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ROLE OF VITAMIN C AND E AGAINST CADMIUM TOXICITY IN FEMALE WISTAR ALBINO RATS OVARIES, LIVER AND KIDNEY

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Abstract:

Cadmium is a heavy metal present almost everywhere in the environment and it causes toxicity to different organs of body in female wistar albino rats. Cadmium exposure causes adverse effect to different target organs like kidney, liver and ovaries. The purpose of present study is to evaluate effect of vitamin C and E against cadmium toxicity in female wistar rats. Rats are divided in four groups and we provide different does of cadmium (3/5/7mg/lit) with vitamin C and vitamin E (100mg/kg b.w.). Vitamin C and E shows recovery effect against cadmium toxicity in different organs. The tissue and blood sample were taken from rats for histological analysis after 14 days. Hematological analysis, serum biochemical analysis histopathology of kidney, liver and ovarian tissue of different group of female treated with 3/5/7 mg/lit and (100 mg/kg) show recovery effect of ovary, liver and kidney. The result obtained from present study show protective effect against cadmium toxicity. Vitamin C and E has beneficial effect in the amelioration of cadmium toxicity in female wistar rats.

Keywords: *Cadmium, vitamin C, Vitamin E, protective effect, wistar rats, ovary, liver, kidney, heavy metal.*

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INTRODUCTION:

Cadmium is a toxic metal present in the environment by many human activities. This metal also works as an environment as well as an industrial pollutant (Layachi N et al, 2012). In water enter through industrial wastes and in soil from sewage sludge leaching. Population affected by cadmium through consumption of food, water, and incidental ingestion of soil contaminated by Cd. Also present in non-ferrous metal smelter and recycling of electronic waste. Forest fire, erosion, and abrasion of rock and soil, volcanic activity is also the reason for increasing Cd concentration in air, soil, and water. Some metals like Zn, Cu, and Pb also contribute to releasing the metal into the environment. The absorption of cd mainly takes place via the respiratory tract and in a small amount through the gastrointestinal tract. Skin absorption of Cd is very rarely. In the body, Cd enters into the blood through erythrocytes and albumin. After entering into the blood it binds to albumin and accumulates into kidneys, gut, and liver (Andjelkovic M. et al 2019). Excretion of Cd from the body is through saliva, milk during lactation, urine, and kidney slowly. Cd causes a variety of adverse effects such as osteomalacia, testicular damage, ovarian damage, pulmonary edema, renal and hepatic dysfunction and damage to adrenals and hemopoietic system, neurological impairment, pancreatic activity changes, coronary heart disease, stroke, peripheral artery disease. Through lipid peroxidation, chronic Cd causes oxidative stress and atherogenic changes in lipid profile. Also affects various structures of the metabolic process such as nucleic acid, carbohydrates, energy metabolism, and enzyme system, and protein synthesis. Rather than the cytotoxic effect it could lead to the necrotic or apoptotic event and is a proven carcinogen (group 1international agency for research on cancer classification).

Cadmium affects cell proliferation and differentiation. Cadmium modifies gene expression and signal transduction, reduces activities of proteins involved in antioxidant defences, generates ROS and interferes with DNA repair mechanism and the induction of apoptotic cell death. Cadmium binds to the mitochondria and is reported to inhibit cellular respiration and oxidative phosphorylation at low concentration (Patrick, 2003). Cadmium can affect apoptosis by modulating the cellular level of Ca^{2+} and caspases and nitrogen-activated protein kinases (MRPKs) activities in the cells. Cadmium is responsible for chromosomal aberrations, sister chromatid exchange, DNA strand breaks and DNA-protein crosslinks in cell lines. It is potent cause of mutations and chromosomal deletions (Joseph, 2009). It interferes with DNA repair. Its toxicity involves depletion of reduced glutathione (GSH), binds sulfhydryl groups with protein, and causes to enhance production of reactive oxygen species (ROS) such as superoxide ion, hydrogen peroxide, and hydroxyl radicals and result in oxidative stress. It reduces activities of proteins involved in antioxidant defencesas catalase, manganese-superoxide dismutase, and copper/zinc-dismutase (Filipic, 2013). Cadmium modulates also gene expression and signal transduction. The cells that contain metallothionein are resistant to cadmium toxicity. On the other hand, the cells that cannot synthesize metallothionein are sensitive to cadmium intoxication (Han et al, 2015).

Vitamin C and E are known to have antioxidant properties, they increase inorganic ion absorption, have essential role in metabolism of hormones. This means they can suppress harmful molecules, known as free radicals, which are produced within cells and which may cause tissue damage or disease.

Vitamin C is an essential co-factor for many enzymes involved in diverse metabolic pathways. In the present study co-administration of vitamin C significantly ameliorated Cd toxicity in rat tissues which were monitored through activity levels of antioxidant enzymes in tissues and in serum. Previous reports suggest that vitamin C significantly protected against Cd toxicity, i.e., activity levels of ALT, AST, SOD, CAT, SGOT, and SGPT were significantly altered in Cd-induced toxicity in rats and rabbits.

Vitamin E is soluble in oil and has high potency for antioxidants. Alpha- tocopherol is one of the isoforms of Vitamin E and it functions by protecting the cell against lipid peroxidation and cell membrane from degenerative effects of free radicals. Studies have shown that Vitamin E is protective against Cd toxicity and reduces oxidative damage. (Nakano et al, 2008).

Because of its potentially harmful effects on human and animal health, Cd is of special interest to researchers and ecologists. The studies on the ameliorating effect of Vitamin C and E on cadmium toxicity are limited and has not been fully elucidated yet. Therefore, this study was designed to elucidate the effect of Vitamin C and E on Cadmium's toxicity in ovaries of female wistar albinorats.

MATERIAL AND METHODS:

1. Experimental animals

For the purpose of study65 albino rats (7- 8 weeks old) of wistar strain were procured from the animal house of Delhi University, India. Healthy adult female albino rats of 100- 180 grams were selected for the study. The rodents were given the balanced mice diet consisting of carbohydrates (69%), proteins (16%), fats (7%), fibre (6%), mineral salt mixture

(2%). The water was given ad libitum. Rodents were maintained in the standard sized polypropylene cages in well-ventilated room. The laboratory conditions were as follows: temperature 23 ± 20°C; relative humidity 50 ± 10%, Light: Dark cycle 12:12.Before separating the animals into experimental groups, they were acclimatized in the laboratory for about a week. The present experiments were conducted under the supervision of lAEC (Institutional Animal Ethics Committee) of the College. The study was carried out in compliance with the international guidelines for the use and care of laboratory animals in research (Sudarshana et.al 2022).

2. Experiment design

In order to study the effect of Vitamin C and E on Cadmium's toxicity in female reproductive system of albino rats, the following 7 experimental groups were made (table 1). The number of rats in each group was 06. The animals were given different doses of Cadmium chloride and Vitamin C and E orally according to their groups.

