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Effect of levofloxacin antibiotic on the body weight and some biochemical parameters in male rats

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Abstract
Levofloxacin (LFX) is one of the antibiotics that belongs to the family of fluoroquinolones and is used to treat several types of diseases caused by bacteria sensitive to these antibiotics, this drug belongs to the third generation of fluoroquinolones which have high activity against most gram- positive and gram-negative aerobic microorganisms**.** In the current study, we evaluated the possible effect of LFX on body weight of male rats. Rats (twenty) were randomly divided into 2 equal groups. Control group the rats were treated orally with distilled water, LFX group; the rats received LFX at a dose of 40ml kg-1 B.W orally day after day for 6 weeks by stomach tube. Intoxication of rats with LFX non significantly resulted in a decrease in the body weight in compared with the control group. Regarding to the liver function biomarkers of rats, LFX has no effect on serum total protein and albumin compared to the control group.

Keywords: Levofloxacin, Body Weight, Hepatic Biomarkers

1. Introduction

Levofloxacin (LFX), a fluoroquinolone antibiotic of the 3rd-generation, is commonly used in respiratory and urinary tract infections, prostatitis and orchitis. LFX has a strong antibacterial action alongside both Gram-positive and Gram-negative bacteria. When compared to other fluoroquinolones, LFX has a substantially higher efficacy in treating typhoid fever. It's commonly used to treat infections like pneumonia, sinusitis, and genitourinary infections. LFX's bactericidal activity is primarily achieved by its interaction with the enzyme DNA gyrase, which inhibits DNA replication and transcription, preventing bacteria from dividing. In general, LFX toxicity in the liver causes the generation of free radicals, the destruction of mitochondria, and lipid peroxidation of membranes or alterations in redox status of glutathione. Fluoroquinolones have been linked to allergic interstitial nephritis, acute tubular necrosis, acute renal failure, and crystalluria. The majority of these reactions are linked to the antibiotic's ciprofloxacin, norfloxacin, ofloxacin, and LFX (Ibrahim *et al*., 2021) [8]. Fluoroquinolones (FQs) are the quinolones with fluorine atom attached to the central ring system, typically at the C-6 position or C-7 position. These are bactericidal drugs that inhibit the bacterial enzymes DNA gyrase and topoisomerase IV and possess a broad spectrum of anti-bacterial activity against a range of bacteria, including the ones resistant to other anti-microbial drugs, despite the basic similarity in the core structure of these molecules, their physiochemical properties, pharmacokinetic characteristics, and anti- microbial activities vary markedly across compounds. Levofloxacin, the active L-isomer of the racemate ofloxacin, has nearly 100% oral bioavailability and is thus preferred over FQs that have broad spectrum of activities, but limited oral bioavailability. It is used alone or in combination with other antibacterial drugs to treat certain bacterial infections, including pneumonia, urinary tract infections, and abdominal infections (Khan and Rampal, 2013) [9], the scientific name of the drug is Levofloxacin, and the drug is also known by many brand names such as Levaquin, Tavanic, Felsin, Voflan and Levoxa, and its chemical formula is C18 H20 FN3O4. 1/2 H2O, molecular weight of it is about (370,38) (Hussein and Al-Essawi, 2021) [7].

Levofloxacin is rapidly absorbed from the gastrointestinal tract after administration and drug concentrations reach their maximum in plasma after 1-2 hours in stable conditions when taking a single dose orally, this drug penetrates well into most body fluids and tissues such as bone and lung tissue and its binding rate with plasma proteins in the blood is about 30-40%. Levofloxacin is excreted mainly from the body by the urinary system through removal by glomerular filtration in the kidneys (Hussein and Al-Essawi, 2021) [7].

overusing antibiotics causes damage to hepatic cells, leading to the destruction of liver tissue. The most widespread effect of overusing antibiotics is to cause antibiotic sensitivity such as skin rash, itching, kidney failure and serious damage to liver. The

activity range of levofloxacin involves a large number of bacterial pathogen species and respiratory system, urinary-reproductive tract, digestive tract and abdominal infections as well as helping to wash away gram-negative bacteria (Eyrisofla *et al*., 2015) [12].

The present study was designed to evaluate the effect of levofloxacin on the body weight of male rats.

2. Materials and methods

Levofloxacin: was purchased from Arabco med company LFG. No (17080173), Diagnostic kits for total protein level (CAT. No: 2020) and albumin level (CAT. No1010) were purchased from Egyptian Company for Biotechnology (Spectrum Diagnostics, Al Obour, Cairo).

2.1 Animals

Twenty of Wistar male rats, age 6 weeks and weighting (110–120 g), were purchased from Experimental Animals Production Center (Giza, Egypt).

