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Research Article

The effect of ciprofloxacin on the lipids and some liver enzymes in albino mice

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Abstract

The current work aimed to study the effects of Ciprofloxacin (80mg/kg body weight) on levels of lipids (Cholesterol, Triglycerides, HDL, VLDL, and LDL) and liver enzymes (GOT, GPT, and Alkaline phosphatase) in albino mice for 3, 7 and 14 days using ΔpH/30 min method. The study was conducted by dividing the albino mice into four equal groups. G-I: control group, G-II: animals were treated with ciprofloxacin as one /day orally for 3 days, G-III: animals were treated with ciprofloxacin as one per/day orally for 7 days, and G-IV: animals were treated with ciprofloxacin one per/day orally for 14 days. The results showed that ciprofloxacin therapy raised the blood total cholesterol considerably and serum HDL, LDL, GOT, GPT, and Alkaline phosphatase significantly. There was a substantial decrease in triglyceride levels in the blood.

Keywords: Parasitic contamination, Vegetable, Worm, Protozoan.

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Introduction

The liver acts as a center for the metabolism of nutrients and secretion of waste metabolites. It also has a critical biochemical role in metabolism and digestion (Widmaier et al. 2006). Liver enzymes are proteins, including the bile and compounds that aid in clotting the blood, digesting food and toxins, and the fight against infection. Alkaline phosphatase (ALP), Alanine transaminase (ALT), Aspartate transaminase (AST), and Gamma-glutamyl transferase are some of the most common liver enzymes (GGT). The ability of liver enzymes to perform metabolic processes such as detoxification and conjugation is measured by monitoring the concentration of chemicals generated by hepatocytes or the serum content released from these cells (Rosenthal 1997). Liver function tests are used for detecting liver disease and following up its progression (Dufour et al. 2000). The most frequent laboratory tests for detecting liver illnesses are serum AST and ALT as excellent markers of hepatocellular injury (Hyeon et al. 2004).

Ciprofloxacin is a fluoroquinolone antibiotic with a wide range of applications. It is used to treat various bacterial illnesses and has a high oral bioavailability (Bertino & Fish 2000). It also has antibacterial action against Gram-positive and Gram-negative bacteria and is used to treat persons who have been exposed to anthrax or plague. Ciprofloxacin extended-release tablets should only be used by adults. The severe disadvantageous effect of its use is liver injury (Chalasani et al. 2000; Zimmerman 2000). The most frequent sign of liver damage caused by ciprofloxacin is an asymptomatic increase in liver

enzymes. It can also manifest as acute hepatitis in rare cases. It is taken orally as it is easily absorbed and penetrates well into tissues. Its antibacterial effect is mainly caused by inhibiting DNA gyrase, which is equivalent to mammalian topoisomerase II (Liu & Wong 1999). Several biochemical, clinical and epidemiologic studies reports indicated that ciprofloxacin treatments might cause serious liver failure. In addition, there has been particular concern about convulsions created after exposure to ciprofloxacin (Chalasani et al. 2000). Although these side effects are uncommon, the high prescription rates for these antibiotics may have significant health consequences for the general public. This work aims to study the effects of Ciprofloxacin on levels of lipids (Cholesterol, Triglycerides, HDL, VLDL, LDL) and liver enzymes (GOT, GPT, Alkaline phosphatase) in albino mice.

Materials and Methods

A total of 150 adult albino mice, female and male, were acquired from Iraq's Ministry of Health's National Center for drug control and research, in the age of 8-12 weeks and weighing 22-28g. They were kept in a plastic box with hardwood chips for bedding in a controlled animal home at 25°C with a 14/10-hour light/dark cycle at Nahrain University's Biotechnology Research Center.

