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A REVIEW ON ORGANOCHLORINE PESTICIDES AND REPRODUCTIVE TOXICITY IN MALES

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ABSTRACT: Today, humans and wildlife are constantly exposed to thousands of chemical residues, through air, food and water. Organochlorines are widespread pollutants and comprise a variety of compounds containing carbon, hydrogen, and chlorine. Chlorinated insecticides, solvents, and fumigants are widely used around the world. Exposure to organochlorine chemicals has been associated with many deleterious effects on human health. Concerns have been raised about their implication in reproductive toxicity and endocrine disruption, because organochlorine chemicals persist in the environment. Organochlorines interfere with normal hormonal function in animals and humans. Reproductive abnormalities, including feminization of males, abnormal sexual behavior, birth defects, altered sex ratios, decreased sperm production, reduced testicular size, infertility, and thyroid dysfunction, have been reported in laboratory animals and wildlife exposed to endocrine-disrupting chemicals. This review deals with adverse effects of different organochlorine chemicals on male reproductive system, thus indicates limited use of organochlorines to improve the quality of life for human welfare.

INTRODUCTION: Severe environmental pollution and health hazards may occur due to the widespread use of pesticides in public health and agriculture; these include cases of severe, sub-chronic and chronic human poisoning [1, 2]. Pesticide hazards to man and environment are extended to developing as well as developed nations [3, 4]. Oxidative stress may be induced by pesticides, leading to generation of free radicals and alteration in antioxidants, oxygen free radicals, the scavenging enzyme system, and lipid peroxidation which may contribute to the toxicity of pesticides [5, 6, 7].

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The four main groups of pesticides are organochlorine, organophosphate, carbamate, and pyrethroid insecticides [8, 9]. Pesticides are still used on a large scale in developing countries and continue to pose severe concern because of their toxicity and persistence in the environment. There is a need to create awareness among the farmers on Integrated Pest Management, as farmers in developing regions seem to treat pesticides as substitutes for fertilizers [10]. Pesticide toxicity can result from ingestion, inhalation or dermal absorption.

In humans, exposure to environmental contaminants may cause impaired fertility, altered birth-sex ratio, declining sperm count and quality, and undescended testes [11]. However, the association between altered reproductive health and exposure to environmental pollutants remains a subject of controversy. One group of environmental

pollutants includes chlorinated pesticides and polychlorinated biphenyl (PCBs), collectively termed organochlorines. Organochlorines are present in the environment and contaminate food chains throughout the world despite being banned in many developed countries because of their resistance to degradation and long-range atmospheric transport [12].

Human exposure to organochlorine insecticides is an important issue in human health. The resistance of these compounds to environmental degradation has raised concerns regarding their ability for bioaccumulation and potential public health impact [13]. Reproductive toxicants may produce an adverse effect by one of several mechanisms. Some xenobiotics interrupt reproduction directly, either by virtue of chemical reactivity or structural similarity to endogenous molecules; and other xenobiotics interrupt reproduction indirectly either by metabolism to a direct-acting toxicant or by endocrine alterations [14]. The toxicity of these agents varies according to their molecular size, volatility, and effects on the CNS. In general, they cause either CNS depression or stimulation, depending upon the agent and dose [15].

Organochlorine compounds can be separated into 5 groups, as follows:

- Dichlorodiphenyltrichloroethane (DDT) and analogues (eg, dicofol, methoxychlor)
- Hexachlorocyclohexane (ie, benzene hexachloride) and isomers (eg, lindane, gamma- hexachlorocyclohexane)
- Cyclodienes (eg, chlordane, heptachlor, aldrin, dieldrin, endrin, endosulfan, isobenzan)
- Chlordecone, kelevan, and mirex
- Toxaphene

Human exposure to organochlorine substances may occur by inhalation of air, ingestion of food and water and skin absorption [16]. Major route of exposure to these substances is via food (and not drinking water) because of the bioaccumulation of organochlorines in fish and other animals that humans consume [17]. Another route of exposure is through the long term and regular skin absorption of cosmetic products that contain organochlorines or other endocrine disrupters [18]. The regular application of a variety of cosmetics with estrogenic activity may lead to the continuous direct dermal exposure and consequently to the absorption and accumulation in underlying tissues [19]. Humans may be poisoned or injured by pesticides. Pesticide poisoning is caused by pesticides that harm internal organs or other systems inside the body. Long term exposure to relatively small amount of organochlorines leads to the accumulation of these substances in human tissues.

Measurements of body burdens of organochlorine substances and their metabolites are good indicators of exposure and help to make associations between exposures and health outcomes [20]. Levels of organochlorines in human tissues are positively associated with age and with rate of consumption of polluted products [21]. It has been observed that vegetarians (i.e. eat all vegetables, fruits and grain with no animal products) have much lower levels of organochlorines compared to individuals who consume animal- based products [22].

1.1. Highly toxic organochlorines

- Aldrin
- Dieldrin
- Endrin (banned by the US Environmental
- Protection Agency [EPA])
- Endosulfan

1.2. Moderately toxic organochlorines

- Chlordane
- DDT (banned by the EPA)
- Heptachlor
- Kepone
- Lindane
- Mirex
- Toxaphene

1.3. Male reproductive toxicity:

Sperm counts are falling at an alarming rate of 2% per annum for the past 20 years [23, 24]. In addition, a significant association was found between exposure to occupationally hazardous chemicals, environmental endocrine disruptors, and decline in semen parameters (sperm count, morphology, and sperm concentration) [25, 26, 27]. The effects of

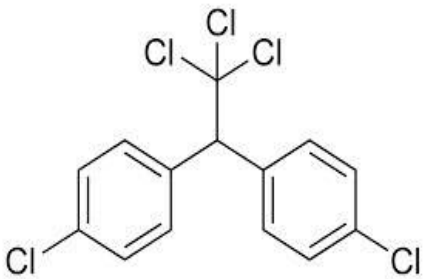
pesticide exposures on male reproductive health are a topic of concern in environmental, occupational and reproductive epidemiology [28-32].

