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Research Article

Protective Effect of Curcumin on Cadmium Chloride Induced Epididymal Toxicity in Swiss Mice (*Mus musculus)*

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ABSTRACT

The monitoring of infertility and its control has become a worldwide issue of apprehension in order to retain fit population. Cadmium, a viable environmental toxicant hinders reproductive functioning which adversely influence the number of spermatozoa and complete organization of connective tissue in the epididymis, where as curcumin is known to be a strong protective herbal remedy which renders protection against numerous toxicants. Hence, in the present research work an effort has been made to evaluate the protective effect of curcumin (10mg/kg/day , for 15 days) prior treatment against a dose of 50mg/kg/animal/day for a day of cadmium chloride induced perturbations in the epididymis. Our results strongly suggest that cadmium intoxication leads to several histopathological alterations in the epididymis of adult male mice that are alleviated by the administration of curcumin.

Keywords: Curcumin, cadmium chloride, epididymis,toxicant, protection

INTRODUCTION

The monitoring of infertility and its control has become a worldwide issue of apprehension in order to retain fit population. Cadmium, a viable environmental toxicant hinders reproductive functioning which adversely influence the process of spermatogenesis.Cadmium is one of the 35 metals that concern humans because of their occupational or residential exposure;23of these are the heavy elements: antimony,arsenic,bismuth,cadmium,cerium,chromium,cobalt,copper,gallium,gold,iron,lead,manganese,mercury,nickel,platinum,silver,tellurium,thallium,tin,uranium,vanadium, and zinc. Heavy metals become toxic when they are not metabolized by the blood and accumulate in the soft tissues. Cadmium is recognized to produce severe toxic effects on humans and 'The Agency For Toxic Substances and Disease Registry'(ATSDR)[1] in Atlanta Georgia has listed cadmium as number 7 in its top 20 list of hazardous substances..Traditionally cadmium toxicity was associated with mining of zinc and lead, and

with the application of municipal sewage. Cadmium has been in industrial use for a long period of time, its serious toxicity moved into scientific focus during the middle of last century. Target organs of cadmium toxicity are liver,placenta, kidneys, lung, brain and bones [2-5].Cadmium is a known Clastogen , Mutagen and a Carcinogen[6]. Human uptake of cadmium takes places mainly through food. In vegetarian diet, cadmium rich foodstuffs are as follows: Mushrooms, cocoapowder,potatoes, fruits, wheat, grains,bran,sugerbeet fibre, carrot,dried seaweeds etc.Similarly in non-vegetarian diets shellfish, mussel, meat, fishes are rich in cadmium[7].Cadmium is of particular concern to mankind because it accumulates in the human body with a half life exceeding 10 years and has been linked with a number of health problems including renal tubular dysfunction ,pulmonary emphysema ,kidney damages ,osteoporosis etc [5,8-10] .Chronic and acute exposure of cadmium leads to oxidative stress and damage various organs of the body [11].Cadmium is a recognized reproductive toxicant and has been reported to reduce male fertility and altered sexual behaviour in both humans and rodents [12]. Epididymis provides a favourable internal milieu for storage of spermatozoa in a motile and fertiliable state. It is most susceptible to cadmium toxicity[13].Cadmium exerts a selective toxic effect on the blood vessels of the caput epididymis [14-16]. There are no substitutes for prompt professional medical attention in cases of heavy metal toxicity. However there are a number of things of a dietary nature that we can do that are beneficial, protective, and supportive of good health and the body's own natural chelation mechanisms. Many herbs and supplements have natural chelating characteristics and properties that help to detoxify the body. Curcumin is one of the herb which is used against cadmium toxicity in this experiment. Curcumin (*Curcuma longa* - Haldi) is derived from the spice turmeric and is used in curries and other spicy dishes from India, Asia and the Middle East. Similar to many other herbal remedies, people first used curcumin as a food and later discovered that it also had impressive medicinal qualities. It has been used extensively in Ayurveda (Indian system of Medicine) for centuries as a pain relieving, anti-inflammatory agent to relieve pain and inflammation in the skin and muscles. It has also been attributed to have anti-cancer properties.It acts as a free radical scavenger Curcumin acts as a strong anti oxidant, anti inflammatory, antibacterial, Antiamoebic, antiHIV27, anticarcinogenic and antibacterial agent [17,18].Histopathological studies help in evaluating the extent of damage caused to any tissue on exposure to toxic substances.[19,20], .Therefore, the present study has been undertaken to evaluate the ameliorating effect of curcumin on cadmium induced oxidative damage in the epididymis of adult male albino mice.

