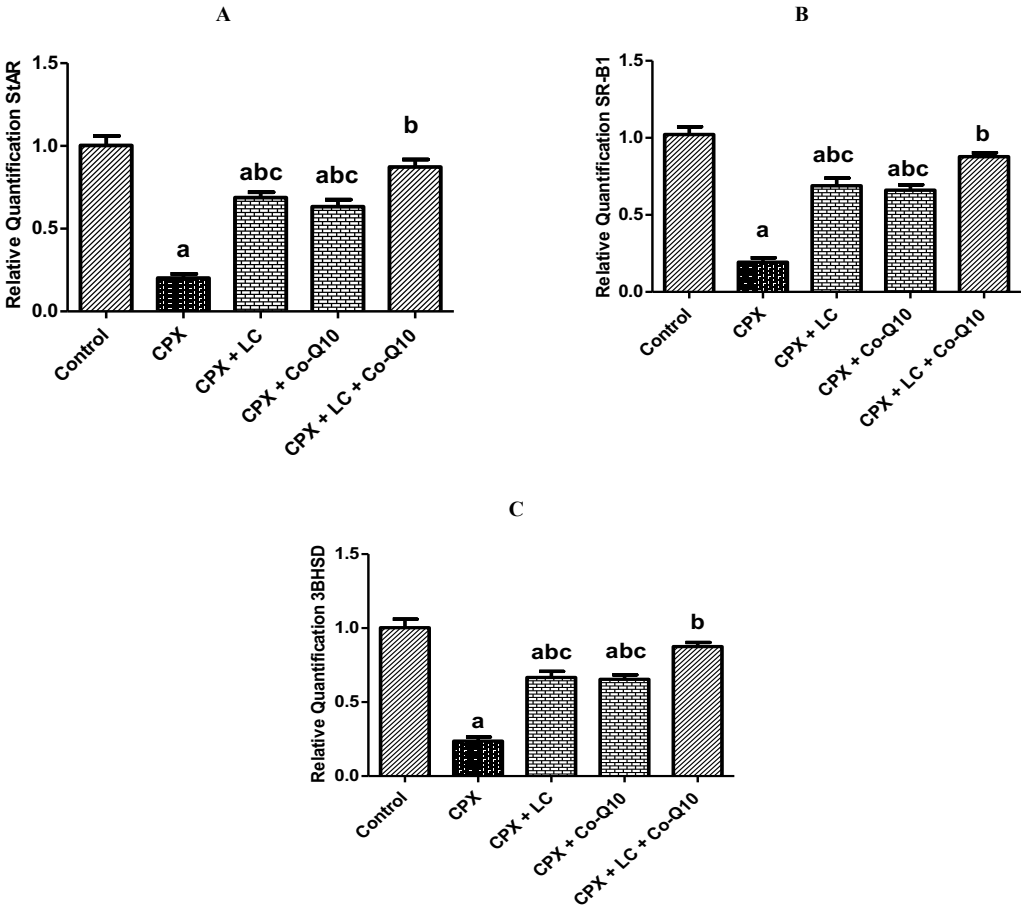

Figure (1): Effect of different treatment on StAR, SR-B1 and 3βHSD

Mean ± SE of StAR, SR-B1and 3βHSD in the studied groups: The data are presented as mean ± SEM **(**n=12 rats/group). The symbols **a:** significant difference from control values; **b:** significant difference from CPX values; **c:** significant difference from CPX +LC + Co-Q10 values