Exposure to environmental contaminants like organochlorines causes decrease in sperm counts, impairment of sperm motility, reduction of fertilization ability, production of abnormal sperm in men and animals. Pesticides exposure cause over-production of reactive oxygen species (ROS), resulting in a decline of sperm count and infertility in wildlife and human [33]. The antioxidant system plays an protective role in testes and other biological tissues [34-36] and ROS has been known to damage macromolecules, including membrane bound polyunsaturated fatty acid (PUFA), causing impairment of cellular function [37]. Spermatozoa are rich in PUFA, and, therefore, could be highly susceptible to oxidative stress. Pesticides affect spermatogenesis through hormonal or genotoxic pathways [38].

The present article reviews the advances in the studies of male reproductive toxicity of the organochlorine pesticides that are widely used and commonly researched in the recent years. The mechanism of male reproductive toxicity of these pesticides is discussed.

1.3.1. DDT:

DDT (1,1,1-trichloro-2,2-bis(p-chlorophenyl) ethane) is the agricultural chemical which was consumed most quantities in the world until the middle of the 1970s. Although it is not so conspicuous to be toxic to the human being, there are several reports concerning carcinogenicity. However, as DDT is a chemically very stable material, the persistence and the accumulation in the body become a problem. The toxicity of DDT analogues is related to a peculiar interaction between the DDT molecule and biomolecules [39].



STRUCTURE OF DDT

DDT, an organochlorine pesticide, has been suspected of having endocrine disrupting effects. According to several researches, DDT and some organic solvents lead to decreased fertility and altered sperm counts [40]. The reproductive toxicity of DDT in adult male rats exposed to 50 and 100 mg/kg body weight (b.wt) day-1 for 10 successive days induced adverse effects on male rat fertility by acting directly on the testes and altering the hormone level. Administration of DDT led to a dose-dependent reduction of testicular weight and the number of motile spermatozoa in the epididymis. Testicular histological observations also revealed a marked loss of gametes in the lumen of seminiferous tubules. In DDT treated animals, testosterone production by testes decreased after pesticide exposure [41].

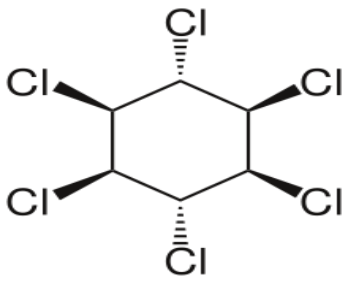
The effects of DDT on workers regularly exposed to it were evaluated by Dalvie *et al.* [42]. The study measured sperm count, density and motility. Normal morphology recording included 2.5 ± 1.8% of the individuals. Most (84%) of the morphological counts were below the WHO and Tygerberg criteria, with the highest individual recording at 6%, which is precisely on the subfertility line according to the Tygerberg criterion. Persistent problems with sexual function extended to 10-20% of the patients. The most prevalent genital abnormality (71%) was abnormal testicular placement.

DDT can also delay puberty [43]. The estrogenic activity of DDT isomers is very weak, but the properties of bioaccumulation and long half-life indicate that human exposure levels can cause estrogenic effects under certain circumstances and act as an androgenic agonist at high doses [44].

Embryonic and postnatal exposure to high doses of insecticides like DDT and its derivatives induced a significant reduction in the seminiferous tubules of the male testis [45]. DDT and its metabolite DDE, have estrogenic effects in males by blocking the androgen receptor [46]. DDT inhibited the cAMP response to follicle-stimulating hormone (FSH), the major endocrine control of Sertoli cell development. DDT exposure decreased the level of FSH binding sites [47].

1.3.2. Lindane:

Lindane, the gamma-isomer of hexachlorocyclohexane, is an organochlorine pesticide widely used as a broad-spectrum insecticide to control pests in agriculture and ectoparasites in both humans and animals [48]. Other uses of lindane include lotions, creams and shampoos for the control of lice and mites (scabies) in humans [49].



Lindane:

Chronic exposure to lindane causes damage to liver, kidney, pancreas, brain, heart, lungs and the nasal mucous membranes [50], and also affects the respiratory, circulatory, excretory and immune systems [51]. Lindane has been reported to cause impairment to various biological functions, including reproduction in humans and animals. It has deleterious effects on various hormone dependent reactions in the male reproductive system. Several studies have revealed that lindane disrupts the reproductive function in male and female animals [52, 53]. In male rats, chronic lindane exposures markedly reduce sperm counts, sperm motility and impair spermatogenesis. In addition, serum testosterone concentrations decrease in lindane intoxication [54-56].

The testes are highly susceptible to lindane as it crosses the blood-testis barrier and depresses spermatogenesis with a numeric reduction in spermatids and fragmentation of Sertoli cells [57]. A few toxicological studies have addressed the possible relationship between reproductive toxicity and exposure to chemicals that generate reactive oxygen species (ROS) [58]. It induces infertility in males and females by decreasing gametogenic and steroidogenic activities in mammals [59, 60]. It causes damage to the male reproduction tract either acting directly on the testes or indirectly through endocrine regulation of the testes [61, 62].

Lindane induces oxidative stress in the testis as well as in the epididymis and sperm dyanamics of adult rats [63-65]. Several studies demonstrated that exogenous treatment with lindane diminishes serum testosterone level, and thus confirmed that lindane acts as an inhibitor on testicular steroidogenesis [66, 67]. It causes alterations in Leydig and Sertoli cells by impairing their functions [68].