MATERIALS AND METHODS

Chemicals: Cadmium chloride (Molecular weight = 201.32) was obtained from Glaxo company (India). Cur cumin was purchased from Loba Chem. Pvt. Ltd . All the other chemicals and solvents used were of analytical grade.

Animals and treatment: The study was conducted after taking prior approval by Institutional Animal Ethical Committee (No.CS\Res\07\759), on adult male Swiss albino mice 32-50 days old and weighing around to 30-40g.These were maintained in plastic cages under controlled lighting conditions (12:12 light: dark cycle) relative humidity (50 ± 5%) and temperature(37 ± 2°C), fed with mice feed and water was given adlibitum..

Experimental Protocol: A group of 6 mice per experiment were taken for the study. The doses of cadmium chloride were prepared fresh in distilled water and were administered by gastric gavages. Different doses were selected for the study and were administered at different time intervals.

Group 1: Mice were administered only the vehicle. The group served as control.

Group 2: Mice were administered cadmium chloride at a dose 50mg/kg/animal/day for a day.

Group 3: Mice were administered curcumin (10mg/animal/day) for 15 days

Group 4 : Mice were pretreated with curcumin (10mg/animal/day) for 15 days and subsequently administered $CdCl_2$ 50mg/kg/animal for a day

HISTOLOGICAL PREPARATION

After administration of last dose, the control and the experimental animals were sacrificed by cervical dislocation. After dissection both the epididymis were taken out, weighed and fixed in Bouins solution for 24 hours and then transferred to 70% alcohol for prolonged washing to remove excess of picric acid from the tissues. Subsequently, the epididymis was further promoted for paraffin embedding. Routine 5-6 µ thick sections were cut with a rotary microtome. The deparaffinized sections were stained with haematoxylin and eosin stains. Appropriate sections were observed under the microscope and photographed.

HISTOPATHOLOGICAL FINDINGS AND RESULTS

The caput, corpus and cauda epididymis of control group mice administered only vehicle showed normal histopathology. Endothelium of the epididymal capillaries appeared normal. Control group did not showed any damage in histopathological profile of epididymis. Clear cells were visible in the cauda epididymis. In control caput epididymis the entire cell types- principal cells, basal cells, apical cells and halo cells were seen distinctly**(Fig.1-4).** .