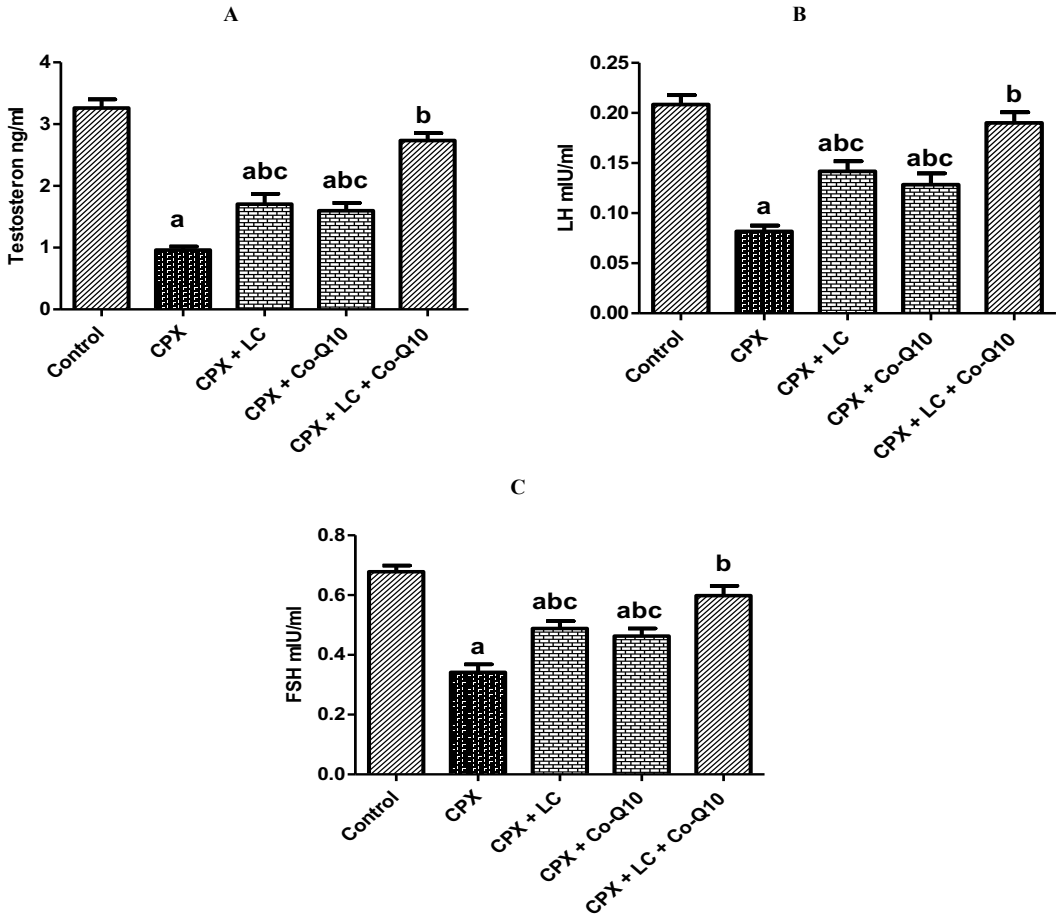

Figure (2): Effect of different treatment on Testosteron, LH and FSH

Mean ± SE of Testosterone, LH and FSH in the studied groups: The data are presented as mean ± SE **(**n=12 rats/group). The symbols **a:** significant difference from control values; **b:** significant difference from CPX values; **c:** significant difference from CPX +LC + Co-Q10 values