Table 1- Number of rats, groups, treatment and doses in the experiment

1	Control group	Distilled Water	Ad libitum	06
2	Experimental group 2	Cadmium chloride + Vitamin C	3mg/ltr + 100mg/kg b.w.	06
3	Experimental group 3	Cadmium chloride + Vitamin C	5mg/ltr + 100mg/kg b.w.	06
4	Experimental group 4	Cadmium chloride + Vitamin C	7mg/ltr + 100mg/kg b.w.	06
5	Experimental group 5	Cadmium chloride + Vitamin E	3mg/ltr + 100mg/kg b.w.	06
6	Experimental group 6	Cadmium chloride + Vitamin E	5mg/ltr + 100mg/kg b.w.	06
7	Experimental group 7	Cadmium chloride + Vitamin E	7mg/ltr +100mg/kg b.w.	06

3 Cadmium Chloride Treatment

The desired concentration of aqueous solution of the cadmium chloride (SDS, Chemicals, India) was prepared by dissolving required amount of cadmium chloride in 1000 ml of the glass distilled water and then administered orally in drinking water for 14 days to different groups of rats. Only the high-grade pure chemicals were used in this study.

4. Vitamin C and E treatment

Vitamin C (Ascorbic acid) procured from Glaxo India Ltd was dissolved in required quantity of water and administered orally for 14 days to different groups of rats. Vitamin E (tocopherol acetate) procured from Merck was dissolved in required quantity of vegetable oil and also administered orally for 14 days to different groups of rats.

RESULTS:

I. Control group- Group 1 served as the control group and photograph below represents ovarian histology of Wistar rats administered only distilled water throughout the experiment. The photograph shows a normal ovary with follicles (F), blood vessels (BV) and corpora lutea (CL) (indicating ovulation).

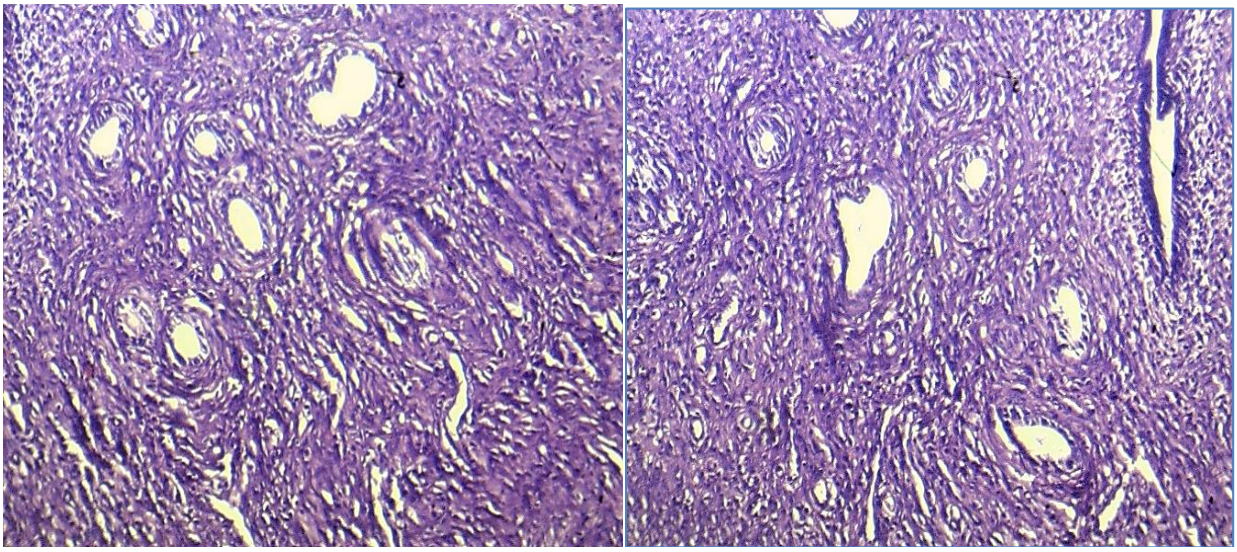

Fig 1- Group 1 (Control) Histological section of ovarian tissue of rats administered only distilled water for 14 days. Photomicrographs of ovary sections stained with hematoxylin and eosin (magnification ×100). The image shows normal ovary with follicles (F) at varying stages of development, blood vessels (BV), and Corpora Lutea (CL).

II. Experimental group 2- Experimental group 2 was the group of female Wistar rats that were administered 3mg/ltr Cadmium chloride + Vitamin C for 14 days.

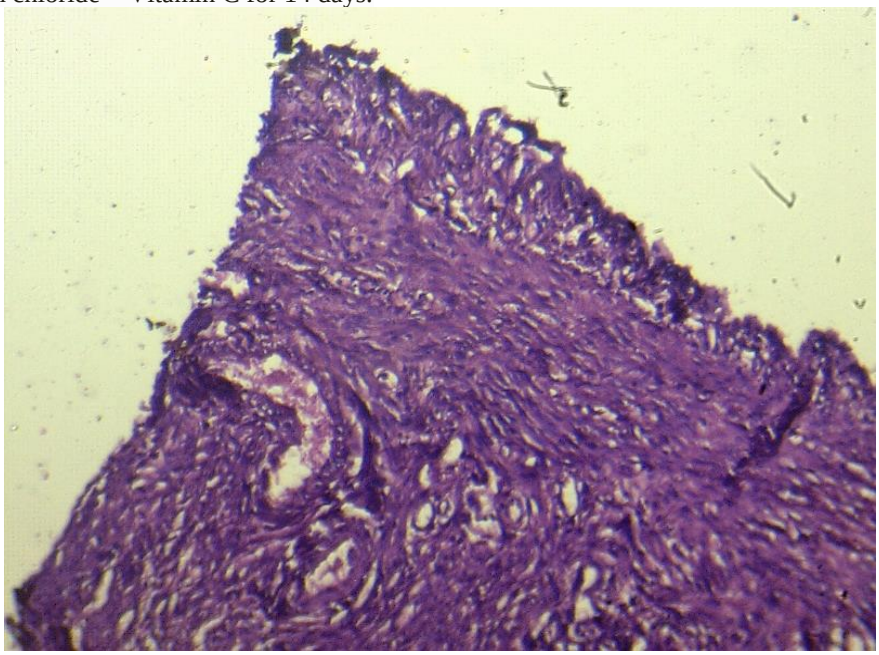

Fig 2. Group 2 (Experimental group) Histological section of ovarian tissue of rat administered 3mg/ltr Cadmium chloride + Vitamin C for 14 days. The section shows improvement in congested blood vessels (CBV), follicles (F) at varying stages of development, and the corpora Lutea (CL).

III. Experimental group 3- Experimental group 3 was the group of female Wistar rats that were administered 5mg/ltr Cadmium chloride + Vitamin C for 14 days.