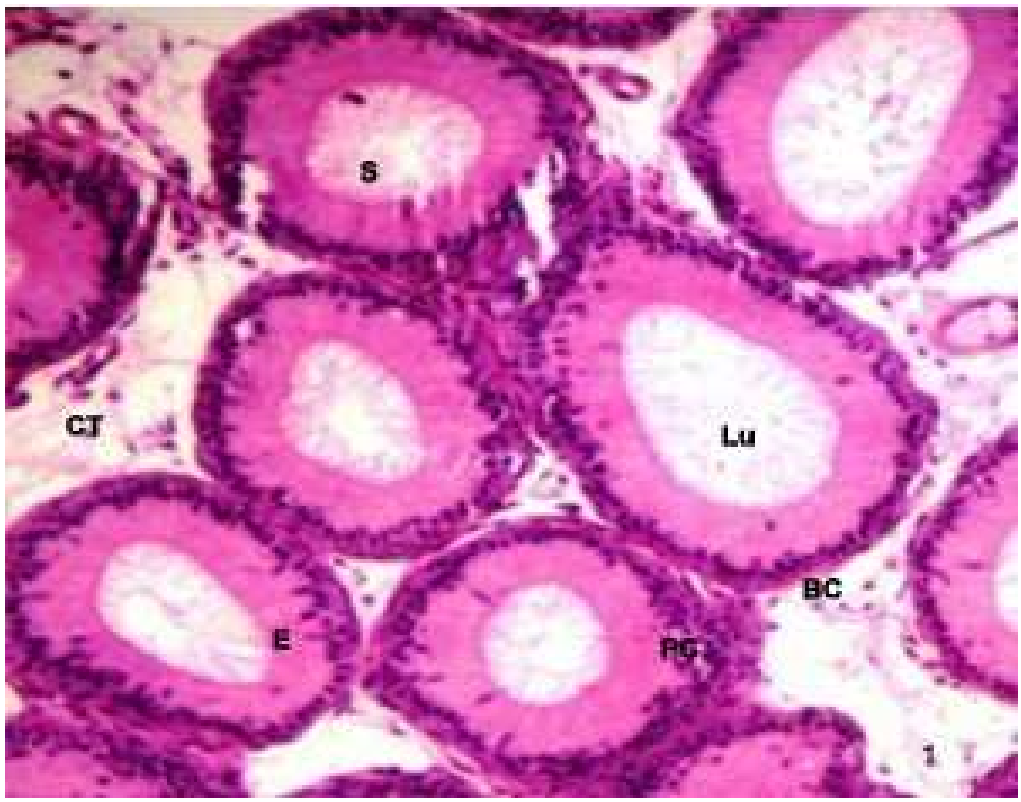

Fig. 1: T.S. of Caput epididymis showing normal histoarchitecture with presence of epithelium (E), sperms (S), basal cells (BC),principal cells (PC) and connective tissue (CT)(10x).

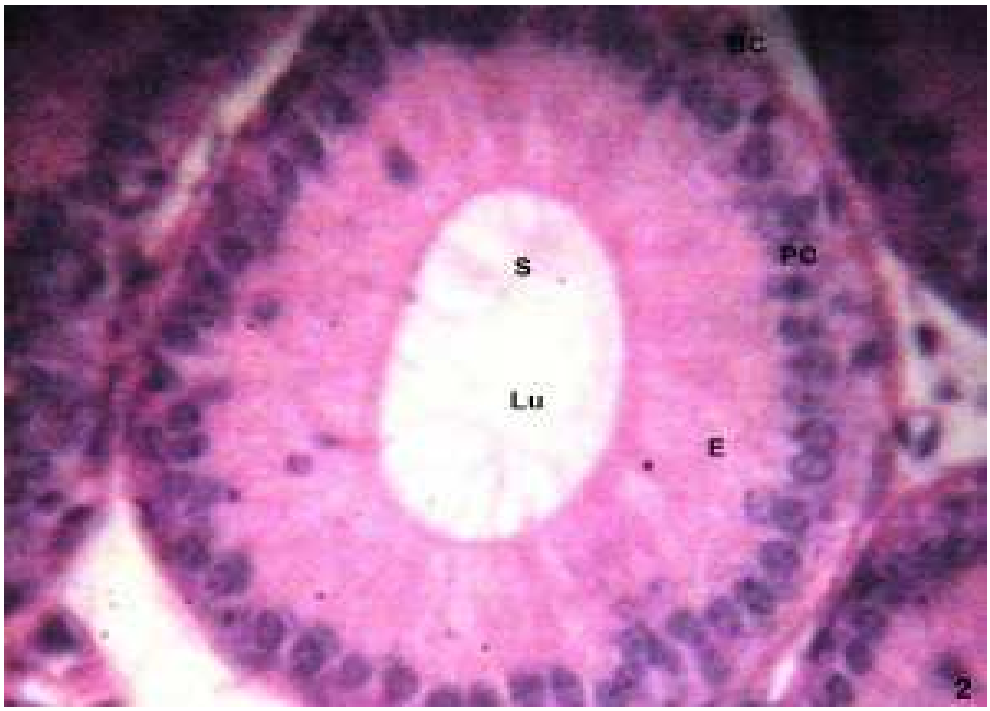

Fig.2 T.S. of Caput epididymis showing normal epithelial (E) histoarchitecture. Sperms(S) are distinctly visible in lumen (Lu) (40x).