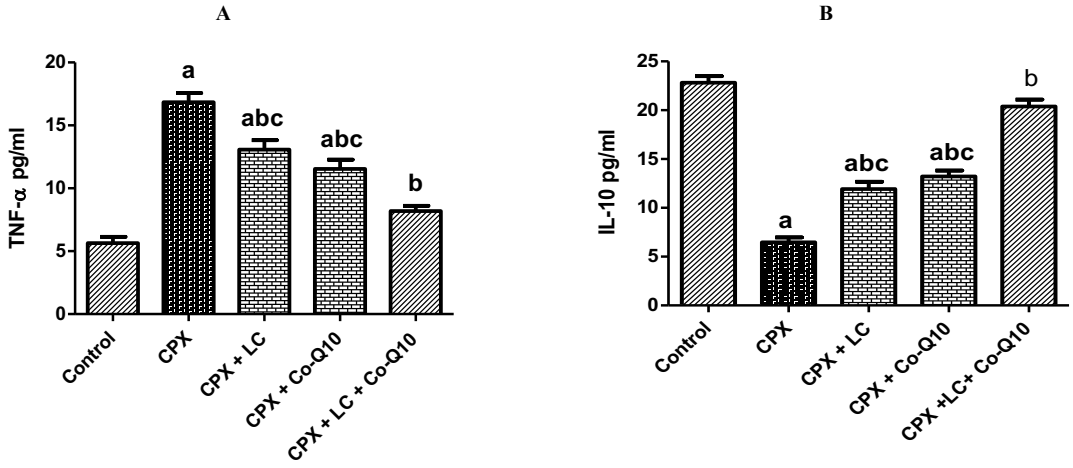

Figure 3: Effect of different treatment on TNF-α and IL-10

Mean ± SE of TNF- α and IL-10 in the studied groups: The data are presented as mean ± SE **(**n=12 rats/group). The symbols **a:** significant difference from control values; **b:** significant difference from CPX values; **c:** significant difference from CPX +LC + Co-Q10 values

DISCUSSION

Ciprofloxacin is one of the best drugs for the treatment of different bacterial infections[18]. However, some reports[19,20] recorded that the administration of CPX significantly impairs testicular structure and function. In the current study, administration of CPX influence the body weight of the animals and caused a significant decrease in the weights of testes, prostate glands and seminal vesicles comparative to the control group[21]. Further, concurrent administration of LC and Co-Q10 with CPX clearly restored the reproductive organ weights towards normal that may be due to their androgenic activity [22]. Epididymal sperm count, motility and viability supply a direct measurement of fertility in animals[23]. Our results were in accordance with,[24] who reported that CPX causing decrease in sperm counts and motility in laboratory animals. On the other hand The obtained data are parallel with[25,26] who reported that LC and Co-Q10 attenuated spermatogenic and testicular damage by returning sperm count, motility and viability towards normal control values. A series of enzymatic reactions are required to synthesize testosterone and estrogen from cholesterol. SR-B1 is a trans membrane protein that mediates selective cholesterol uptake by steroidogenic tissues, including Leydig cells[27]. StAR transport of cholesterol across the mitochondrial membrane is generally considered the rate-limiting step in steroidogenesis, followed by the conversion of cholesterol to pregnenolone [28]. Pregnenolone is metabolized into testosterone mainly by 3β -HSD in the smooth endoplasmic reticulum [29]. Our report is the first that describes the exposure of male rates to CPX for 30 days has important effects on these key steroidogenic testicular genes that causing a decrease in expression of genes involved in cholesterol transport and steroidogenesis with a resultant reduction in testosterone production in the testes. The concurrent treatment of CPX with LC and/or Co-Q10 increase StAR, SR-B1 and 3βHSD relative quantification compared to the positive group. Normal testicular function is dependent on testosterone, FSH and LH which are absolutely required for normal spermatogenesis [30]. Our results were in accordance with [31] who recorded that CPX induced a significant decrease in the testosterone, LH and FSH levels associated with degenerative changes in the seminal vesicle. The present study was supported by[32] who found that, the levels of FSH and testosterone increased in the LC treated group. Also, [33] reported that Co-Q10 significantly increased serum testosterone level. The results obtained in this study parallel with[34] who reported that Co-Q10 suppressed the production of inflammatory mediators such as TNF- α and the expression of IL-10 was increased significantly. Also, with [35] who reported that carnitine therapy reduced levels of pro-inflammatory cytokines as TNF- α, moreover enhancement of IL-10.The present study was supported by[21] who found that the oxidative stress marker in the rat testes of CPX group resulted in increased MDA levels as well as decreased GSH hormone as the plasma membrane in the sperm contains a high proportion of polyunsaturated fatty acids that are easily susceptible to oxidized lipid peroxide[36]. The obtained results were parallel with[8] who reported that LC affects these sperm parameters mainly by increasing the activity of antioxidant enzymes, which is reflected in the increased levels of GSH and TAC. [22,28] reported that Co-Q10 reduced MDA level and protected against peroxidative damage.

CONCLUSION

Our study revealed that the thirty-day administration of CPX to adult male rats promotes reproductive toxicity in rats, while LC and Co-Q10 co-administration could effectively prevent the reproductive toxicity induced by CPX on the male reproductive system.