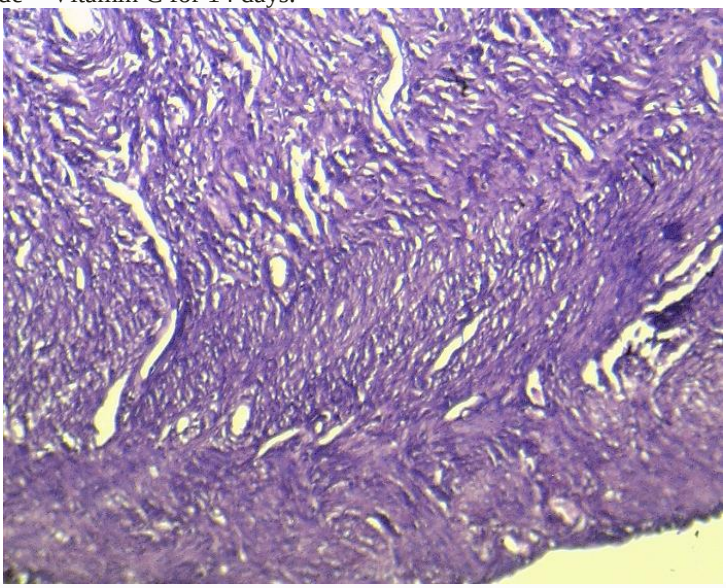

Fig 3. Group 3 (Experimental group) Histological section of ovarian tissue of rat administered 5mg/ltr Cadmium chloride + Vitamin C for 14 days. The section shows recovery in congested blood vessels (CBV), follicles (F) at varying stages of development, and the corpora Lutea (CL).

IV. Experimental group 4- Experimental group 4 was the group of female Wistar rats that were administered 7mg/ltr Cadmium chloride + Vitamin C for 14 days.

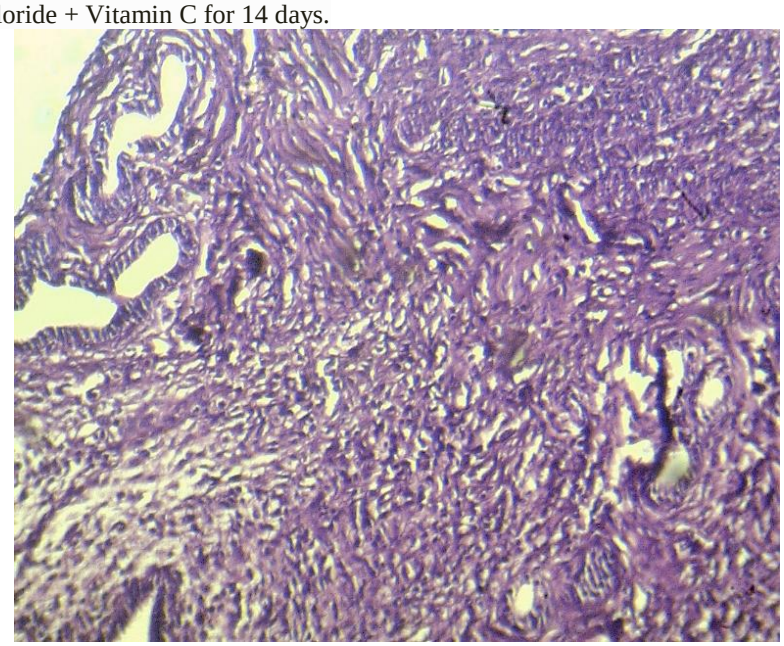

Fig 4. Group 4 (Experimental group) Histological section of ovarian tissue of rat administered 7mg/ltr Cadmium chloride + Vitamin C for 14 days. The section shows improvement in congested blood vessels (CBV), follicles (F) at varying stages of development, and the corpora Lutea (CL).

V. Experimental group 5: Experimental group 5 was the group of female Wistar rats that were administered 3mg/ltr Cadmium chloride + Vitamin E for 14 days.

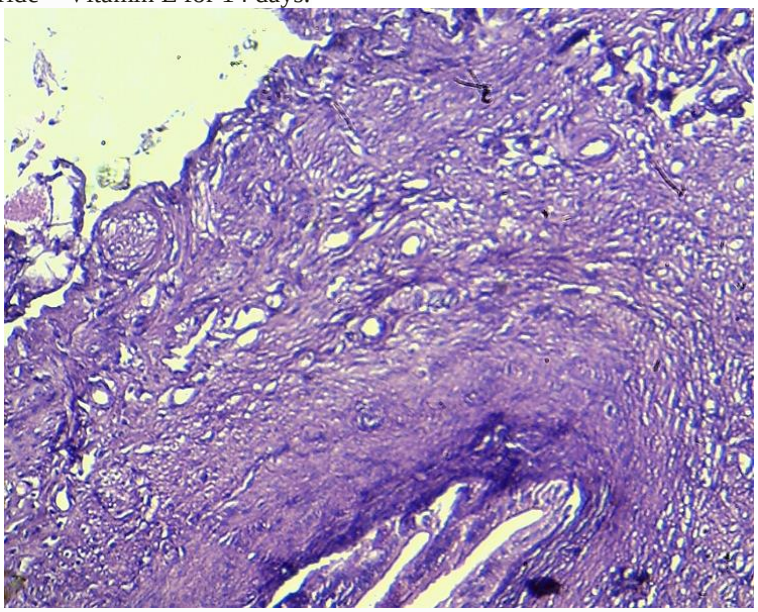

Fig5. Group 5 (Experimental group) Histological sections of ovarian tissue of rat administered 3mg/ltr Cadmium chloride + Vitamin E for 14 days. The section shows improvement in congested blood vessels (CBV), follicles (F) at varying stages of development, and the corpora Lutea (CL)

VI. Experimental group 6- Experimental group 6 was the group of female Wistar rats that were administered 5mg/ltr Cadmium chloride + Vitamin E for 14 days.

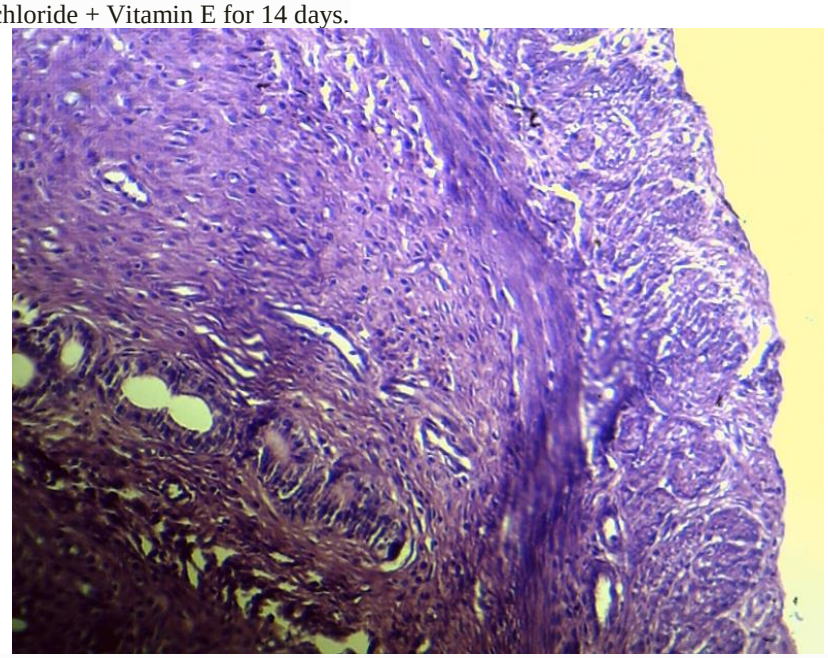

Fig 6. Group 6 (Experimental group) Histological section of ovarian tissue of rat administered 5mg/ltr Cadmium chloride + Vitamin E for 14 days. The section shows recovery in congested blood vessels (CBV), follicles (F) at varying stages of development, and the corpora Lutea (CL)

VII. Experimental group 7- Experimental group 7 was the group of female Wistar rats that were administered 7mg/ltr Cadmium chloride + Vitamin E for 14 days.