Ciprofloxacin (Cipro) ($C_{17}H_{18}FN_3O_3 \cdot HCl \cdot H_2O$) (as ciprofloxacin hydrochloride tablets, Bayer healthcare pharmaceuticals) were given orally three times a day for three, seven, and fourteen days. According to the Guidance for industry and reviewers (2002), the indicated dosages are comparable to the human therapeutic quantity (Food and Drug Administration 2005).

Experimental design: The trials were aimed to study ciprofloxacin effects on lipid levels (cholesterol, triglycerides, HDL, VLDL, and LDL) and liver enzymes (GOT, GPT, and alkaline phosphatase) in albino mice and therefore, the treatments were considered as Group I: the animals did not treat with drug (control), Group II: animals were treated with ciprofloxacin as 80mg/100g body weight (Dosage one per/day Orally) for 3 days, Group III: animals were treated with ciprofloxacin as 80mg/100g body weight (Dosage one per/day Orally) for 7 days, and Group IV: animals were treated with ciprofloxacin as 80mg/100g body weight (Dosage one per/day Orally) for 14 days.

Serum profile assay: One ml of blood was obtained from each animal through heart puncture using disposable tiny (insulin) syringes (1ml) placed in Eppendorf tube and permitted to clot at room temperature for around 10min, then centrifuged at 4000rpm for 10min to extract serum for further use.

Cholesterol was measured using a commercially available kit (2-1-3) following enzymatic hydrolysis and oxidation, and the absorbance was set at 500nm. In the presence of phenol and peroxidase, the indicator quinonimine is produced from hydrogen peroxide and 4-Amino Phenazone (Schettler & Nussel 1975) if the indicator is converted. For measurement of serum triglyceride, after enzymatic hydrolysis with lipase, triglycerides were assigned. Under the catalytic action of Peroxidase, the indicator was quinonimine, which was made from hydrogen peroxide, 4-Amino-Antipyrine, and 4-Chlorophenol (Schettler & Nussel 1975). The total serum concentration of Triglycerides was determined at 500nm with a commercially available kit (2-1-3). For measurement of Serum high-density lipoprotein-cholesterol, phospho-tungstic acid, and magnesium chloride are used to deposit Chylomicrons, VLDL (very low-density lipoproteins), and LDL (low-density lipoproteins). The HDL (high-density lipoproteins) portion of the supernatant liquid is tested for HDL-Cholesterol using a cholesterol liquid-color test kit after centrifugation (Gordon et al. 1977). The total cholesterol (TC), high-density lipoprotein (HDL), and triglyceride concentrations were used to compute the LDL cholesterol concentration (TG) according to Friedwald equation (Friedewald et al. 1972) and calculated aa:

$$LDL\ (mg/dl) = TC - HDL - (TG / 5)$$

ALT was determined using a colorimetric method

Table 1. Effect of ciprofloxacin on cholesterol, triglyceride, HDL, VLDL and LDL.

Parameter	Control (Mean±SE)	Ciprofloxcin		
		3 day (Mean±SE)	7 day (Mean±SE)	14 day (Mean±SE)
Cholesterol (g/dL)	173.3±1.76	177.3±1.2	179.3±1.2	181±2.08*
Triglyceride (g/dL)	99.3±0.66	96.3±0.66	96±1.15	94.3±0.66*
HDL (g/dL)	40.6±0.66	49±1**	51.3±0.88**	54.3±0.88**
VLDL (g/dL)	20.6±0.33	21±1.52	21.6±1.45	25.6±1.45
LDL (g/dL)	113.3±0.88	122.3±0.88**	125.3±1.45**	131.6±1.45**

Significant * ($P \leq 0.05$) and ** ($P \leq 0.01$) differences between sample with control.

Table 2. Effect of ciprofloxacin on Got, GPT and alkaline phosphatase.