Treatment with 1-40 mg of lindane/kg b.wt. disrupts testicular morphology, decreases spermatogenesis, inhibits testicular steroidogenesis, reduces plasma androgen concentrations and may adversely affect reproductive performances in males [69]. Reduced sperm count and an increased incidence of sperm abnormalities have been evidenced as the consequences of exposure to lindane [70]. Furthermore, as an endocrine disrupting chemical, it may interfere with male reproductive performance and fertility.

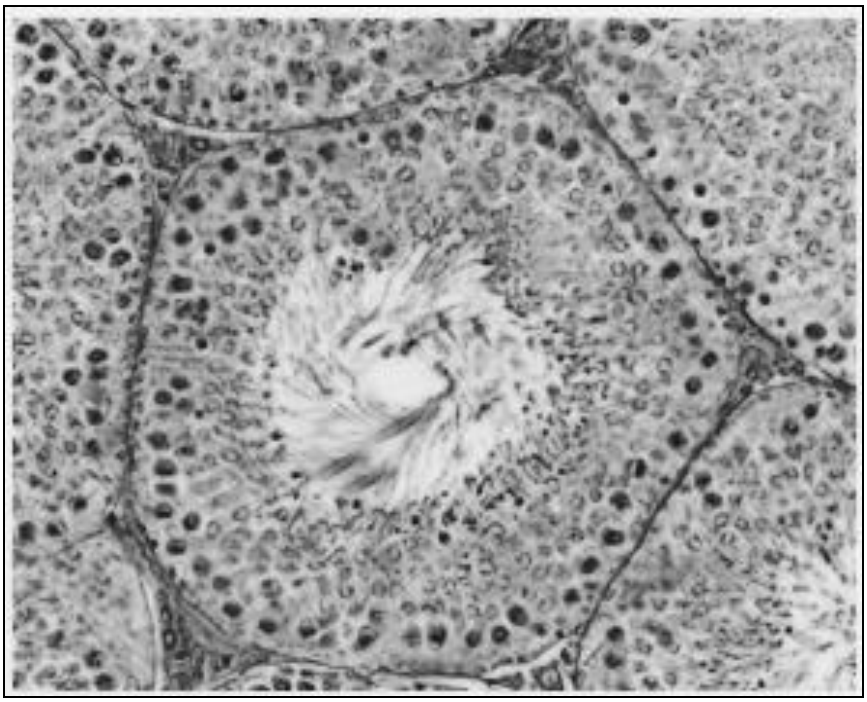
After i.p. treatment of lindane at concentrations of 9 and 18 mg/kg body wt, twice a week for 60 days, sperm numbers decreased by 42% at low lindane dose, while the drop in sperm count in the animals exposed to the higher dose extended to about 50%. Motility decreased by about 45% to 68% at 9 and 18mg/kg b.wt, respectively. After the treatment, relative masses of epididymis and testis also decreased. A histopathological analysis of testicular tissue showed cell disorganization, irregularly shaped cells, with marked intercellular space between the spermatogenic cells [71].

Exposure to lindane during lactation induces reproductive hazards to male offspring rats which are detectable at adulthood. The dams treated with a single dose of 6mg/kg on day 9 or 14 of lactation, or with 1mg/kg on days 9 to 14 of lactation showed reduction in testicular weight and the number of sperm and spermatids in all treated groups at adulthood. The testosterone level of the treated groups significantly reduced to approximately 50% [62].

Oral doses of 6 mg lindane/kg for 5 days or a single dose of 30 mg/kg body weight caused decrease in sperm count in the testes. Histological investigation by electron microscopy revealed a pronounced

ballooning of Sertoli cells accompanied by fragmentation or complete loss of organelles [61].

In our lab, Lindane was evaluated for its effect on reproductive function in male rats. The results revealed that lindane was found to induce marked histopathological and biochemical changes in testes and epididymis (**Fig. 1, 2, 3**). There was a significant decrease in sperm density, sperm motility and serum testosterone level after lindane (10 mg/kg/day for 15 and 45 days) exposure in rats. Mating exposure test revealed that control rats showed 100% positive fertility, whereas 20% and 50% levels of negative fertility were found in rats exposed to lindane for 15 and 45 days at 10 mg/kg dose (**Table 1**).