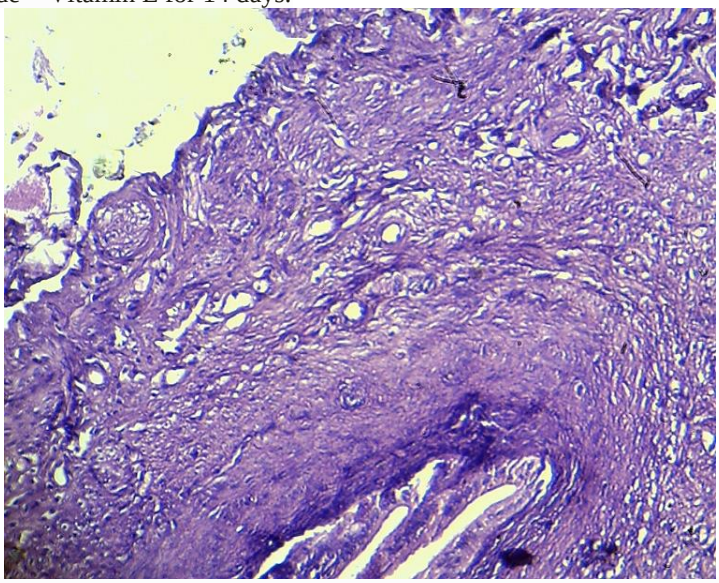

Fig 7. Group 7 (Experimental group) Histological section of ovarian tissue of rat administered 7mg/ltr Cadmium chloride + Vitamin E for 14 days. The section shows recovery in congested blood vessels (CBV), follicles (F) at varying stages of development, and the corpora Lutea (CL).

Histology of liver and kidney tissues

Histopathological observation indicated severe changes in the liver and kidney under Cadmium toxicity. The liver tissue was completely damaged and in kidney severe tubular injury associated with glomerulus with a thickened capsule and a small area of edema was observed (Fig. 16)

I. Control group- Group 1 served as the control group and microphotograph below represents liver and kidney histology of wistar rats administered only distilled water throughout the experiment. Liver section shows normal uninterrupted compact field of hepatocytes, blood sinusoids, and sporadic islands of connective tissues enclosing the bile ducts, venous, and arterial vessels. While no abnormal renal histological structures have been observed in the kidney of the control groups.

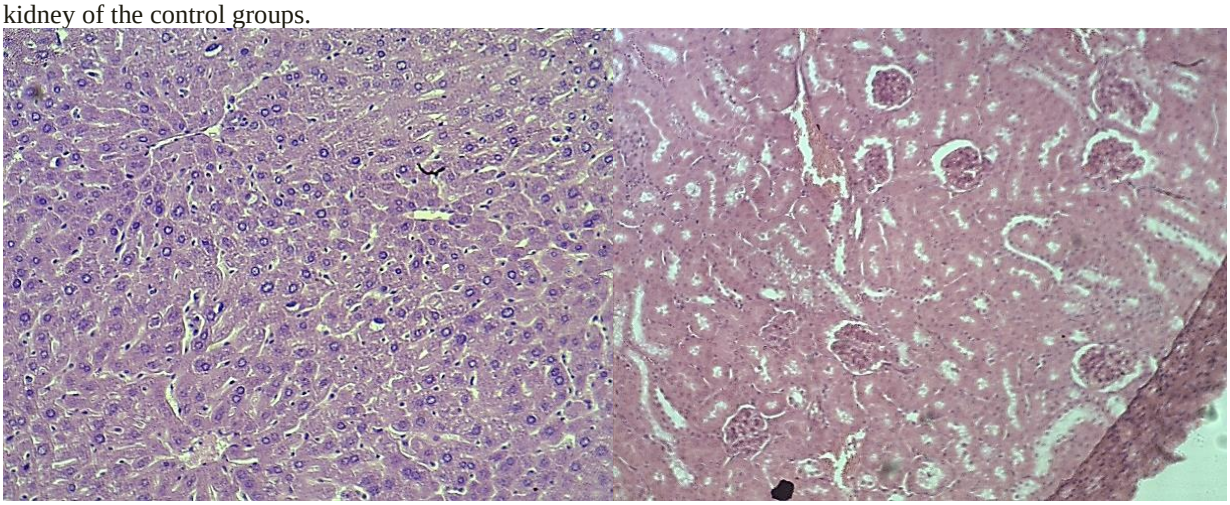

Fig 8.Group 1 (Control)- Histological section of liver (left) and kidney(right) tissue of rats administered only distilled water for 14 days. Photomicrographs of liver and kidney sections as seen with light microscope stained with hematoxylin and eosin (magnification ×100).

II. Experimental group 2- Experimental group 2 was the group of female Wistar rats that were administered 3mg/ltr Cadmium chloride for 14 days.

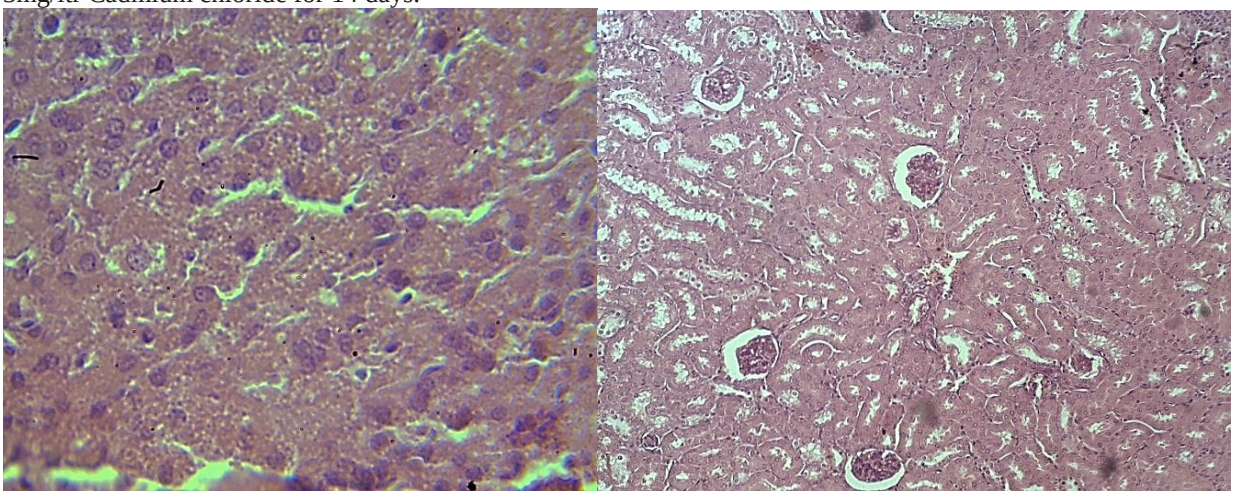

Fig 9.Group 2 (Experimental group)- Histological section of liver (left) and kidney (right) tissue of rat administered 3mg/ltr Cadmium chloride for 14 days. The liver section shows generalized degeneration, necrosis and depletion while the kidney section shows slight tubular necrosis, some glomeruli had an increased and the sections of the renal cortex and medulla displayed mild vascular degeneration and necrosis.