Parameter	Control (Mean±SE)	Ciprofloxcin		
		3 day (Mean±SE)	7 day (Mean±SE)	14 day (Mean±SE)
GOT Ph/30 min	13.5±0.2887	18.6667±0.8819 **	21.6667±0.3333 **	23.6667±0.8819 **
GPT- Ph/30 min	12.2±0.1155	15.6667±0.8819	15.6667±1.2019	19.6667±1.2019 **
Alkaline phosphatase-Ph/30 min	12±0.3464	15±0.7506	16±0.5774 *	16.3333±0.8819 **

Significant * ($P \leq 0.05$) and ** ($P \leq 0.01$) differences between sample with control.

according to of Reitman & Frankel (1957) using a commercial assay kit (2-1-3). The concentration of pyruvate hydrazone produced with 2,4 dinitrophenyl hydrazine was used to determine ALT/GPT. AST was determined using a colorimetric method according to the method of Reitman & Frankel (1957) using a commercial assay kit (2-1-3). The concentration of Oxaloacetate Hydrazone produced with 2,4 Dinitrophenyl Hydrazine was used to compute AST/GOT. Calculation of /GOT (units /ml) of serum was done using the Standard Curve. The colorimetric method by Belfield & Goldberg, (1971) was used to determine serum alkaline phosphatase (ALP) (Belfield & Goldberg 1971).

Statistical analysis: Data were analyzed using the statistical software IBM (SPSS version 18). The parameters were given in terms of Mean±standard error, and differences between means of all parameters were carried out using analysis of variance (ANOVA). Differences were considered statistically significant at $P<0.05$.

Results

A significant ($P \leq 0.05$) increase was found in the cholesterol of the treated animals with Ciprofloxacin, as 181 at 14 days, while in triglyceride was decreased significantly at 14 days, as 94.3 than control one (Cholesterol 173.3; Triglyceride 99.3) (Table 1). In treatment with Ciprofloxacin for 3, 7, and 14 days, the level of HDL were significantly ($P \leq 0.01$) increased (as 49, 51.3, and 54.3, respectively) and the LDL as 122.3, 125.3, and 131.6, respectively in comparison to control group (HDL 40.6and LDL 113.3) (Table 1).

In the treated animals with ciprofloxacin, a significant difference was observed in the Got between 3, 7 and 14 days (18.6, 21.6, and 23.6, respectively) compared with control (13.5), and for GPT (19.6) and Alkaline phosphatase enzymes (16.3), significant differences were found in the treated animal for 14 days compared to control one (Got = 13.2 and GPT = 12). (Table 2).

Discussion

Ciprofloxacin is used to treat many bacterial infections. The results of the present study were in agreement with the findings of (AL-Rikaby et al. 2016) indicating that Ciprofloxacin has potential hepatotoxicity as evidenced by increased enzymes activities of GOT, GPT, and ALP and cholesterol by using 100mg/kg B.W in male rabbits. Additionally, Aqeel & Atallah (2021) reported that ciprofloxacin has shown the ability to change the level of Cholinesterase enzyme in the liver.

Ciprofloxacin is an important anti-microbial because it affects a wide variety of organisms (Dana et al.

2001). Adikwu & Brambaifam (2012) was found that ciprofloxacin has the potential toxicity effects to induce hepatotoxicity. The result of the present work was similar to that of Bergan et al. (1987). The effect of the antibiotics, especially ciprofloxacin, is the main cause of many liver diseases, and the symptoms after use in different treatments to elevated hepatic enzymes with abdominal pain indicate liver disease, as the possible diagnosis of hepatotoxicity caused by ciprofloxacin (Qutrio et al. 2017). In conclusion, the administration of ciprofloxacin increases lipid profile in the blood having harmful effects on health. In addition, the effects of ciprofloxacin were more effective on liver enzymes. Further descriptive studies are suggested to understand of the toxic effect of ciprofloxacin on other organs.

References

Adikwu, E. & Brambaifam, N. 2012. Ciprofloxacin cardio- toxicity and hepatoxicity in human and animals. Pharmacology 3: 207-213.