The animals were housed in cages with temperature regulated at 23 ± 2

°C, dark periods of 12-h light/12-h and, 55 ± 5% relative humidity and had free access to a standard Commercial diet of pellets and provided with water adlibitum. The rats have been acclimatized to laboratory conditions for one week before the beginning of the experiment. and had free access to a standard Commercial diet of pellets. The study was ethically approved by the International Animal Care and Use Committee (IACUC)(VUSC-016-1-20), Faculty of Veterinary Medicine, University of Sadat City.

2.2 Experimental design and animal grouping

Animals were allocated into2 groups, 10 Rats) as follows:

Control group, rats received distilled water orally, day by day for 6 weeks.

LFX-treated group, rats received levofloxacin dissolved in distilled water at a dose of 40 mg/kg BW orally by gastric tube day by day for 6 weeks (Afalobi and Oyewo, 2014) [2].

2.3 Sample Collection

Blood samples were collected after the 6th week from the beginning of the experiment. Animal were anaesthetized by diethyl ether. The blood samples were withdrawn from orbital sinus. Then, samples were left at room temperature to clot and centrifuged at 3000 rpm for 15 min. The clear supernatant serum was collected and kept at − 20 °C until used for assaying the biochemical parameters.

2.4 Determination of serum total protein

Serum total protein measured according to (Gornal *et al*., 1949) [6] by colorimetric method.

Calculation:

Protein concentration(g/dl) =A sample / A standard X 5

2.5 Determination of serum albumin

Serum albumin measured according to (Doumas B.T *et al*., 1971) [5].

Calculation:

Serum albumin(g/dl) =A sample /A standard X 4

2.6 Statistical analysis

Values are presented as mean ± standard error (SE). Statistical significance of data was determined by one-way ANOVA (Analysis of Variance) followed by Duncan's Multiple range test for post hoc analysis. All statistical analyses were performed using SPSS (Statistical Package for Social Sciences) Version 16 released on 2007.

3. Results

3.1 Evaluation of body weights

A non-significant difference in the body weight gain at the end of the experimental period was observed in treated groups when compared with the control group, Table 1 showed LFX intoxication non significantly decrease the body weight gain all over the experimental period compared with the control rats.

LFX group show no significant changes in the serum albumin and total protein compared to the control group showed in table (2)

Table 1: Effect of levofloxacin on body weight compared to control group

Weeks	Control group	Levofloxacin treated group
Week 1	192± 1.1[a]	190.6 ± 1.63[a]
Week 2	211.8 ± 0.9[a]	209 ± 8.1[a]
Week 3	232± 3.6[a]	236.8± 7.6[a]
Week 4	254.3± 9.5[a]	257.8 ± 7.7[a]
Week 5	263 ± 8.01[a]	263.6 ± 8.09[a]
Week6	285± 9.2[a]	278.9± 9.4[a]

Table 2: Effect of levofloxacin on serum albumin and total protein

Test/group	control	Levofloxacin treated group
Albumin	3.28±0.05[a]	3.35±0.03[a]
Total protein	7.05±0.02[a]	7.50±0.3[a]

4. Discussion

Although fluoroquinolone antibiotics are being extensively used to treat serious and life-threatening infections but most of them are known to be consolidated with inimical effects (Ara *et al*., 2020) [3]. Body weight of animal is one of the pragmatic parameters towards antibiotics induced toxicity. Current study exhibited detrimental effects of levofloxacin on weight of rats, as the body weights declined significantly after exposure to different concentrations of levofloxacin (LFX). These findings are un like the observations of (Ray, 2012) [11] who reported that the relative body weights of antibiotic exposed mice were increased. According to literature, it has been reported that fluoroquinolone antibiotics generate reactive oxygen species that ultimately result in oxidative stress and cellular damage to liver and kidney.

The present study was a Trial to evaluate the toxicity of LFX on body weight and hepatic biomarkers in male rats

The body weight of treated LFX rats in the present study was non significantly lower than that of the control group. Levofloxacin is amember of quinolones which act as an anti-bacterial agent with broad spectrum activity (Abd-Allah, *et al*., 2000) [1] quinolones are named flur-quinolones,4 quinolones or quinolone carboxylic acids. they contain ofloxacin, ciprofloxacin, perfloxacin, norfloxacin, enoxacin, difloxacin, fleroxacin, temofloxacin, levofloxacin and other compounds (Aral *et al*., 2008) [4].

Levofloxacin is one of the antibiotics which is used widely in treatment of genitourinary and lower respiratory tract

infections (Eyrisofla *et al*., 2015) [12] as in case of pneumonia, chronic bronchitis and sinusitis. LFX act on both Gram-Psitive and Gram–negative bacteria. It is the drug of choice for treatment of typhoid fever. LFX is achiral fluorinated Carboxyquinolone with fluorine at position 9, and pure (-)-S-enantiomer of the racemic drug substance of Ofloxacin (Olayinka *et al*., 2014) that lead to lowering its phototoxic potential.

The mode of action of Levofloxacin: it targets bacterial topoisomerase IV and DNA gyrase in Gram – Positive and Gram-negative bacteria respectively (Olayinka *et al*., 2014).

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