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PROTECTIVE EFFECT OF *EMBLICA OFFICINALIS* ON HISTOPATHOLOGICAL CHANGES IN RATS INDUCED WITH POTASSIUM DICHROMATE

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ABSTRACT

Potassium dichromate is a common inorganic chemical reagent, most commonly used as an oxidizing agent in various laboratory and industrial applications. Prolonged exposure to the chemical causes hepatotoxicity, nephrotoxicity and oxidative stress damage of reproductive organs of both male and female. A single dose of Potassium dichromate (15mg/kg, b.w.i.p) dissolved in sterile saline (0.9% Nacl) induced histological alterations in liver, kidney and testis of male wistar rats. Pretreatment with Emblica officinalis at doses of 250 mg/kg body weight, prior to intoxication of Potassium dichromate prevented tissue damage. The results obtained in the study revealed the protective effect of Emblica officinalis.

KEYWORDS: Potassium dichromate, *Emblica officinalis*, Hepatotoxicity, Nephrotoxicity, Testicular damage.

INTRODUCTION

Oxidative stress and cellular damage in major organs like liver, kidney and reproductive organs caused by toxins are increasing every year due to modern life style, junk food consumption, inhalation of certain chemicals, chemicals used for food colouring and house hold items. Prolonged exposure to these chemicals may cause hepatotoxicity, nephrotoxicity and oxidative stress damage in reproductive organs. Potassium dichromate ($K_2Cr_2O_7$) is a chemical compound widely used in metallurgy, chrome plating, chemical industry, textile manufacture, wood preservation, photography and photoengraving, refractory and stainless steel industries and cooling systems.[1] Potassium dichromate is a hexavalent form of Chromium and has been demonstrated to induce oxidative stress and carcinogenic in nature.[2,3,4] Emblica officinalis Garten plays a vital role to challenge many diseases in human body. Emblica officinalis Garten, commonly known as amla (synonym Indian gooseberry), is one of the fruits which contain bioactive components that is thought to have antioxidative properties is widely used in India as a traditional medicine.[5,6] The present study is aimed to evaluate the protective effect of Emblica officinalis in potassium dichromate induced damage in liver, kidney and testis of male wistar rats. Pretreatment with *Emblica officinalis* improved the histological changes in liver, kidney and testis of potassium dichromate administered male wistar rats.

MATERIALS AND METHODS

Preparation of extract

The powder of dried fruit of Emblica officinalis (EF) was obtained from Ayurvedic pharmacy, Chennai and was extracted with 50% ethanol 25 g/ 100ml in soxhlet extraction assembly. The fruit extract powder dosage was fixed as 250mg/kg from previous literature.

Animals and experimental protocol

24 Male wistar rats weighing 150-200g and the age of 12-22 weeks were obtained from BRULAC, Saveetha University, chennai-77 and were housed in a ventilated room at 25 ± 5°C under a 12 h light/dark cycle. The animals were accessed free to standard laboratory feed and water *ad libitum.* The study was approved by the Committee for the Purpose of Control and Supervision of Experimental Animals (CPCSEA) having Registration number and date of registration: SU/BRULAC/RD/005/2014, March 20th, 2014. CPCSEA guidelines were followed for animal handling and treatment. Rats were divided into four groups of 6 animals each.Group I (Control) received normal laboratory feed and water,Group II (toxic) received 15mg/kg/bwt of potassium dichromate dissolved in sterile saline(0.9% Nacl) as single IP injection,Group III received 250mg/kg/bwt of EF in water through oral gavage for 14 days and at the end of 14th day the rats are treated with 15mg/kg/bwt potassium dichromate in water through oral gavage for 14 days and Group IV received 250mg/kg/bwt of EF in water through oral gavage for 14 days.

Histological Evaluation

At the end of the experimental periods, rats of all four groups were sacrificed by cervical dislocation. Liver, kidney and testis was collected immediately after sacrifice, cleaned of fats and fixed in 10% (v/v)formalin in phosphate buffered saline (PBS) (pH 7.4),dehydrated, embedded in paraffin, sectioned at 5 mm thickness, and stained with hematoxylin-eosin to make the permanent glass slides. Sections of liver, kidney and testes were examined under a microscope equipped with a digital camera.