AL-Rikaby, A.A.; Ghadhban, R.F. & Majeed, S.K. 2016. The effects of ciprofloxacin on male rabbits: Biochemical and histopathological study. Al-Qadisiyah Journal of Veterinary Medicine Sciences 15(1): 38-44.

Aqeel, H. & Atallah, A. 2021. Study the Effect of Ciprofloxacin on Cholinesterase in Different Organs of Mice. Iraqi Journal of Science 56(2A): 21456

Belfield D.M. 1971. Goldberg, colorimetric determination of alkaline phosphatase activity. Enzyme 12(5): 561-568.

Bergan, T.; Thorsteinsson, S.B.; Solberg, R.; Bjornskau, L.; Kolstad, I.M. & Johnson S. 1987. Pharmacokinetics of ciprofloxacin: intravenous and increasing oral doses. American Journal of Medicine 82: 97-102.

Bertino Jr, J. & Fish, D. 2000. The safety profile of the fluoroquinolones. Clinical therapeutics 22(7): 798-817.

Chalasani, N.; Fontana, R.J.; Bonkovsky, H.L.; Watkins, P.B.; Davern, T. & Serrano, J. 2000. Drug induced liver injury network (DILIN) causes, clinical features, and outcomes from a prospective study of drug-induced liver injury in the United States. Gastroenterology 135(6): 1924-1934.

Dana, E.K.; Robb, M. & Sandra, H.L. 2001. New classification and update on the quinolone antibiotics. Amer. Fam. Physic.

Dufour, R.; Lott, J.; Nolte, F.; Greth, D.; Koff, R. & Seef, L. 2000. Dignosis and monitoring of hepatic injury performance characteristic of laboratory test. Clinical Chemistry 46: 2027-2068.

Food and Drug Administration. 2005. Estimating the safe starting dose in clinical trials for therapeutics in adult healthy volunteers. Rockville, Maryland, USA: US: Food and Drug Administration.

Friedewald, W.T.; Levy, R.T. & Frederickson, D.S. 1972. Estimation of the concentration of low-density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge Clinical Chemistry 18: 499-502.

Gordon, T.; Castelli, W.P.; Hjortland, M.C.; Kannel, W.B. & Dawber, T.R. 1977. High density lipoprotein as a protective factor against coronary heart disease: the Framingham Study. The American Journal of Medicine 62(5): 707-714.

Hyeon, C.K.; Chung, M.N.; Sun, H.J.; Kwang, H.H.; Oh, D.K. & Suh, I. 2004. Normal serum aminotransferase concentration and risk of mortality from liver diseases: prospective cohort study. BMJ 328(7446): 983.

Liu, Q. & Wong, J.C. 1999. Similarity in the catalysis of DNA breakage and rejoining by type IA and IIA DNA topoisomerase. Proceedings of the National Academy of Sciences 96: 881-886.

Qutrio Baloch, Z.; Raza, M.A. & Abbas, S.A. 2017. Ciprofloxacin-induced Hepatotoxicity in a Healthy Young Adult. Cureus 9: e1016.

Reitman, S. & Frankel, S. 1957. A Colorimetric Method for the Determination of Serum Glutamic Oxalacetic and Glutamic Pyruvic Transaminases. American Journal of Clinical Pathology 28: 56-63.

Rosenthal, P. 1997. Assessing liver function and Hyperbilirubinemia in the newborn. Clinical Chemistry 43(1): 228-234.

Schettler, G. & Nussel, E. 1975. Determination of serum total cholesterol by enzymatic Colorimetric test. Arbeitsmedizin, Sozialmedizin, Präventivmedizin Sonderheft 10: 25.

Widmaier, E.P.; Raff, H. & Strang, K.T. 2006. *Vander's Human Physiology, the Mechanisms of Body Function.* 10th ed., McGraw-Hill, pp. 575-583.

Zimmerman, H.J. 2000. Drug-induced liver disease. Clinics in Liver Disease 4.1(2000): 73-96.