REFERENCES

1. Khojasteh SMB, Khameneh RJ, Houresfsnd M, Yaldagard E. A review on medicinal plants used for improvement of spermatogenesis. Biol Med. 2016;8(4).
2. Agarwal A, Makker K, Sharma R. Clinical Relevance of Oxidative Stress in Male Factor Infertility : An Update. 2008;59:2–11.
3. Drobnis EZ, Nangia AK. Advances in Experimental Medicine and Biology 1034 Impacts of Medications on Male Fertility [Internet]. 2017. 131-161 p.
4. Singh K, Mishra A, Singh A. Synthesis Characterization and In Vitro Release Study of Ciprofloxacin-Loaded Chitosan Nanoparticle. Bionanoscience. 2018;8(1):229–36.
5. Eskandari M, Jani S, Kazemi M, Zeighami H, Yazdinezhad A, Mazloomi S, et al. Ameliorating effect of ginseng on epididymo-orchitis inducing alterations in sperm quality and spermatogenic cells apoptosis following infection by uropathogenic Escherichia coli in rats. Cell J. 2016;18(3):446–57.
6. El-sherbini E, El-sayed G, El R, Gheith N. Ameliorative effects of L -carnitine on rats raised on a diet supplemented with lead acetate. Saudi J Biol Sci [Internet]. 2017;24(6):1410–7.
7. Liu L, Zhang DM, Wang MX, Fan CY, Zhou F, Wang SJ, et al. The adverse effects of long-term l -carnitine supplementation on liver and kidney function in rats. Hum Exp Toxicol. 2015;34(11):1148–61.
8. Khushboo M, Murthy MK, Devi MS, Sanjeev S, Ibrahim KS, Kumar NS, et al. Testicular toxicity and sperm quality following copper exposure in Wistar albino rats: ameliorative potentials of L-carnitine. Environ Sci Pollut Res. 2018;25(2):1837–62.
9. Al-Shammari MHM, Yenzeel JH, Fakhrildin M-BM-R. Effect of L- Carnitine and COQ10 Addition to SMARTProMedium on Human SpermConcentration,SpermMorphology and Chromatin StructureduringIn VitroSperm Activation. IOSR J Pharm Biol Sci [Internet]. 2017;12(02):51–5.
10. Lafuente R, González-Comadrán M, Solà I, López G, Brassesco M, Carreras R, et al. Coenzyme Q10 and male infertility: A meta-analysis. J Assist Reprod Genet. 2013;30(9):1147–56.
11. Nadjarzadeh A, Sadeghi MR, Amirjannati N, Vafa MR, Motevalian SA, Gohari MR, et al. Coenzyme Q 10 improves seminal oxidative defense but does not affect on semen parameters in idiopathic oligoasthenoteratozoospermia : A randomized double-blind , placebo controlled trial. 2011;224–8.
12. Talevi R, Barbato V, Fiorentino I, Braun S, Longobardi S, Gualtieri R. Protective effects of in vitro treatment with zinc , d-aspartate and coenzyme q10 on human sperm motility , lipid peroxidation and DNA fragmentation. 2013;1–10.
13. Paget GE and Barnes JM. Interspecies dosage conversion scheme in evaluation of results and quantitative application in different species. Eval drug Act pharmacometrics. 1964;1:160–2.
14. Bearden HJ and Fluquary J. Applied Animal Reproduction. Appl Anim Reprod. 1980;158–60.
15. Barth AD and Oko RJ. Abnormal Morphology of Bovine Spermatozoa. In: Iowa State University Press Ames, Iowa, USA. 1994. p. 8–12.
16. Loftis AD, Reeves WK. Principles of real-time PCR. Vet PCR Diagnostics. 2012;15(March 2012):3–17.
17. Armitage, P. and Berry G. Statistical methods in Medical Research. Blackwell, Oxford, UK. 1987;93–213.