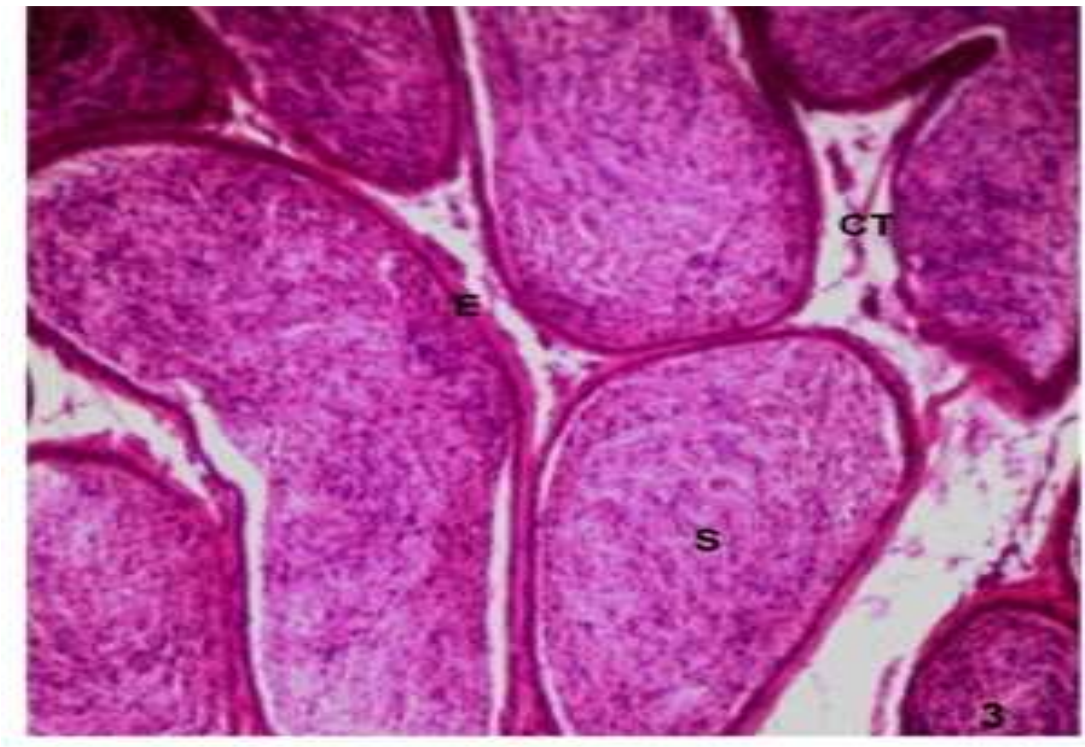

Fig.3. T.S. of Cauda epididymis showing lumen filled with mature sperms (S). (10x).

