

Does coenzyme Q10 protect testicular function and spermatogenesis in rats receiving levofloxacin-containing therapy?

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Objective: Levofloxacin (LVFX), a fluoroquinolone antibiotic, is used in the treatment of urogenital tract diseases affecting the reproductive system. This study aimed to examine the protective effects of coenzyme Q10 (CoQ10) against LVFX-induced side effects using stereological methods.

Methods: Eighty rats were divided into eight groups: control (distilled water), CoQ10 (10 mg/kg/day), and low dose (25 mg/kg/day), medium dose (50 mg/kg/day), and high dose (100 mg/kg/day) of LVFX (low dose [LD]-LVFX, medium dose [MD]-LVFX, and high dose [HD]-LVFX) with or without CoQ10 administration. Treatments were performed daily for 4 weeks. Sperm parameters, serum testosterone levels, testicular oxidative stress markers, and testicular histology were evaluated.

Results: Sperm count, motility, normal morphology, and viability, as well as serum testosterone levels, were reduced, while malondialdehyde concentrations increased in MD-LVFX and HD-LVFX treated animals compared to controls. MD-LVFX and HD-LVFX treatments produced a 6% to 56% reduction in the volumes, lengths, and diameters of seminiferous tubules and their epithelium, whereas the interstitial tissue volume increased by 43% to 53% in these groups. The numbers of spermatogonia, spermatocytes, spermatids, Sertoli cells, and Leydig cells were reduced by 23% to 76% in animals treated with MD-LVFX and HD-LVFX compared to controls. Notably, all changes observed in the rats receiving CoQ10 were similar to those in the control group, and although most parameters decreased in animals that received LD-LVFX, the differences were not statistically significant relative to controls.

Conclusion: LVFX treatment for 28 days, regardless of dose, adversely affected sperm parameters and testicular tissue. CoQ10 exhibited a protective effect by mitigating the structural and functional impairments induced by LVFX.

Keywords: Coenzyme Q10; Levofloxacin; Rat; Spermatogenesis; Stereology

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Introduction

Infertility is a global health issue that affects both men and women of reproductive age. It remains one of the major challenges in modern medicine. Male infertility, which accounts for approximately half of all infertility cases, is a disorder of the reproductive system. Male infertility may result from endocrine disorders, infections, physical damage, exposure to toxic substances, medication side effects, or idiopathic causes [1]. Additional contributing factors include sleep deprivation, environmental pollution, elevated scrotal temperature, and increased levels of reactive oxygen species (ROS) [2]. These factors negatively impact sperm quality, and many cases of male infertility are linked to sperm disorders [1]. Certain therapeutic drugs may

et al. [12], Eid et al. [13], and Iftikhar et al. [10] further indicate that CoQ10 prevents testicular tissue alterations in rats exposed to methotrexate, cadmium chloride, cyclophosphamide, and bisphenol A. Based on our findings, CoQ10 prevented histological changes in the seminiferous tubules, interstitial tissue, and cell numbers in LVFX-treated rat testes, most likely due to its ability to mitigate oxidative stress.

These results are consistent with those reported by other researchers, who showed that CoQ10 could mitigate the unfavorable changes induced in rat testis tissue after exposure to free radicals by inhibiting oxidative stress [10–14].

The current study confirmed that treating rats with MD-LVFX (50 mg/kg/day) and HD-LVFX (100 mg/kg/day) for 4 weeks induced testicular toxicity. The reduction in sperm parameters appears to result from a decline in the germinal epithelium volume following LVFX exposure. The rat testis is composed primarily of seminiferous tubules separated by interstitial tissue containing blood vessels and Leydig cells. Damage to the seminiferous tubules leads to reductions in their length, diameter, and volume, while degeneration of the seminiferous epithelium reduces spermatogenic and Sertoli cell numbers—a finding consistent with reports by Ahmadi et al. [7] and Zaki et al. [6]. Sertoli cells support spermatogenic cells and facilitate spermatogenesis; thus, their reduction likely contributes to the decline in spermatogenic cell numbers. Furthermore, an increase in connective tissue may explain the observed reduction in Leydig cells, as LVFX has been shown to cause Leydig cell damage and interstitial edema [6,7]. Oxidative stress, evidenced by elevated MDA levels, may also contribute to these effects [10–14].

In conclusion, LVFX treatment disrupts testicular tissue and function in rats, whereas CoQ10 ameliorates LVFX-induced impairments in sperm parameters, serum testosterone, MDA levels, and testicular histology. Therefore, CoQ10 may be a suitable dietary supplement to prevent testicular disorders and reduce fertility problems associated with LVFX treatment in animals. Further preclinical and clinical studies in humans are needed to determine whether CoQ10 supplementation can protect testicular tissue in patients receiving LVFX.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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References

- Podgrajsek R, Hodzic A, Stimpfel M, Kunej T, Peterlin B. Insight into the complexity of male infertility: a multi-omics review. *Syst Biol Reprod Med* 2024;70:73–90.
- Abad Paskeh MD, Babaei N, Entezari M, Hashemi M, Doosti A. Protective effects of coenzyme Q10 along with Fe2O3 nanoparticles on sperm parameters in rats with scrotal hyperthermia: effects of CoQ 10 and Fe2O3 nanoparticles on sperm parameters. *Galen Med J* 2022;11:1–7.
- Ding J, Shang X, Zhang Z, Jing H, Shao J, Fei Q, et al. FDA-approved medications that impair human spermatogenesis. *Oncotarget* 2017;8:10714–25.
- El-Demerdash FM, Ahmed MM, Baghdadi HH. Punica granatum peel extract modulates levofloxacin-induced oxidative stress and testicular damage in rats. *Tissue Cell* 2023;85:102227.
- 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;6:294–303.
- Zaki NF, Orabi SH, Abdel-Bar HM, Elbaz HT, Korany RM, Ismail AK, et al. Zinc oxide resveratrol nanoparticles ameliorate testicular dysfunction due to levofloxacin-induced oxidative stress in rats. *Sci Rep* 2024;14:2752.
- Ahmadi R, Ahmadifar M, Safarpour E, Vahidi-Eyrisofla N, Darab M, Eini AM, et al. The effects of levofloxacin on testis tissue and spermatogenesis in rat. *Cell J* 2016;18:112–6.