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# A Study of the Effect of Combination of Coenzyme Q-10 and Dehydroepiandrosterone on Some Biochemical and Reproductive Parameters on $CCl_4$ Induced Toxicity in Albino Male Rats, and its Effect on Embryotoxic and Teratogenic of Norfloxacin in Pregnant Female Albino Rats

**Abstract:**

The present study was conducted at College of Veterinary Medicine/ University of Basrah to investigate the effect of CoQ10, DHEA and their combination on some biochemical aspects such as total serum cholesterol (TCh), triglycerides (TGs), high density lipoprotein (HDL), low density lipoprotein (LDL), very low density lipoprotein (VLDL), liver enzymes function such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), malondialdehyde (MDA), kidney function tests such as blood urea (BUr), blood urea nitrogen (BUN), and creatinine (Cr) were also evaluated. The antioxidant enzymes activity like glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase (CAT) were performed. Sperm viability such as sperm concentration, individual sperm motility, live sperm, and abnormal sperm morphology were measured. Fertility and reproductive efficiency which includes reproductive hormones such as FSH, LH, and testosterone, number of pregnant female, fertility percentage (%), number of litters, weight of litters, and sex ratio (%) were calculated. Body and internal organs weight such as liver, kidney and testes were also calculated. The histopathological changes to the liver, kidney and testes in normal and treated male rats, and the effect of CoQ10, DHEA and their combination were observed. Furthermore, CoQ10, DHEA and their combination as antioxidant agents and to improved reproductive efficiency parameters on CCl4 induced toxicity in male rats were studied. In addition, study its ameliorating effect as anti-fetotoxic and anti-teratogenic agents in pregnant female rats and their fetuses treated orally with norfloxacin.

The experiment was divided into three parts.

The first part was conducted to study the effect of CoQ10, DHEA and their combination as a powerful antioxidant substance. Thirty male rats were divided into five equal groups, each group consisted of 6 adult male rats as in the following: Control group (G1): 6 male rats received orally DMSO 0.5 ml/ animal/day. First treated group (T1): 6 male rats received 1ml/kg CCl4 IP (olive oil 1:1v/v). Second treated group (T2): 6 male rats received CCl4 1ml/kg and after 1hour later injected daily with CoQ10 200 mg/kg IP. Third treated group (T3): 6 male rats received CCl4 1ml/kg and after 1hour later injected daily with DHEA 25 mg/kg IP. Fourth treated group (T4): 6 male rats received CCl4 1ml/kg and after 1hour later injected daily with combination of CoQ10 200 mg/kg + DHEA 25 mg/kg IP. The experiment lasted for 28 successive day and biochemical parameters which include the measurement of [TCH, TGs, HDL-C, LDL-C,VLDL-C, ALT, AST, ALP, BUr, BUN, Cr, FSH, LH, T, GPx, SOD, CAT, and MDA]. The body and internal organs weights such as liver, kidney and testes were measured. The histopathological changes to the liver, kidney and testes in normal and CCl4 treated male rats were also done.

The second part was conducted to study the effect and ability of CoQ10, DHEA and their combination to improve fertility and reproductive efficiency in CCl4 treated male rats. Thirty male and female rats (10 male vs. 20 female) which were randomly divided into five equal groups, each group consisted of 6 rats (2 male vs. 4 female) as in the following: Control group (G1): 2 normal male mated with 4 normal female rats received orally DMSO 0.5ml/animal/day. First treated group (T1): 2 treated male received CCl4 1ml/kg IP mated with 4 normal female rats. Second treated group (T2): 2 treated male received CCl4 1ml/kg IP and after 1hour later injected daily with CoQ10 200 mg/kg mated with 4 normal female rats. Third treated group (T3): 2 treated male received CCl4 1ml/kg IP and after 1hour later injected daily with DHEA 25 mg/kg mated with 4 normal female rats. Fourth treated group (T4): 2 treated male received CCl4 1ml/kg IP and after 1hour later injected daily with combination of CoQ10 200 mg/kg + DHEA 25 mg/kg mated with 4 normal female rats. The male and female were allowed to mate, and then

separated after 16 days to let females deliver freely. The seminal parameters were reported for all male rats which include measurement of sperm concentration, individual sperm motility, live sperm, and abnormal sperm morphology. The reproductive efficiency for female rats were expected after delivery such as: number of pregnant female, fertility percentage (%), number of litters, weight of litters, and sex ratio (%) were also calculated.