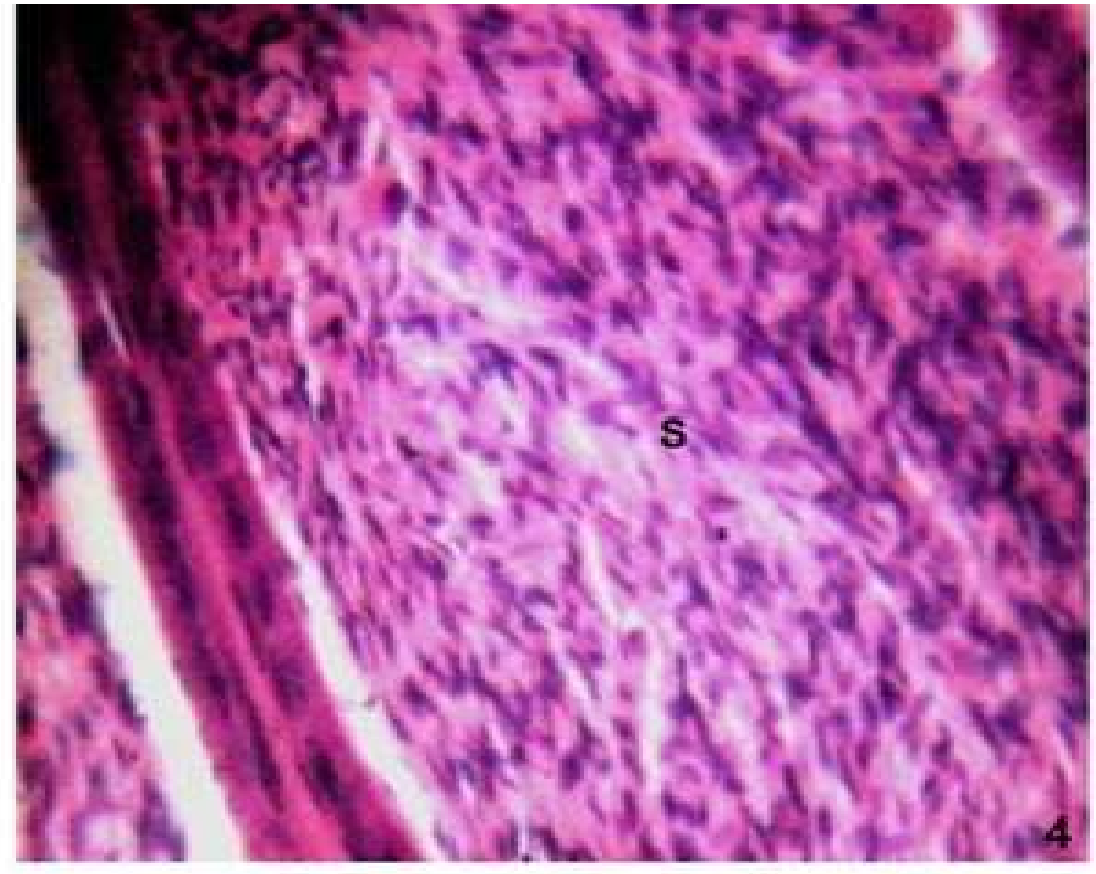

Fig.4. T.S. of normal cauda epididymis showing lumen filled with mature sperms (S). (40x).

In parallel experimental groups which were treated with curcumin (10 mg/animal/day), it was discerned that the histoarchitecture of epididymis was same as that of the control group animals. There was no discernible microscopic alterations in either the spermatozoa or the epithelial lining cells of the cauda epididymidis The lumen was seen to be full of spermatozoa**.(Fig,1-4)**

Mice which were administered with a dose of cadmium chloride 50 mg/kg/ animal for a day showed altered histopathological profile with induction of necrosis and degenerative changes of different degrees as evidenced by oedematous swelling, milieu cytostatic and cytotoxic changes in the cauda epididymis etc. hemorrhage of its vasculature and degenerated epithelium was also observed and the overall shape of epididymis was not altered. Caput epididymis showed degenerated empty tubules. **(Fig. 5-6).** Cauda epididymis showed thickening of muscular layer and spermatozoan population appeared to be pushed to a side in the lumen **(Fig.9)**

In this study, treatment of mice with cadmium chloride caused marked changes in the histology of both the caput and cauda epididymis. It is likely that these structural alterations would affect its epithelium and biochemical makeup and subsequently its internal structure thereby making it nonconductive for sperm maturation and survival**.(Fig.5-6 and Fig.9).**

Pre treatment with curcumin for 15 days did not cause any structural distortion and the normal histoarchitecture of epididymis was maintained. Lumen showed presence of sperms and overall degeneration and disarrangement was checked to some extent **(Fig.7-8 and Fig.10).**