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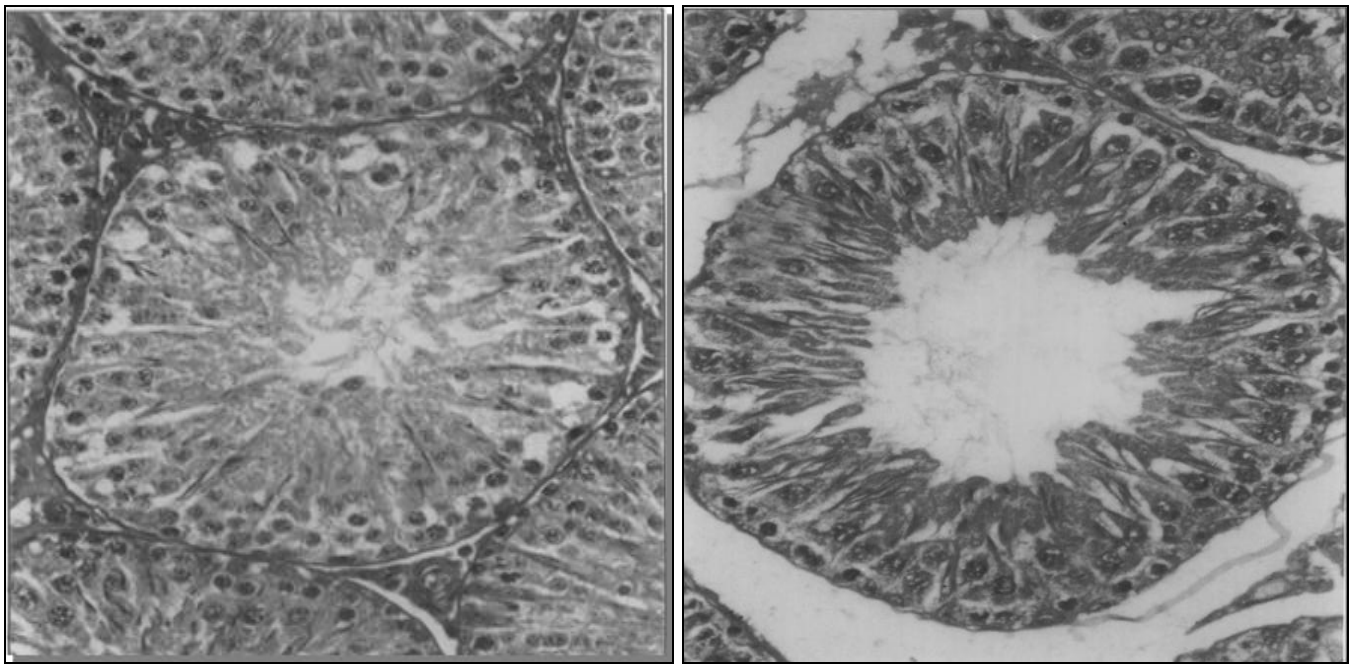
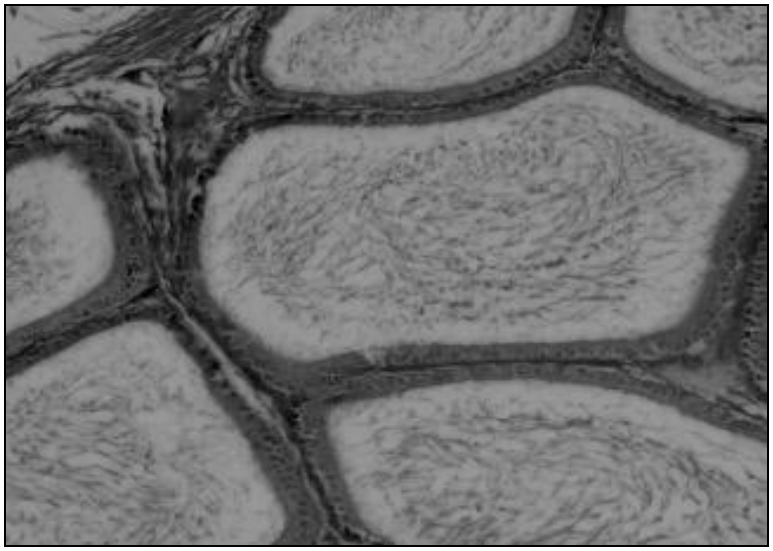


(b) **(c)**

FIG.1: HISTOPATHOLOGY OF TESTES AFTER EXPOSURE WITH LINDANE IN RATS. (a) Testes of control rat, (b) Testes of rat treated with Lindane 10mg/kg b.wt./day for 15 days, and (c) Lindane 10 mg/kg b.wt./day for 45 days



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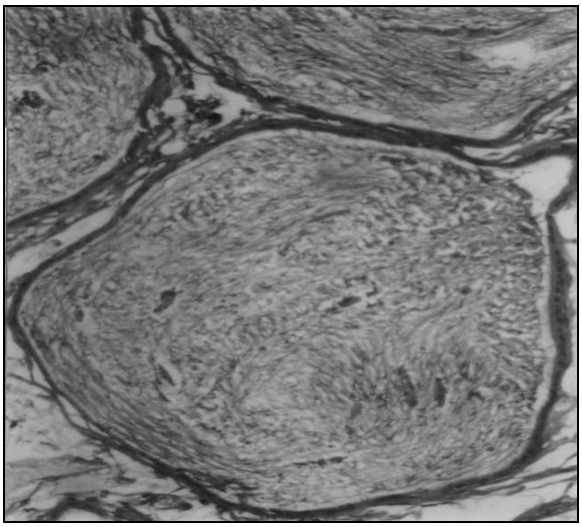

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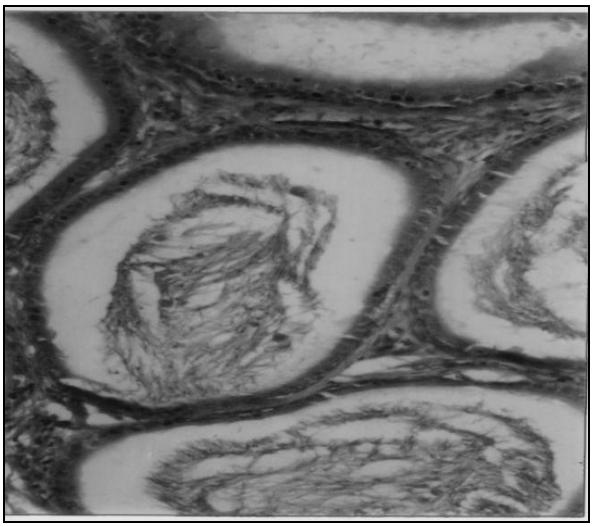
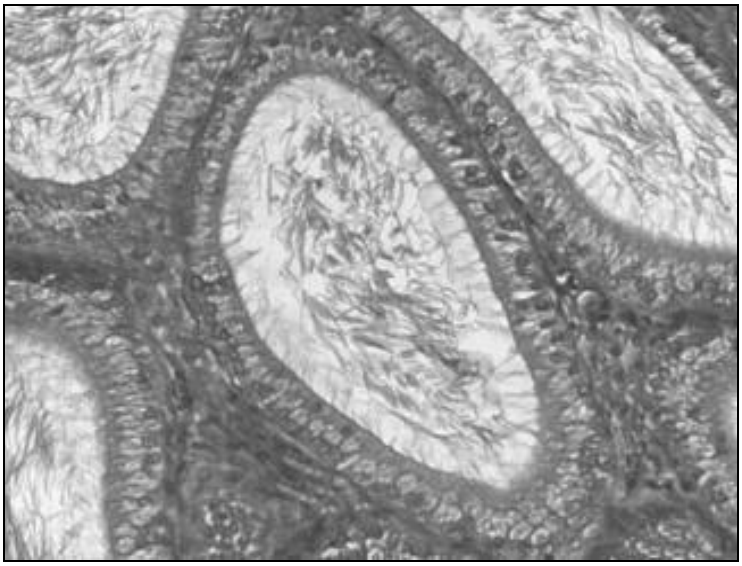