III. Experimental group 3- Experimental group 3was the group of female Wistar rats that were administered 5mg/ltr Cadmium chloride for 14 days.

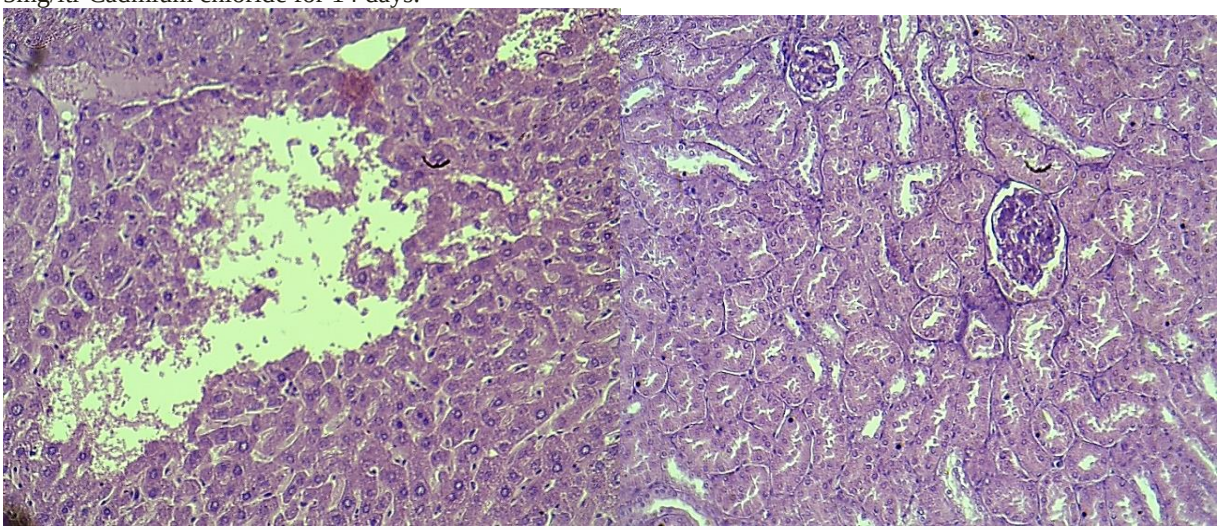

Fig 10.Group 3 (Experimental group)- Histological section of liver (left) and kidney (right) tissues of rat administered 5mg/ltr Cadmium chloride for 14 days. The liver section shows cellular swelling and necrosis of hepatocytes with clear nuclear hypertrophy. The kidney section shows characteristic tubular injury, increased number of lesions noted in addition to the glomerular changes.

IV. Experimental group 4- Experimental group 4was the group of female Wistar rats that were administered 7mg/ltr Cadmium chloride for 14 days.

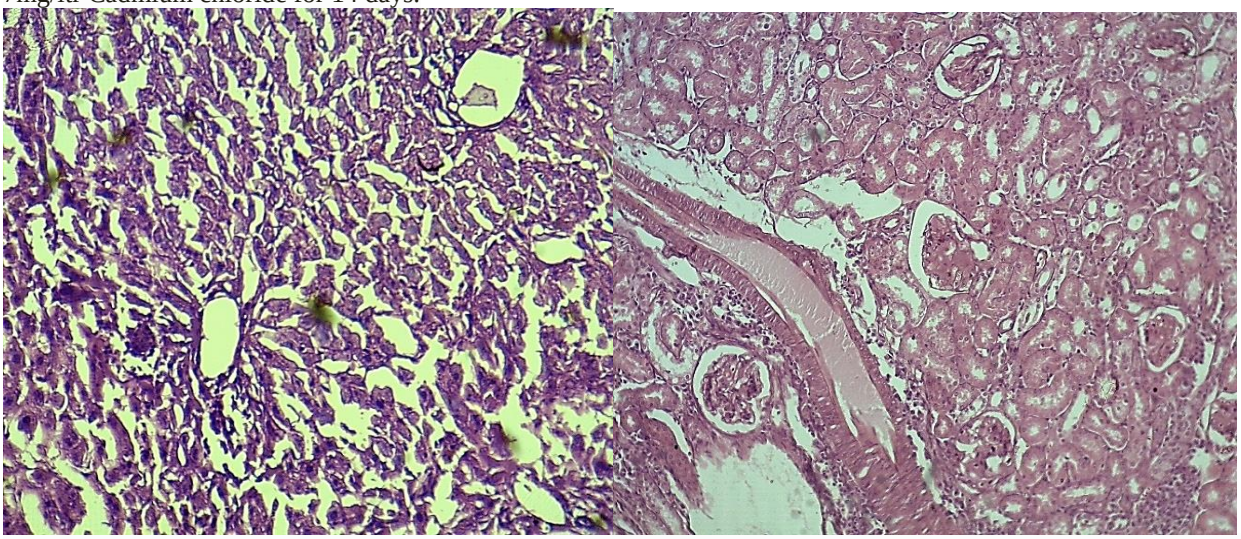

Fig11.Group 4 (Experimental group)- Histological section of liver (left) and kidney (right) tissues of rat administered 7mg/ltr Cadmium chloride for 14 days. The section of liver shows severe cellular swelling of hepatocytes, marked nuclear hypertrophy, and necrosis of hepatocytes with tissue depletion. The kidney shows stronger tubular necrosis, vascular changes with interstitial edema and glomerular fibrosis and cell hypertrophy.

V. Experimental group 5- Experimental group 5 was the group of female Wistar rats that were administered 3mg/ltr Cadmium chloride + Vitamin C for 14 days.