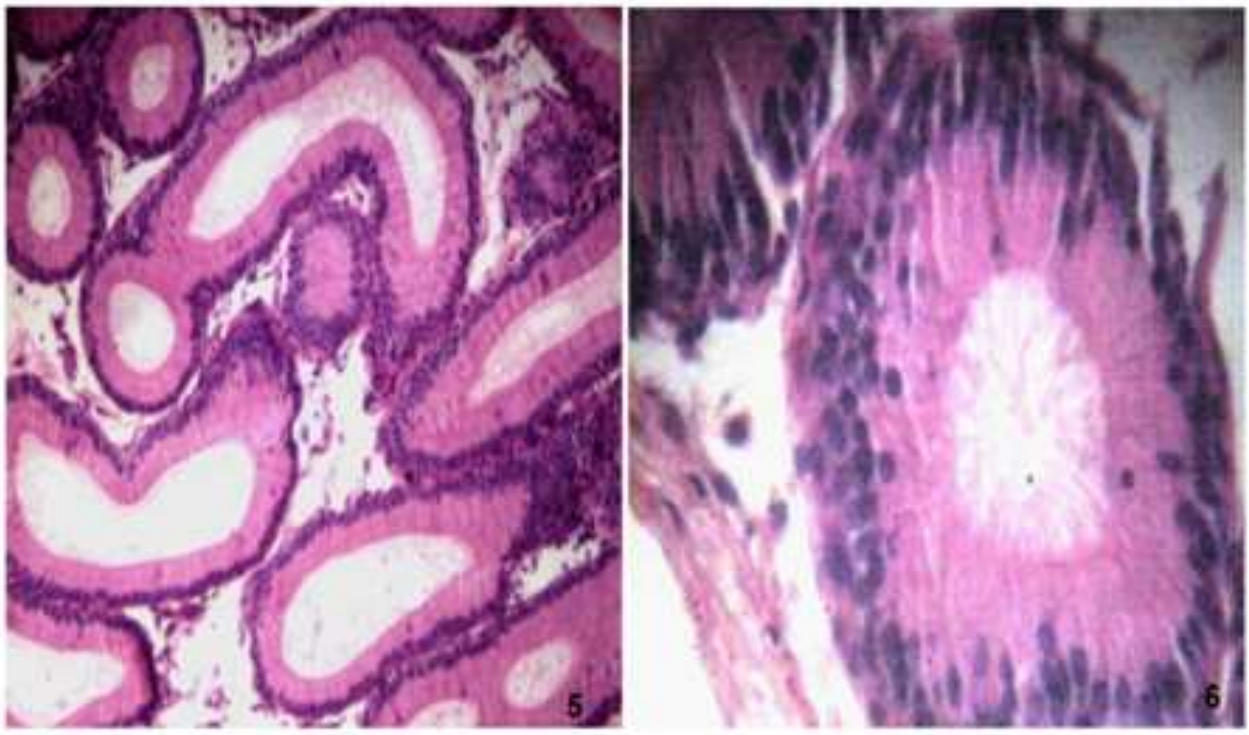

Fig. 5 and 6: T.S. of caput epididymis of Cd treated groups showing degenerated interstitial layer (b) and dearrangement of cells (c). (40x).