RESULTS

Histological evaluation of rat liver

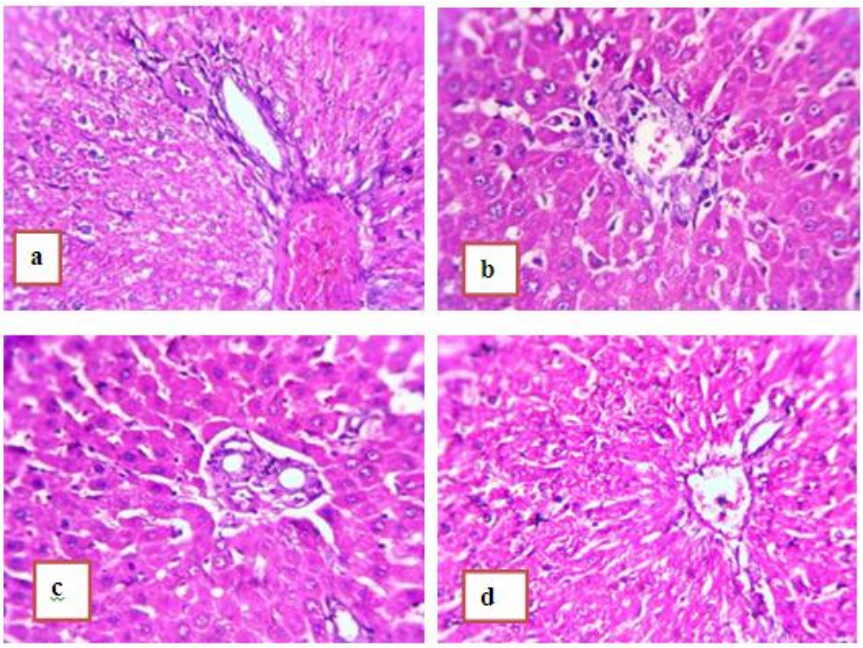

Figure 1: Photomicrographs of liver sections stained with hematoxylin and eosin. (a) Control group, (b) potassium dichromate (15mg/kg/bwt)treated rat liver with periportal inflammation,(c)potassium dichromate(15mg/kg/bwt)+ Emblica officinalis extract (250mg/kg/bwt) treated liver demonstrate mild periportal inflammation and (d) Emblica officinalis extract (250mg/kg/bwt)treated group.

Histological evaluation of rat kidney

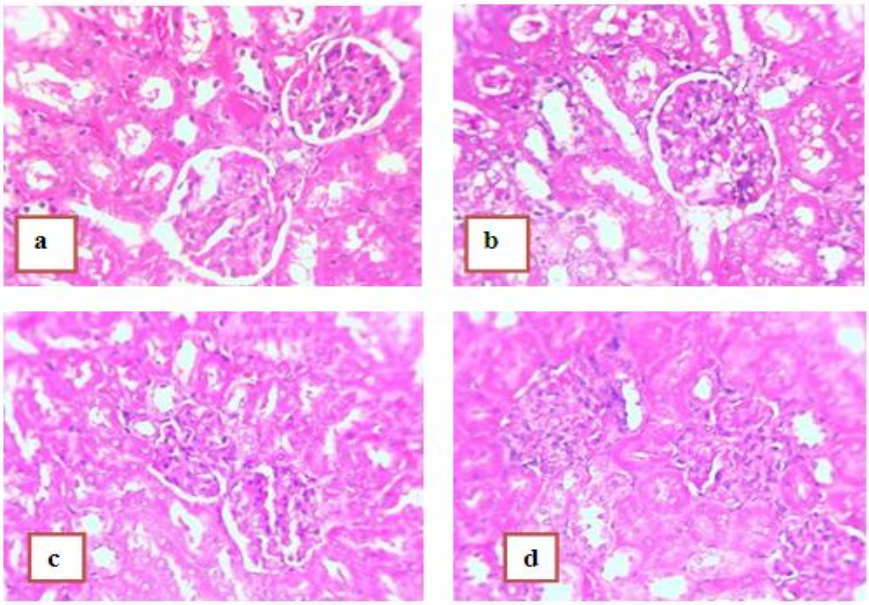

Figure 2: Photomicrographs of kidney sections stained with hematoxylin and eosin. (a) Control group, (b) potassium dichromate (15mg/kg/bwt)treated group demonstrate glomeruli with focal thickening of membrane,(c) potassium dichromate(15mg/kg/bwt) +Emblica officinalis extract (250mg/kg/bwt)treated with normal glomerulus and tubules and (d) Emblica officinalis extract (250mg/kg/bwt)treated group.