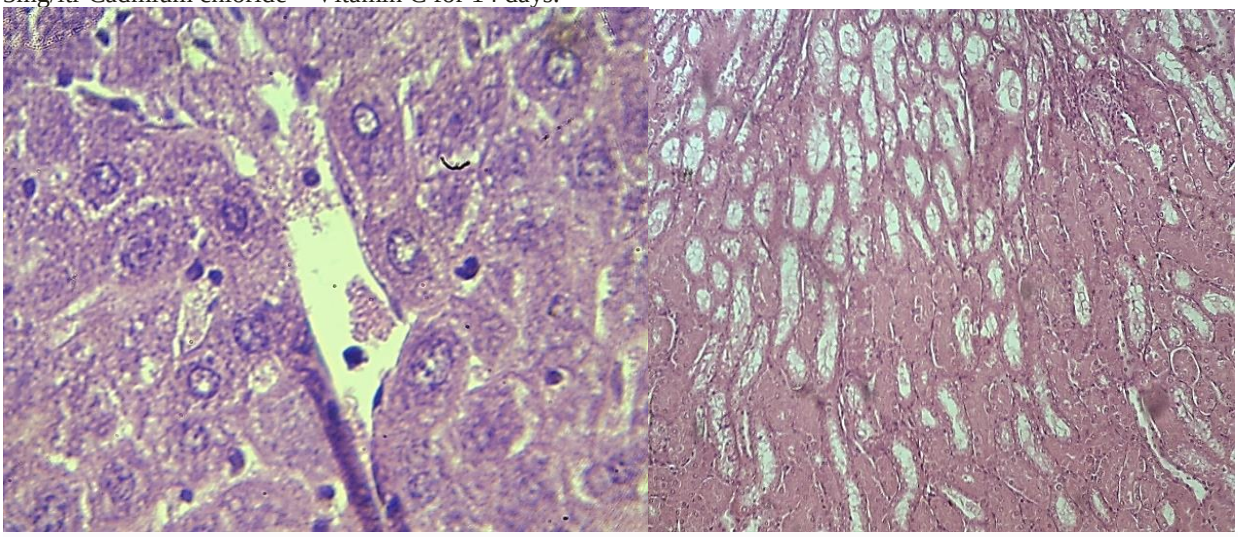

Fig12.Histological section of liver (left) and kidney (right) tissues of rat administered 3mg/ltr Cadmium chloride + Vitamin C for 14 days. In kidney renal injury was slightly recovered and the liver tissues demonstrated disappearance of the degenerative changes in hepatocyte.

VI. Experimental group 6- Experimental group 6 was the group of female Wistar rats that were administered 5mg/ltr Cadmium chloride + Vitamin C for 14 days

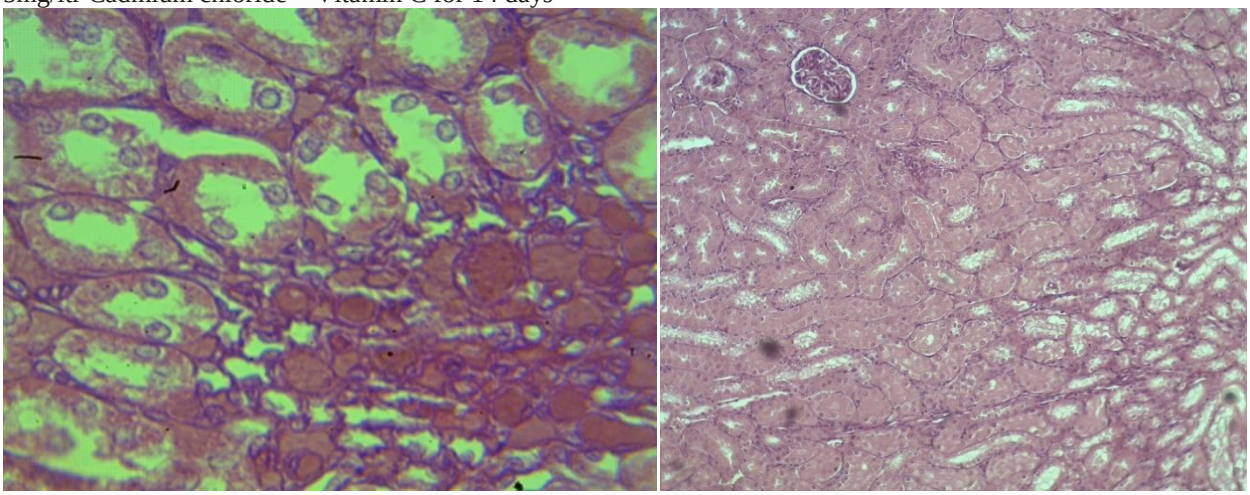

Fig.13. Histological section of liver (left) and kidney (right) tissues of rat administered 5mg/ltr Cadmium chloride + Vitamin C for 14 days. The kidney and liver tissues showed considerable recovery

VII. Experimental group 7- Experimental group 7 was the group of female Wistar rats that were administered 7mg/ltr Cadmium chloride + Vitamin C for 14 days

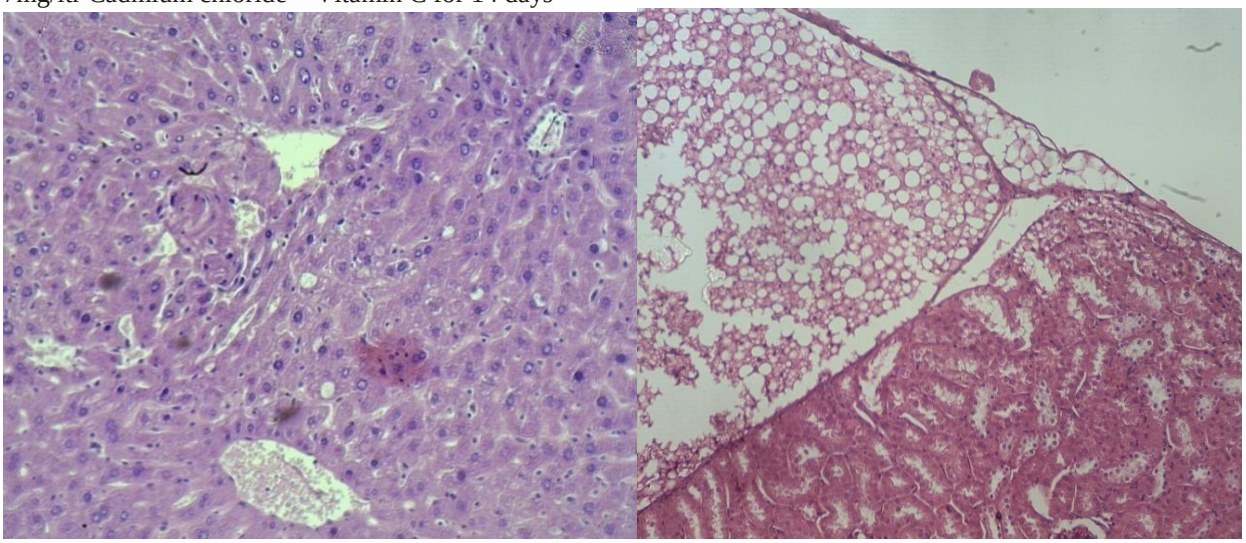

Fig 14.Histological section of liver (left) and kidney (right) tissues of rat administered 7mg/ltr Cadmium chloride + Vitamin C for 14 days. There recovery of kidney renal injury was maximum and the liver tissues also demonstrated disappearance of the degenerative changes in hepatocytes**.**

VIII. Experimental group 8-Experimental group 8 was the group of female Wistar rats that were administered 3mg/ltr Cadmium chloride + Vitamin E for 14 days.