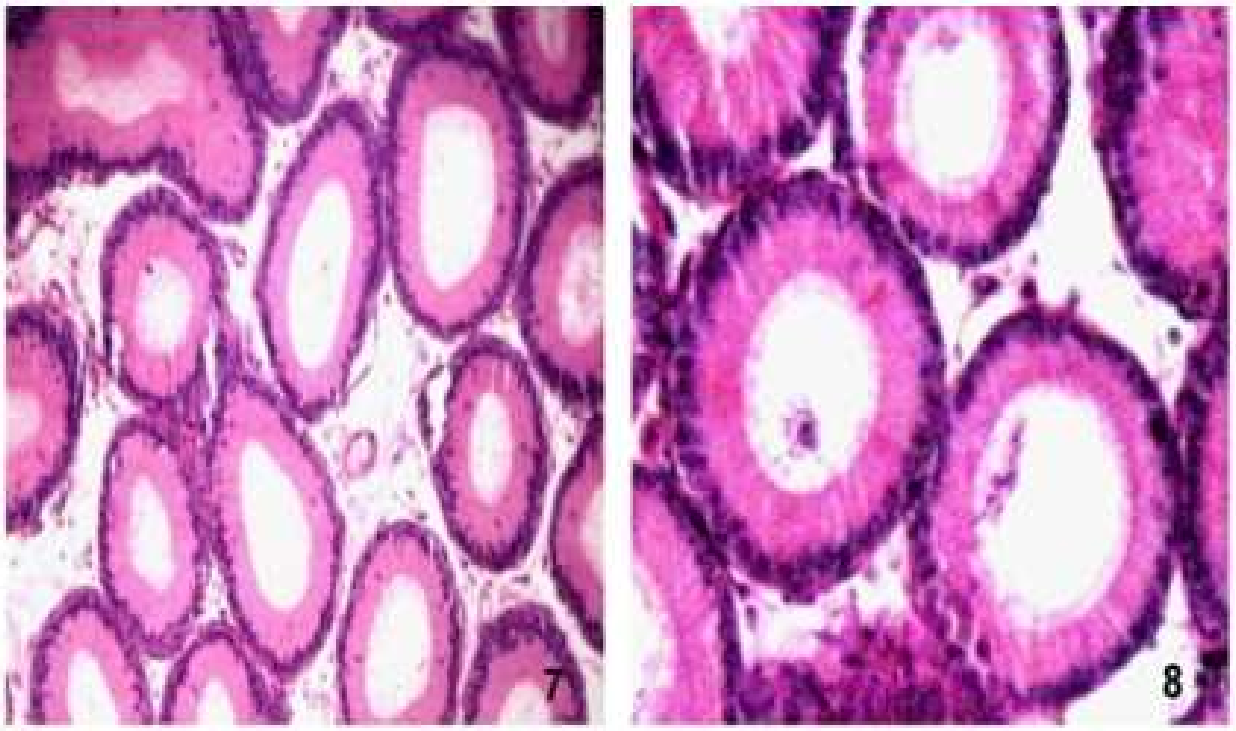

Fig. 7 and 8: T.S. of caput epididymis of pre treated groups showing less degeneration of interstitial layer. (10x, 40x).

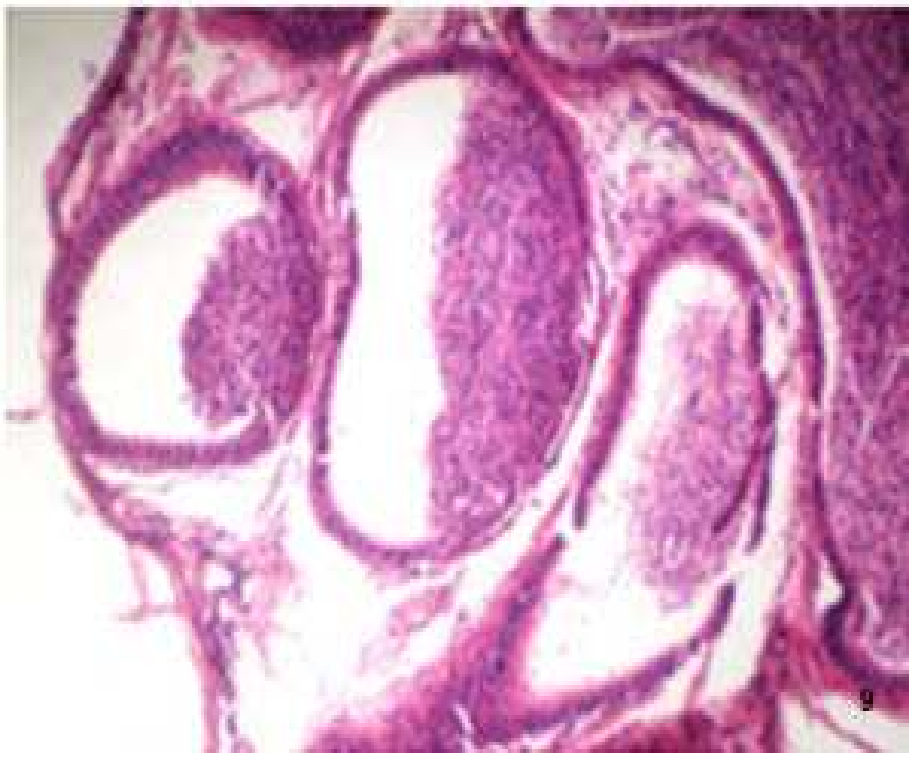

Fig. 9. T.S. of cauda epididymis of cadmium treated group showing empty lumen. (40x).