(c)

FIG.2:HISTOPATHOLOGY OF CAUDA EPIDIDYMIS AFTER EXPOSURE WITH LINDANE IN RATS. (a) Cauda epididymis of control rat, (b) Cauda epididymis of rat treated with Lindane 10 mg/kg b.wt./day for 15 days, and (c) Lindane 10 mg/kg b.wt./day for 45 days



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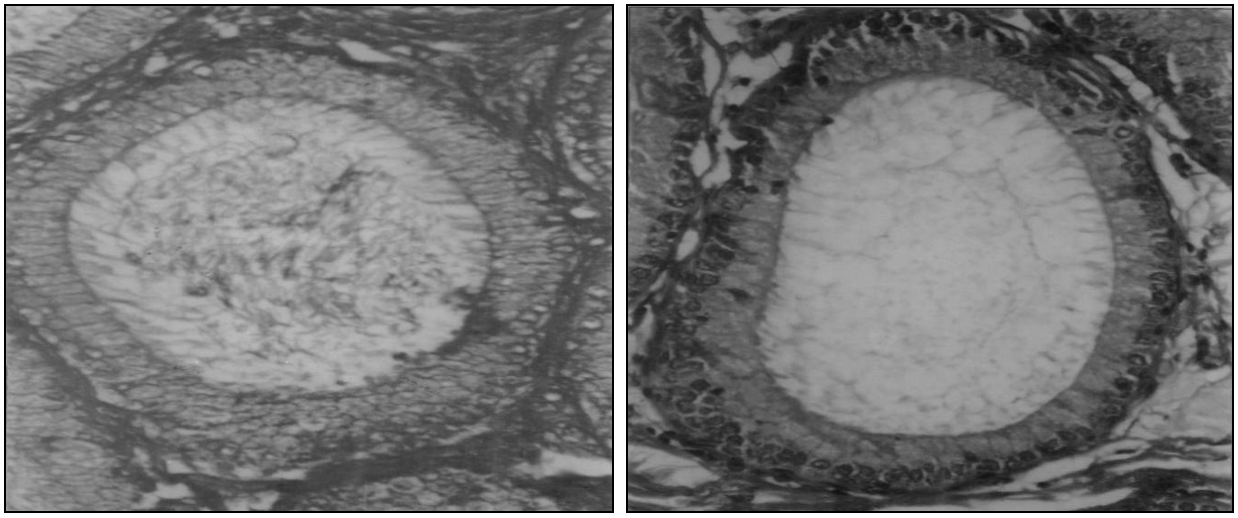


(b) **(c)**

FIG.3: HISTOPATHOLOGY OF CAPUT EPIDIDYMIS AFTER EXPOSURE WITH LINDANE IN RATS. (a) Caput epididymis of control rat, (b) Caput epididymis of rat treated with Lindane 10 mg/kg b.wt./day for 15 days, and (c) Lindane 10 mg/kg b.wt./day for 45 days

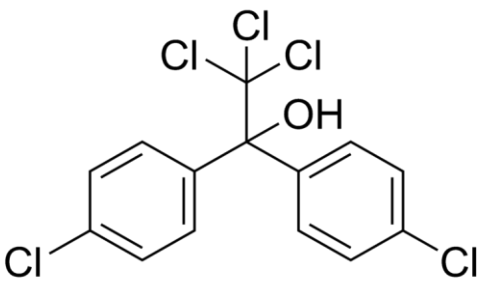
TABLE 1: SPERM DYNAMICS, FERTILITY ANALYSIS AND TESTOSTERONE LEVEL AFTER EXPOSURE TO LINDANE

Treatment	Sperm motility (%)	Sperm density (million/ml)	Sperm density (million/ml)	Fertility (%)	Testosterone
	Cauda epididymis	Cauda epididymis	Testes		
Group I (Control: vehicle treated)	66.83 ± 1.39	20.92 ± 1.69	4.32 ± 0.12	100%(+)ve	2.65 ± 0.02
Group II (10 mg/kg b.wt./day for 15 days)	63.64 ns ± 1.30	16.31 ± 0.69	4.20ns ± 0.06	20%(-)ve	2.50ns ± 0.05
Group III (10 mg/kg b.wt./day for 45 days)	32.42** ± 8.03	10.93** ± 1.73	1.76** ± 0.67	50%(-)ve	0.86** ± 0.06

(Mean ±SEM of 10 Animals), Group II and III compared with group I, ns = non-significant, * = significant (P<0.01), ** = highly significant (P<0.001)

Dicofol:

Dicofol, an organochlorine acaricide, is used widely on agriculture crops and ornamentals and in or around agricultural and domestic buildings for mite control [72]. It tends to accumulate in steroid producing organs such as adrenal gland, testes and ovary [73], and has antispermatogenic and antiandrogenic properties [74].