18. Calogero AE, Condorelli RA, Russo GI, Vignera S La. Conservative Nonhormonal Options for the Treatment of Male Infertility: Antibiotics, Anti-Inflammatory Drugs, and Antioxidants. Biomed Res Int. 2017;2017.
19. Demir A, Türker P, Önol FF, Sirvanci S, Findik A, Tarcan T. Effect of experimentally induced Escherichia coli epididymo-orchitis and ciprofloxacin treatment on rat spermatogenesis. 2007;(March 2006):268–72.
20. Khaki A, Sohrabi Haghdoust I, Ghaffari Novin M, Azarmi Y HM. Effect of ciprofloxacin in rat spermatogenesis. ISMJ. 2014;17(2):173–81.
21. Khaki A. Assessment on the adverse effects of aminoglycosides and flouroquinolone on sperm parameters and male reproductive tissue: A systematic review. Iran J Reprod Med. 2015;13(3):125–34.
22. Mahat RK, Kumar S, Arora M, Bhale D V., Mehta R, Jyoti Batra. Role of Oxidative Stress and Antioxidants in Male Infertility. Int J Heal Sci Res. 2015;5(3):324–33.
23. El-Sayed MG KM and ED. Ceftiofur Sodium Induced Changes In Sperm Characteristics, Reproductive Organs' Histopathology And Oxidative Stress In Adult Male Rats. WORLD J Pharm Pharm Sci. 2017;6(1):179–95.
24. Merino G. & Carranza-lira S. Infection and Male Infertility : Effect of Different Antibiotic Regimens on Semen Quality. Arch Androl. 2009;5016.
25. Saygin M, Caliskan S, Ozguner MF, Gumral N, Comlekci S, Karahan N. Impact of L-carnitine and selenium treatment on testicular apoptosis in rats exposed to 2.45 GHz microwave energy. West Indian Med J. 2015;64(2):55–61.
26. Festa R, Giacchi E, Raimondo S, Tiano L, Zuccarelli P, Silvestrini A, et al. Coenzyme Q<inf>10</inf> supplementation in infertile men with low-grade varicocele: An open, uncontrolled pilot study. Andrologia. 2014;46(7):805–7.
27. Manna PR, Stetson CL, Slominski AT, Pruitt K. Role of the steroidogenic acute regulatory protein in health and disease. Endocrine. 2016;51(1):7–21.
28. Abdollahzad H, Aghdashi MA, Asghari Jafarabadi M, Alipour B. Effects of Coenzyme Q10Supplementation on Inflammatory Cytokines (TNF-α, IL-6) and Oxidative Stress in Rheumatoid Arthritis Patients: A Randomized Controlled Trial. Arch Med Res [Internet]. 2015;46(7):527–33.
29. Horie S, Yamaki A, Takami S. Presence of Sex Steroid-Metabolizing Enzymes in the Olfactory Mucosa of Rats. Anat Rec. 2017;300(2):402–14.
30. Salman TM, Alagbonsi IA, Olayaki LA, Ayobami S, Salahdeen HM, Olowu OA. Biokemistri enhancing testosterone production . 2013;25(August):39–44.
31. Zobeiri F, Sadrkhanlou RA, Salami S, Mardani K. Long-term effect of ciprofloxacin on testicular tissue: Evidence for biochemical and histochemical changes. Int J Fertil Steril. 2013;6(4):294–303.
32. Tanis D OD and LD. The Effects of a Dietary Supplement, Free Test™, on Serum Free and Total Testosterone Levels in Weight-Trained Male Subjects. Appl Nutr. 2010;
33. Fouad AA, Al-Sultan AI, Yacoubi MT. Coenzyme Q10 counteracts testicular injury induced by sodium arsenite in rats. Eur J Pharmacol [Internet]. 2011;655(1):91–8.
34. Fan L, Feng Y, Chen GC, Qin LQ FC and CL. Effects of coenzyme Q10 supplementation on inflammatory markers: a systematic review and meta-analysis of randomized controlled trials. Pharmacol Res. 2017;119:128–36.
35. Li J, Wang Q, Luan H, Kang Z, Wang C. Effects of L-carnitine against oxidative stress in human hepatocytes : involvement of peroxisome proliferator-activated receptor alpha. 2012;1–9.
36. Zahedi A, Khaki A, Ahmadi-Ashtiani HR RH and RS. Zingiber officinale: Protective Effects on Gentamicin's Toxicity on Sperm in Rats. J Med Plants. 2010;3(35):93–8.

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