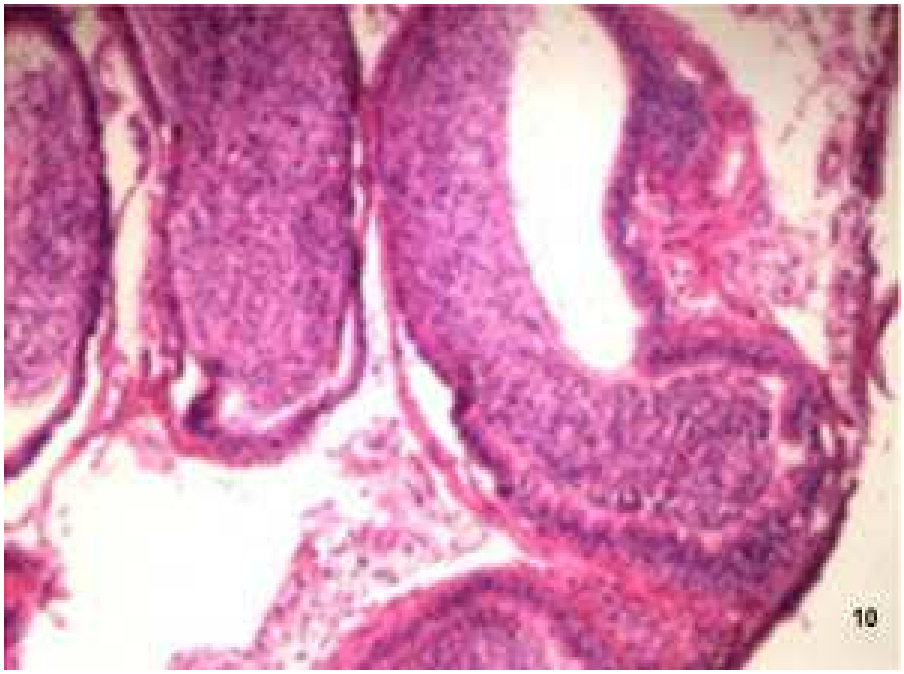

Fig. 10. T.S. of cauda epididymis of pre treated groups showing normal spermatozoan population. (40x)

It is well evidenced that epididymis is the organ of sperm maturation and any structural alteration would adversely affect its function. In the present study it was observed that cadmium exposure results in alteration of epididymis histoarchitecture and these observation are similar to the observation of Gunn[14] who emphasized that the spermatozoa of the proximal end of the caput are completely destroyed with in the first two days after the administration of cadmium ,the more distil part of epidedymis appear

unharmed at this time. It was also observed that cadmium exerts a selective toxic effect on the blood vessels of the caput epididymis [14, 16, 21].

Mason et al[21]. reported that a single peritoneal administration of soluble cadmium causes an acute haemorrhage reaction in proximal end of caput epididymis .It was reported that the epididymis 40 hr after cadmium revealed changes in one area onlya haemorrhagic reaction in the proximal end of the proximal end of the caput .The lining epithelium of the proximal caput was atrophied , the tubules were dilated and spermatozoa within the lumina were disintegrated. Gunn et al[22] and . Saksena [23] reported an injection of 5 mg $CdC1_2$ caused severe histopathological alterations in epididymis. Seven days after the treatment of 1 mg $CdC1_2$, the weights of the caput and cauda epididymis were not affected; however, significant weight loss was that of the cauda epididymis but not that of the caput epididymis which was recorded 15 days after treatment of 1 mg $CdC1_2$ administration. Dose and time dependent response on sperm population in different segments of the reproductive track was observed. Substantial loss of spermatozoa occurred in each segment of the epididymis. Ibrahim and Sameh[13] reported exposure to cadmium can negatively affect the male reproductive system via degenerative changes in epididymis. Amara et al [24] reported subchronic exposure to cadmium significantly decreased epididymal sperm number,percentage of total motile spermatozoa. Borde et al[25] reported that cadmium chloride causes reduction in weight of epididymis which was ameliorated on administration of Withania somniera. Monsefi et al [26.] reported that the high dose administered cadmium group show decrease sperm count, sperm motility and sperm maturity. All these reports justify the results of the present study where a single exposure to cadmium resulted in gross alteration in histopathological profile of epididymis.

In the present study it was also discerned that curcumin has the potential to protect epididymis from cadmium induced toxicity ,however no deliberations are possible due to paucity of available information. Hence this study is making available primary information in this field.

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