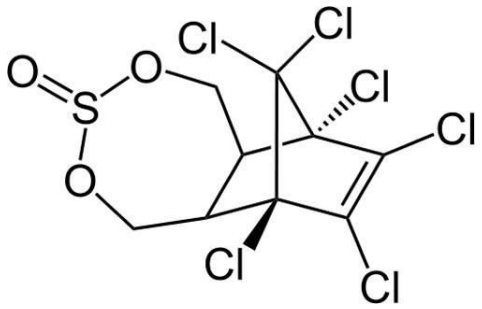
DICOFOL

Organochlorine pesticides caused impairment of the testicular functions through altering the activities of relevant enzymes [75, 76]. Male albino rats orally administered with dicofol at 4.19 and 16.75 mg/kg body weight/day through drinking water (30 and 120 part per million, respectively) for consecutive 90 weeks showed decrease in sperm count, sperm motility, viability and maturity and increased abnormal sperm morphology.

Moreover, decline in serum testosterone, FSH and LH levels. An elevated LPO index associated with depletion in glutathione level were also observed. Dicofol increased total protein level in testes and decreased the activities of the enzymes responsible of spermatogenesis, i.e. lactate dehydrogenase, acid and alkaline phosphatase activities [77].

Endosulfan:

Endosulfan (6, 7, 8, 9, 10, 10–hexachloro–1, 5, 5a, 6, 9, 9a–hexahydro–6, 9–methano–2, 4, 3–benzodioxathiepin–3–oxide) is a pesticide belonging to the chemical family of organochlorines. Endosulfan is a contact and stomach insecticide for food and non–food crops and it is toxic to fish and other aquatic organisms. It consists of two isomers (alpha-: 64–67%; beta-: 29–32%), the alpha-isomer is more toxic to insects and mammals than the beta-isomer [78].



ENDOSULFAN

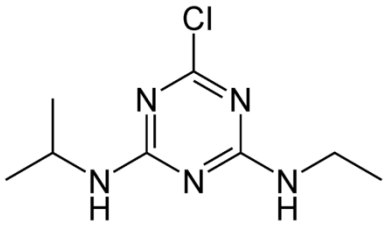
According to Saiyed *et al.*,, in boys exposure to endosulfan can delay sexual maturity and interfere with hormone synthesis [79]. Endosulfan exposure may delay sexual maturity and interfere with hormone synthesis in male children [80]. Endosulfan may cause decrease in semen quality, increase in testicular and prostate cancer and an increase in defects in male sex organs [81]. Biochemical changes in endosulfan treated testes of rats were observed. Endosulfan treatment in pubertal rate inhibits testicular functions [76].

After treatment of male mice with the dose of 3 mg/Kg b.w of endosulfan for 35 days, loss of sperm tail, degenerated acrosome, coiled tail and declined Testosterone and inclined LH were observed which confirm the testicular dysfunctions and finally leads to infertility [82]. In testes, degenerative areas and decreased number of spermatozoon are noticeable in subacute poisoning in male rabbits [83].

Endosulfan exposure to younger animals (3 weeks old) at a dose of 2.5 mg/kg/day revealed marked decrease in daily sperm production [84]. Exposure of pregnant rats to endosulfan at 1 mg/kg/day from day 12 through parturition leads to decreased spermatogenesis in offspring [85, 86].

Atrazine:

Atrazine (2 – Chloro – 4 ethylamino -6-isopropylamino-S-trazine) is a selective, pre and post–emergence herbicide used on a variety of food crops, non-food crops, forests, residential turf, golf course turf, and recreational areas [87].



ATRAZINE

Adult rats were treated i.p. with 60 and 120 mg atrazine kg (-1) body wt. twice a week over 60 days revealed increased testicular sperm number with the treatment time due to the reduced sperm motility [88]. Histological analysis of testicular tissue from treated rats showed the cell disorganization and cell clusters together with spermatocytes. Leydig cells of irregular shape were evaluated by electron microscopy. In Sertoli cell cytoplasm, atrazine treatment caused degenerative changes. Atrazine reduced the semen quality in workers exposed to it [89]. *In vivo* exposure to atrazine affects Leydig cell steroidogenesis due to inhibition of steroidogenesis gene expression, which is accompanied by decreased androgenesis as atrazine might have the ability to interfere with testicular steroidogenesis [90].

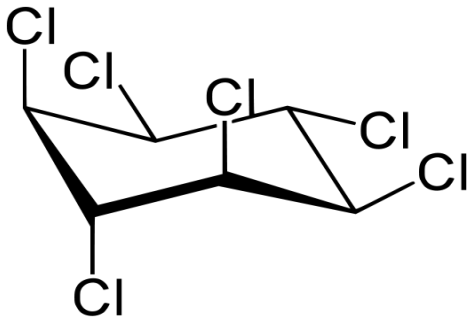
Atrazine could disrupt endocrine function of male reproduction at doses of 200 and 300 mg/kg BW for 28 days for 1, 14 and 28 days. Treated groups revealed that sperm count, number of viable sperms and number of normal moving sperms were significantly decreased but number of abnormal sperms was high. Histological examination also showed decreased number of spermatid and spermatocyte layers [91]. Chronic exposure to ATR can cause histological damages on testicular tissue by inducing remarkable inflammation associated with severe oxidative stress. Also it could be considered as a potent toxic compound against sperm quality [92].