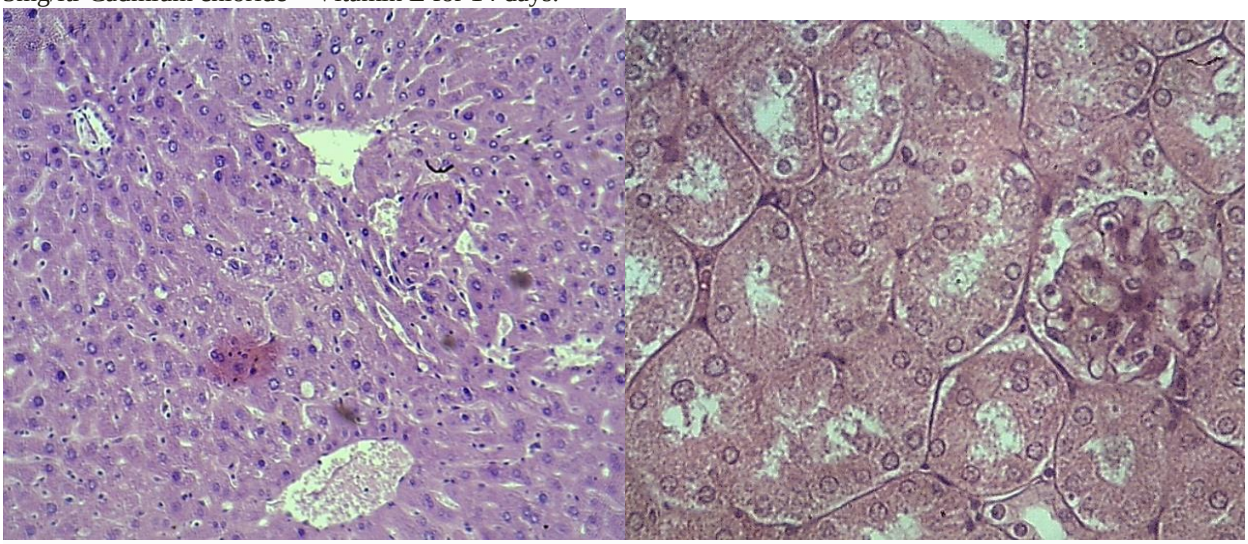

Fig15.Group 8 (Experimental group)- Histological section of liver (left) and kidney (right) tissues of rat administered 3mg/ltr Cadmium chloride + Vitamin E for 14 days. The observed morphological changes had reduced from the liver and from the kidney. The Vitamin E induced recovery and regeneration in renal structure of kidney.

IX. Experimental group 9- Group 9 was the group of rats that were administered 5mg/ltr Cadmium chloride + Vitamin E for 14 days.

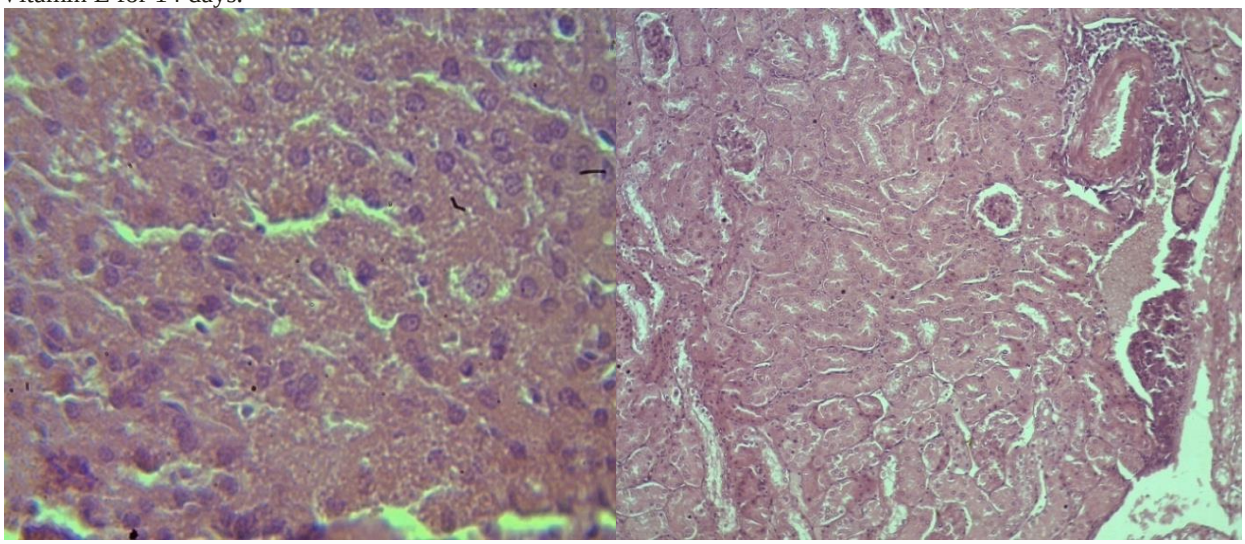

Fig.16. Histological section of liver (left) and kidney (right) tissues of rat administered 5mg/ltr Cadmium chloride + Vitamin C for 14 days. The Vitamin E induced recovery and regeneration in kidney and liver tissues.

X. Experimental group 10- Group 10 was the group of rats that were administered 7mg/ltr Cadmium chloride + Vitamin E for 14 days.

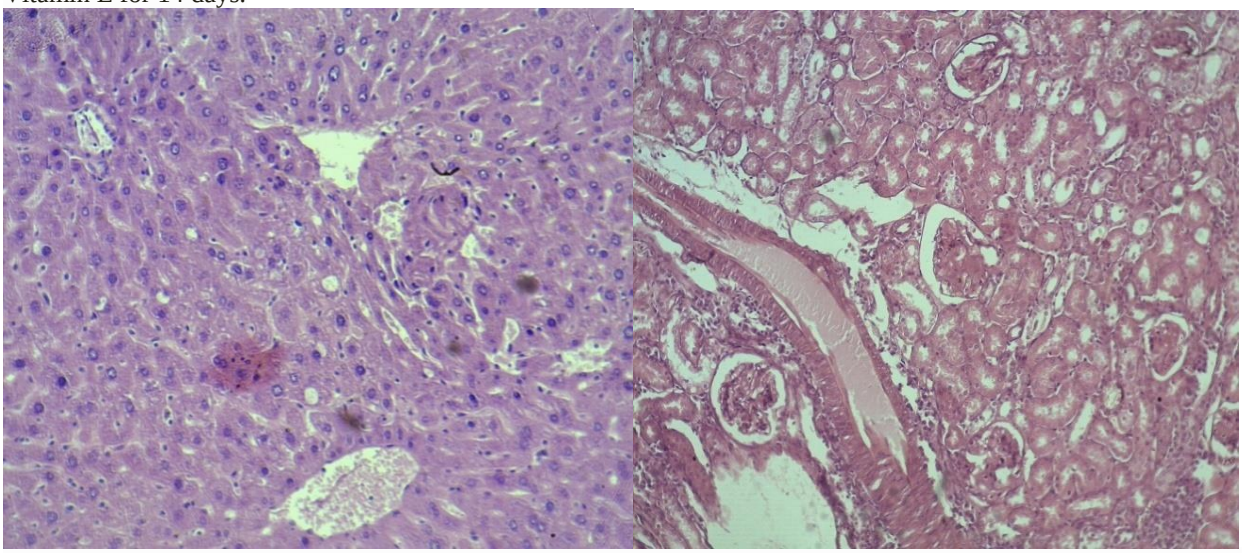

Fig. 17. Histological section of liver (left) and kidney (right) tissues of rat administered 7mg/ltr Cadmium chloride + Vitamin C for 14 days. The effect of Vitamin E showed maximum recovery due to cadmium toxicity in both the tissues.