The third part was conducted to study the effect and activity of CoQ10, DHEA and their combination as anti-fetotoxic and anti-teratogenic substances for prevented and repaired the embryotoxicity and teratogenicity induced by norfloxacin in pregnant female rats and their fetuses. Thirty male and female rats (10 male vs. 20 female) were randomly divided into five equal groups, each group consisted of 6 rats (2 male vs. 4 female). After detection the first day of gestation for all females, 20 pregnant dams had been divided randomly and equally into 5 groups, 4 pregnant female in each group as in the following: Control group (G1): 4 normal pregnant female received orally DMSO 0.5 ml/ animal/day from 5th - 19th day of gestation. First treated group (T1): 4 normal pregnant female received orally 400 mg/kg norfloxacin once daily from 5th - 19th day of gestation. Second treated group (T2): 4 normal pregnant female received orally norfloxacin 400 mg/kg once daily from 5th - 19th day of gestation and after 1hour later injected daily with CoQ10 200 mg/kg IP. Third treated group (T3): 4 normal pregnant female received orally norfloxacin 400 mg/kg once daily from 5th - 19th day of gestation and after 1hour later injected daily with DHEA 25 mg/kg IP. Fourth treated group (T4): 4 normal pregnant female received orally 400 mg/kg norfloxacin once daily from 5th - 19th day of gestation and after 1hour later injected daily with combination of CoQ10 200 mg/kg + DHEA 25 mg/kg IP. The dams were sacrificed at 20th day of gestation and their fetuses were removed from uterus and subjected to morphological and morphometric examination represented by fetal mortality rate (resorped or still birth fetuses) and growth retardation rate (fetal body weight, fetal body length and fetal tail length), fetal external signs, living fetuses, maternal weight changes and placental weight were recorded. In addition to, skeletal examination were estimated by using double special staining technique (Alizarin red

stain) for bone and (Alcian blue stain) for cartilage and whole mount transparency technique.

The results of this study pointed out that male rats treated with CCl4 caused significant increased (P≤ 0.05) in TCH, TGs, LDL, VLDL, ALT, AST, ALP, MDA, CAT, BUr, BUN, Cr, liver and kidney weight, abnormal sperm morphology, significant decreased (P≤ 0.05) in HDL, GPx, SOD, FSH, LH and testosterone, testes weight, and sharp significant decreased (P≤0.05) in sperm concentration, individual sperm motility, live sperm, number of pregnant females, fertility percentage (%), number of litters, weight of litters, and sex ratio (%). The results also indicated that CoQ10, DHEA and their combination shows ameliorating effect, and it was able to improved all parameters above and almost return to its normal values compared to control.

The histopathological examination revealed that male rats which were treated with CCl4 caused various injurious effect in tissues of liver, kidney and testes such as dilation and congestion of central vein, clear fatty degeneration, and infiltration of inflammatory cells in the liver. Whereas the renal changes involved complete loss of glomerulus, aggregation of mesangial cells, and infiltration of inflammatory cells. In the testes, complete loss of spermatogenesis stages, congestion of blood vessels with inflammatory cells in lumen of seminiferous tubules. When CoQ10, DHEA and combination of CoQ10 and DHEA was administered, it really ameliorated the histological consistency of the liver, kidney and testes toward its normal, where it's clearly reduce injury induced by CCl4 intoxication. Results also showed that the combination of CoQ10 and DHEA caused a highly significant increased (P≤0.05) in all parameters compared to control and other treated groups. Furthermore, study also indicated that CoQ10, DHEA and their combination acting as anti-fetotoxic and anti-teratogenic substances throughout prevented and treated fetal morphological and skeletal abnormalities compared to the fetuses obtained from pregnant dams received norfloxacin.

It was concluded from the current study that CCl4 has very deleterious effects on various body systems and it was a major cause of hyperlipidemia, hepatic and renal damage, reproductive insufficiency and male infertility. As well as, norfloxacin also

caused embryotoxicity and teratogenicity in fetuses obtained from pregnant female rats. On the contrary, CoQ10, DHEA and their combination was originated to be as a potent antioxidant which prevents or protective all the deleterious effects induced by CCl4 and NFX administration to the male and pregnant female rats.