Nanomolar concentration of atrazine has deleterious effects on testicular structure including fine morphology and severely impaired the

spermatozoa formation and finally affects the reproductive potential [93]. Atrazine probably decreases the secretion of LH, FSH and testosterone concentrations through reducing the pituitary weight and secretion of GnRH from hypothalamus, thereby, decreasing the activities of pituitary-testis axis and spermatogenesis processes [94, 95].

Hexachlorocyclohexane (HCH):

HCH exposure at dose level of 50 mg or 100 mg/kg body weight/day (5 days in a week for 120 days) results in a decrease in epididymal sperm count, sperm motility and an increase in the percentage of abnormal sperm. Significant quantities of HCH and its isomers accumulated in testes as well as sperm of treated rats. HCH exposure also led to a decrease in serum testosterone levels [54].

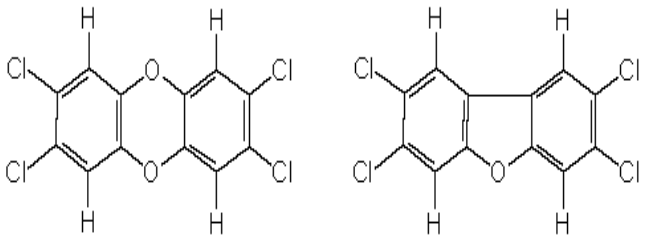


HEXACHLOROCYCLOHEXANE

HCH testicular toxicity may be due to induction of oxidative stress in rat testis following acute and chronic treatment of the pesticide [96, 97]. HCH is known to affect the testicular function in both rats and mice [98, 99]. A direct inhibitory action of g-HCH on testicular steroidogenesis through reduction in the classical second messenger (cAMP) production has also been reported in cultured rat Leydig cells [66].

Dioxin:

Dioxin is the popular name for a class of organochlorines known as polychlorinated dibenzo-p-dioxins (PCDDs) or dibenxofurans (PCDF). Dioxins are a class of persistent polychlorinated aromatic hydrocarbons and some of the most potent environmental contaminants that induce a wide spectrum of toxic responses in experimental animals, including reproductive, developmental and immunologic toxicities as well as carcinogenicity [100].



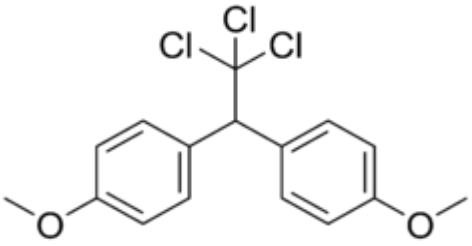
2,3,7,8-TCDD 2,3,7,8-TCDF

Dioxins can affect libido and fertility, causing changes in the sexual behavior of male fish, birds, mammals, and reptiles. The reproductive system has even been considered the most sensitive "end point" for dioxins [44].

2,3,7,8 Tetrachlorodibenzo- p-dioxin (TCDD) is a well known dioxin formed as an unwanted byproduct in the manufacture of chlorinated hydrocarbons. TCDD can interfere with libido. The effects of high exposure to TCDD and "TCDD-like" compounds on important sites for development and reproduction have been also been evaluated by Eskenazi and Kimmel [101]. It decreases the antioxidant enzymes through induction of reactive oxygen species and thus induces oxidative stress in the epididymis and epididymal sperm [102]. TCDD exposed male rats displayed decreased numbers of sperm and increased numbers of abnormal sperm in the epididymis [103]. Male rats exposed to TCDD showed reduced fertility, delayed puberty and altered reproductive organ weights [104]. TCDD can have an anti-androgenic and anti-estrogenic effect [101], inducing a decrease in the testicular response to LH [105].

Methoxychlor:

Methoxychlor (MXC; 1,1,1-Trichloro-2,2-bis(4-methoxyphenyl)ethane) is an estrogenic organochlorine pesticide that has been shown to cause adverse reproductive outcomes in mammalian males and females [106,107].



METHOXYCHLOR

Methoxychlor has gained immense attention due to its widespread usage as an insecticide. It is widely used as a substitute for non-degradable DDT and is now considered to be a major endocrine disruptor. Methoxychlor is weakly estrogenic [108], but its metabolite, 2,2-bis-(p-hydroxyphenyl)-1,1,1-trichloroethane (HPTE) exhibits more potent estrogenic, anti-estrogenic, and antiandrogenic activities than the parent compound [109].

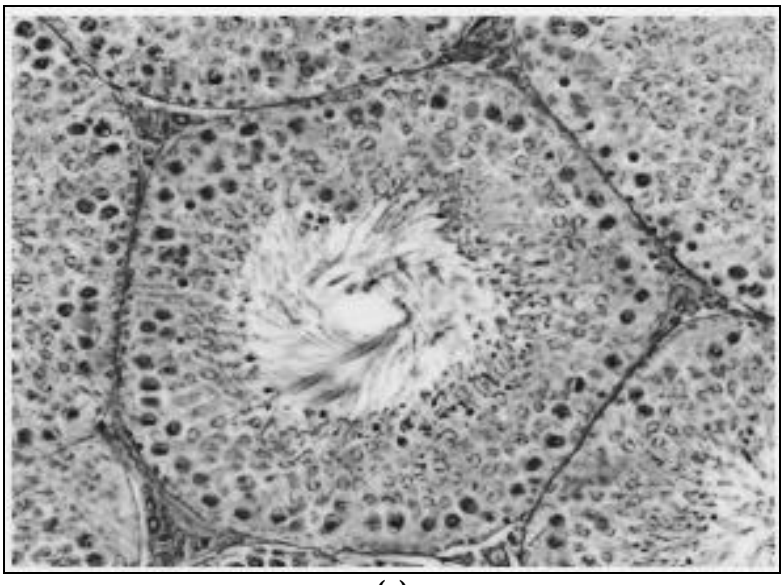
Latchoumycandane and Mathur reported decreased weights of the testis, epididymis, seminal vesicles and ventral prostate in methoxychlor treated rats [110]. The activities of antioxidant enzymes such as superoxide dismutase, catalase, glutathione reductase and glutathione peroxidase decreased in testes. The levels of hydrogen peroxide generation (H2O2) and lipid peroxidation increased in testis of the rats treated with methoxychlor [111].