Vitamin C (ascorbic acid) and E (α-tocopherol) is an important dietary antioxidant which significantly decreases the adverse effects of reactive species, including reactive oxygen and nitrogen species known to cause extensive damage to several macromolecules, such as lipids, proteins and DNA, which are implicated in chronic diseases, including cardiovascular disease, stroke, cancer, neurodegenerative diseases and cataractogenesis. Ascorbic acid is a potent, water-soluble antioxidant capable of scavenging or neutralizing an array of ROS, including hydroxyl, alkolyl, peroxyl, superoxide anion, hydroperoxyl radicals and reactive nitrogen radicals, such as nitrogen dioxide, nitroxide, and peroxynitrile at very low concentrations.

DISCUSSION:

Though, the actual mechanisms of cadmium that effects hormone production in female reproductive system have still remained unclarified. In another study by Sengupta et al, 2004 Vitamin C was found to decrease lipid peroxidation when there is cadmium induced toxicity and this study showed that vitamin C could play protective role against the steroidogenesis. In experimental studies on female rats, it was reported that Cd supresses ovulation, thereby reducing production of progesterone by acting directly on granulosa cell morphology and steroid biosynthesis (Peter et al, 1995).Another in vivo study on female rabbits reported that when Cd chloride was administered at a dose of 1.5 mg/kg, there was a decrease in the number of primary follicles and an increase in the number of atretic follicles in the ovary (Massanyi 2007). Since ovulation is hindered by Cadmium toxicity, a small amount of corpus luteum is produced and it further leads to the decrease in the level of progesterone. Ovulation is also affected by thelow levels of LH serum, which is attributed to the formation of large cystic antral follicles. Cadmium has been found to disrupt the hormonal function (Pollack et al, 2014) and isable to inhibit the ovulation.

Bernard et al. (1981) produced proteinuria in rats by exposing them to cadmium in drinking-water at a dose of 200 µg/L for up to 11 months. Thus, cadmium produces renal tubular dysfunction in non-human mammalian species that is analogous to the effect in humans of exposure to low concentrations of cadmium.

Serum alkaline phosphatase and acid phosphatase were also increased when cadmium at different doses were given to rats. Study indicated that vitamin C and E may have protective effect, even against low dosage of Cadmium (Omonkhua et al. 2013).Our study also suggested that Cadmium toxicity causes significant elevation in liver enzymes like SGOT, SGPT clearly indicating liver dysfunction.

Mattie *et al. also* confirmed that Vitamin E and aspirin exert their protective effect via antioxidation (Mattie and Freedman, 2001). Our results corroborate with a study by Ognjanovic, 2006 where he also indicated that vitamin E could reduce the toxicity caused by high cadmium doses. Many other studies have applied the use of antioxidant substances like

Vitamin E 100 and beta-carotene independently or in combination to adjust the toxic effect of cadmium chloride and reported an increase in liver enzymes, creatinine, urea, bilirubin and decrease in haemoglobin (Rafati et al, 2017)

The findings from this study are in sync with an experiment by Poli et al, 2022 where the workers had also reported that a combination of Vitamin C&E enhances the biological recovery induced by Cadmium,

Our work revealed that vitamin C and E supplement caused decrease in the Cadmium toxicity of liver and kidney. Therefore, it can be concluded that vitamin C and vitamin E have protective effect on the female reproductive system of rats. Furthermore, the effects of Cadmium toxicity in the liver and kidney, and the pathology related to both nephrotoxicity and hepatotoxicity, requires further in-depth investigation

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REFERENCES:

1. Andjelkovic M., Djordjevic A.B., Antonijevic E., Anttonijevic B., Stanic M., Stevulijevic J.K., Kalimanovska V., Jovanovic M., Boricic N., Wallace D., Bulat Z., 2019. Toxic effect of acute cadmium and lead exposed in rat blood, liver and kidney. Review, International Journal of environmental and public health, 16(2), 1-21.
2. Bernard A., Lauwerys R., & Gengoux P.,1981. Characterization of the proteinuria induced by prolonged oral administration of cadmium in female rats. Toxicology, 20 (4), 345-57.
3. Filipic M., 2012. Mechanisms of cadmium induced genomic instability. Mutation research / Fundamental and molecular mechanism of mutagenesis, 733(1-2), 69–77.
4. Han Y.L., Sheng Z., Liu G.D., Long L.L., Wang Y.F., Yang W.X, Zhu J.Q., 2015 Cloning, characterization and cadmium inducibility of metallothionein in the testes of the mudskipper Boleophthalmus pectinirostris. Ecotoxicol Environmental Safety, 119, 1–8.
5. Joseph P., 2009. Mechanisms of cadmium carcinogenesis. Toxicology and Applied Pharmacology, 238 (3), 272–279.
6. Layachi N., and Kechrid Z., 2012. Combined protective effect of vitamins C and E on cadmium-induced toxicity liver injury in the rat. African Journal of Biotechnology, 11(93), 16013-16020.
7. Mattie M.D., Freedman J.H., 2001. Protective effects of aspirin and vitamin E (α-tocopherol) against copper-and cadmium-induced toxicity. Biochemical and Biophysical Research Communications 285(4), 921–925.
8. Nakano M, Onodera A, Saito E, Tanabe M, Yajima K, Takahashi J., Chuyen N.V.,2008. Effect of astaxanthin in combination with alpha-tocopherol or ascorbic acid againt oxidative damage in diabetic ODS rats. J Nutr Sci Vitaminol (Tokyo), 54(4), 329–334.
9. Omonkhua, A.A., Obi F.O., 2012. Effects of Vitamin C on Kidney and Bone of Rats Exposed to Low Doses of Cadmium. Nigerian Journal of Basic and Applied Sciences. 20 (4), 297-304.
10. Patrick L., 2003. Toxic metals and antioxidants: Part II The role of antioxidants in arsenic and cadmium toxicity. Alternative Medicine Review, 8(2), 106–28.
11. Peter M., Róbert T., Ferdinand N., 1995. Concentrations of cadmium in ovary, oviductus, uterus, testis and tunica albuginea of testis in cattle. Journal of Environmental Science Health. Part A: Environmental Science and Engineering and Toxicology, 30(8), 1685–1692.
12. Pollack A.Z., Ranasinghe S., Sjaarda L.A., Mumford S.L., 2014. Cadmium and reproductive health in women: a systematic review of the epidemiologic evidence. Current Environmental Health Reports 1(2), 172–184.
13. Poli, V., Aparna, Y., Madduru R., Motireddy S.R., 2022. Protective effect of Vitamin C and E on enzymatic and antioxidant system in liver and kidney toxicity of Cadmium in rats. Applied Food Research, 2 (1), 100098.
14. Rahimzadeh M. R., Rahimzadeh M. R., Kazemi S, Moghadamnia A., 2017 Cadmium toxicity and treatment: An update. Caspian Journal of Internal Medicine, 8(3), 135–45.
15. Gupta R. S., Kim J., Gomes C., Oh S., Park J., Im W.B., Seong J.Y., Ahn R.S., Kwon H.B., Soh J., 2004. Effect of ascorbic acid supplementation on testicular steroidogenesis and germ cell death in cadmium-treated male rats. Molecular and Cellular Endocrinology 221(1-2), 57–66.
16. Sudarshana, Kumar P., Yadav K.K., 2023. Role of cadmium in inhibiting female fertility in wistar rats. International journal of food and nutritional sciences, 2(1), 1175-1185.