Histological evaluation of rat testis

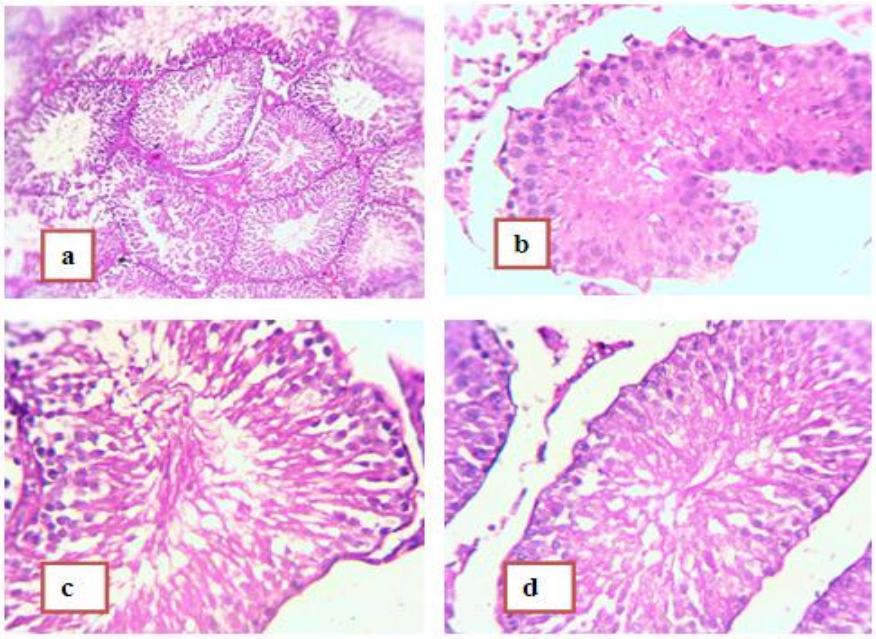

Figure 3: Photomicrographs of testis sections stained with hematoxylin and eosin. (a) Control group, (b) potassium dichromate (15mg/kg/bwt)treated group shows atrophy of seminiferous tubules, (c) potassium dichromate (15mg/kg/bwt)+Emblica officinalis extract (250mg/kg/bwt)treated shows normal seminiferous tubules with spermatocytes of mature spermatids and (d) Emblica officinalis extract (250mg/kg/bwt)treated group.

Histopathological Examination.

Histology of the liver sections of rats of different groups is shown in Figure 1. Examination of the liver in animals of normal control group showed normal histoarchitecture of hepatic parenchyma with hepatocytes arranged in cord like fashion around the central vein.The nucleus and cytoplasm showed normal histological features with intactness and normal morphology of cytoplasm and blood vessels and bile duct in portal triad.The liver sections from group II (potassium dichromate induced) showed moderate degree of damage to hepatic parenchyma with periportal inflammation. As compared to group II the histological evaluation from liver sections of group III showed only minimal changes in hepatic parenchyma with mild periportal inflammation.In group IV normal liver architecture demonstrate the protective role of Emblica officinalis against potassium dichromate induced toxicity.

Histological evaluation of kidney sections as represented in Figure-2 illustrate normal glomerulus and tubular structure in group I. Kidneys sections in (potassium dichromate treated) group II revealed glomerulus with focal thickening of membrane. Pretreatment with 250mg/kg/bwt of EF in group III rats attenuated the renal tissue damage when compared with group II.Normal renal structure in group IV indicate the protective effect of Emblica officinalis.

The preventive effects of Emblica officinalis extract on testicular damage were evaluated in histopathological structures as represented in Figure -3. The result in potassium dichromate induced rats (groupII) showed atrophy of seminiferous tubules. Normal seminiferous tubules with spermatocytes of mature spermatids were observed in testicular sections of rats (group III) pretreated with250mg/kg/bwt of EF extract. Histology of Group IV testis showed normal appearance of seminiferous tubules which emphasize the ameliorative effect of Emblica officinalis.

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DISCUSSION

Chromium compounds induce oxidative stress leading to tissue damage,[7] the formation of chromium (V) intermediates from chromium (VI) produce reactive oxygen species (ROS) including superoxide anion, singlet oxygen and hydroxyl radicals.[8] Its toxic effects contributed to its ability to induce oxidative stress leading to enhanced production of ROS, this result in decreased cell viability, enhanced intracellular oxidized state, membrane damage and apoptotic and necrotic cell death.[4] Renal necrosis and hepatic damage in chromium exposure have been attributed to the stronger oxidizing power of hexavalent chromium and its high transport across the cell membrane.[9] Workers exposed to chromium in welding industry suffered from increased risk of reduced semen quality and sperm abnormalities leading to infertility.[10] *Emblica officinalis* commonly known as amla is one of the fruits which contains an array of bioactive components showing antioxidative property and is widely used in India as a traditional medicine.[5,6] The fruit extract has also been reported to have potent hepato-protective property owing to its antioxidative nature. [11] The present study is aimed to

evaluate the protective effect of Emblica officinalis in potassium dichromate induced hepatotoxicity, nephrotoxicity and testicular damage in male wistar rats.

Liver plays a major role in metabolism and has number of functions in the body, including glycogen storage, decomposition of RBC, protein synthesis, hormone production and detoxification.[12] Treatment with potassium dichromate (15mg/kg/body weight) generated focal centrolobular hepatocytes death within 24 h and 48 h, in a time-dependent fashion and the cells showed extensive cytoplasmic vacuolation with pyknotic nucleus.[13] Rats subjected to potassium dichromate(15mg/kg/ body weight) showed coagulative necrosis in most of the convoluted tubules at the cortex and the loss of the nuclei in the lining epithelium of the necrotic tubules.[14] Administration of EFE to alcohol treated rats improved the histomorphology of the liver near to normal. The EFE administrated rats indicate the hepatoprotective effect as well preserves the structural integrity of the liver from the adverse effects of alcohol.[15] Marked ameliorative effect on the cadmium (cadmium chloride (15 mg/kg body weight/day) induced histopathology was observed in 200 mg/kg of amla fruit extract treated group. Amla fruit extract restored the normal hepatic architecture with hepatic strands radiating from central vein (CV) with binucleated hepatocytes. [16] Chaphalkar etal.[17] have demonstrated hepatoprotective activity of hydroalcoholic bark extract of *P. emblica* (PEE) in rats intoxicated with ethanol. Liver sections from animals of PEE 500 mg/kg group and 1000 mg/kg group showed minimal to mild degree of histopathological changes in the hepatic parenchyma.

Kidney contributes major role in electrolyte balance and maintains homeostasis of the body. [18] The kidney is a critical organ greatly affected by exposure to chromium compounds. Administration of potassium dichromate is toxic to the kidney and results in acute renal failure (ARF).[19] The fruit extract of amla (200 mg/kg) showed a noticeable restoration in the renal architecture caused by cadmium (cadmium chloride (15 mg/kg body weight/day) treatment.[16] Pretreatment with PE extract 250 mg and PE extract 500 mg in rats with CI-AKI induction significantly attenuated the development of these lesions when compared with the CM (intravenous contrast media) group.[20]

The histopathological evaluation of control and EO only groups demonstrated normal architecture of tubules with no evidence of inflammation The kidney sections from the cisplatin(8mg/kg b.w)-control rats showed tubular atrophy, denudation of epithelium and infiltration of inflammatory cells.In the groups, pretreated with 150 and 300 mg/kg dose of EO, there was marked and moderate tubular damage and inflammation respectively.However, the highest dose of EO (600 mg/kg) exerted significant nephroprotection and a marked absence of tubular necrosis and inflammation in the kidneys was observed.[21]

Saxena et al.,[22] suggested a risk to growing testes, if rats are exposed to hexavalent chromium during the pre-pubertal stages of their development, which in turn, may disturb normal testicular physiology in adulthood. A significant higher numbers of morphologically abnormal sperm were noticed in a group occupationally exposed to chromium in compare to the unexposed persons.[23] Jeber et al.,[24] reported potassium dichromate (24 mg/kg orally for 60 day s) treated animals, showed severe changes in seminiferous tubules, including sertoli cells, interstitial edema and germinal epithelium degeneration.

Emblica officinalis fruit extract of 20mg/kg for 30 days are found to be effective on reproductive injury and oxidative testicular toxicity in male wistar rats.[25] Chakraborty and Verma[26] reported oral administration of aqueous extract of *Emblica offcinalis* along with ochratoxin for 45 days, significantly mitigated ochratoxin-induced alterations in reproductive parameters of mice. Iamsaard, et al.,[27] demonstrated the protective effect of *Phyllanthus emblica* L. branch (PE) extract in Valproic acid (VPA) (500 mg/kg BW) treated rats. Testicular histopathology was improved in PE branch extracts (250 mg/kg BW), PE50+VPA PE branch extracts (50 mg/kg BW), PE100+VPA PE branch extracts (100 mg/kg BW) and PE250+VPA PE branch extracts (250 mg/kg BW groups signifying the preventive role of Phyllanthus *emblica*. The study clearly shows that pre-treatment of experimental rat models with *Emblica officinalis* prior to potassium dichromate injection mitigated the pathological changes caused by potassium dichromate envisaging its protective effect.The ameliorative effect suggest *Emblica officinalis* as a potential therapeutic in Indian medicine.

CONCLUSION

The results of the present study demonstrate that Emblica officinalis provides significant protection against potassium dichromate treated liver, kidney and testicular damage. Histopathological observations revealed Emblica officinalis extract restored the normal architecture of liver, kidney and testis tissues. The protective activities of Emblica officinalis extract (EF) can be attributed to the presence of gallic acid, ellagic acid, polyphenols, and flavonoids. The therapeutic potential of Emblica officinalis can be exploited in treating liver, kidney and testicular damage disorders.

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