Administration of methoxychlor at a dose level of 200 mg/kg body weight for 7 days has been shown to reduce seminal vesicle weight, serum testosterone and dehydroepiandrosterone levels in rats [112]. In rats exposed to methoxychlor during the developmental period, reproductive impairment was observed [113].

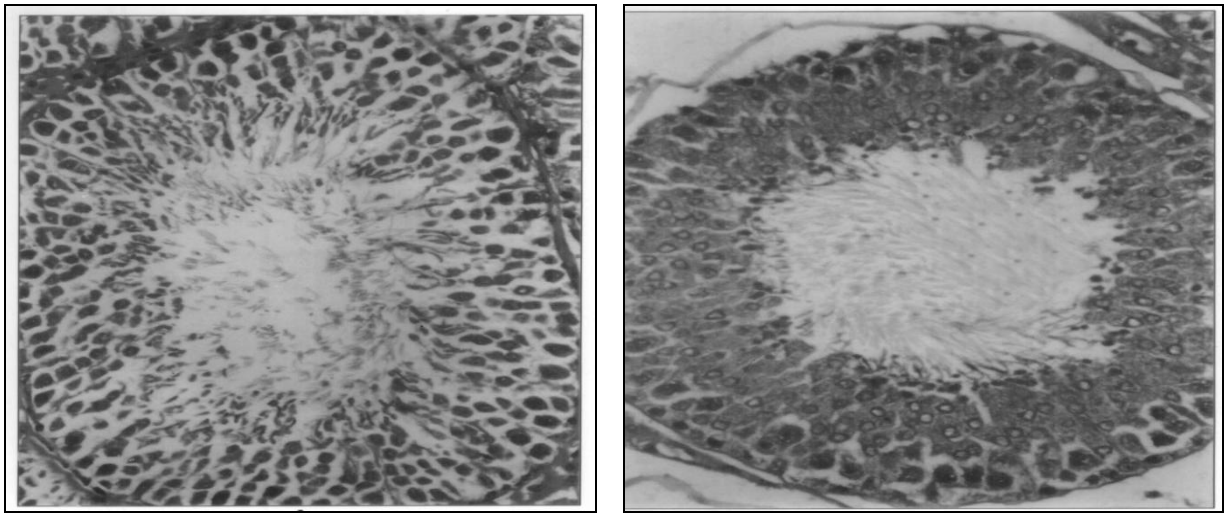
Methoxychlor reduced testicular steroidogenesis, interstitial fluid testosterone content, and spermatogenesis when administered to prepubertal rats, suggesting a direct effect on Leydig cells [114]. In addition, *in vitro* exposure to HPTE has been reported to inhibit side-chain cleavage enzyme (P450scc) and decrease utilization of cholesterol in Leydig cells of rat [115]. It has been shown that methoxychlor induce oxidative stress in the epididymal sperm of goat. The excessive generation of ROS has been shown to cause peroxidative damage to the plasma membrane, which leads to impaired sperm function [116].

HPTE (2,2 - bis(*p*-hydroxyphenyl) - 1,1,1-trichloroethane), the biologically active metabolite of methoxychlor, has the capacity for direct inhibition of 3β-HSD and 17β-HSD3 enzyme activity. Inhibition of enzyme activity is presumably associated with suppression of steroidogenesis in gonadal tissues and has implications for testis function [117].

Methoxychlor was evaluated in our lab for investigating its effect on reproductive function in male rats. The methoxychlor caused marked histopathological changes in testes and epididymis (**Fig. 4, 5, 6**). There was a significant decrease in serum testosterone after methoxychlor (20 mg/kg/day for 15 and 45 days) exposure in rats (**Table 2**). Mating exposure test revealed that control rats showed 100% positive fertility, whereas 40% and 70% levels of negative fertility were found in rats when exposed to methoxychlor for 15 and 45 days at 10 mg/kg dose. Reductions in sperm motility and sperm count in cauda epididymides and testicular ducts were also seen (**Table 2**).

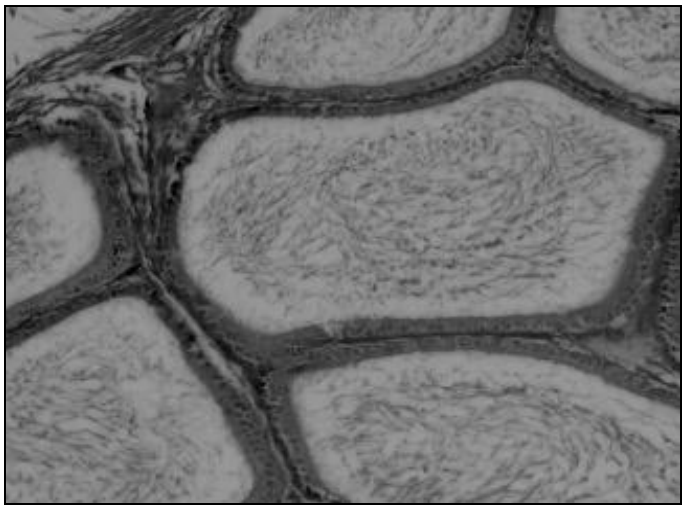


(a)

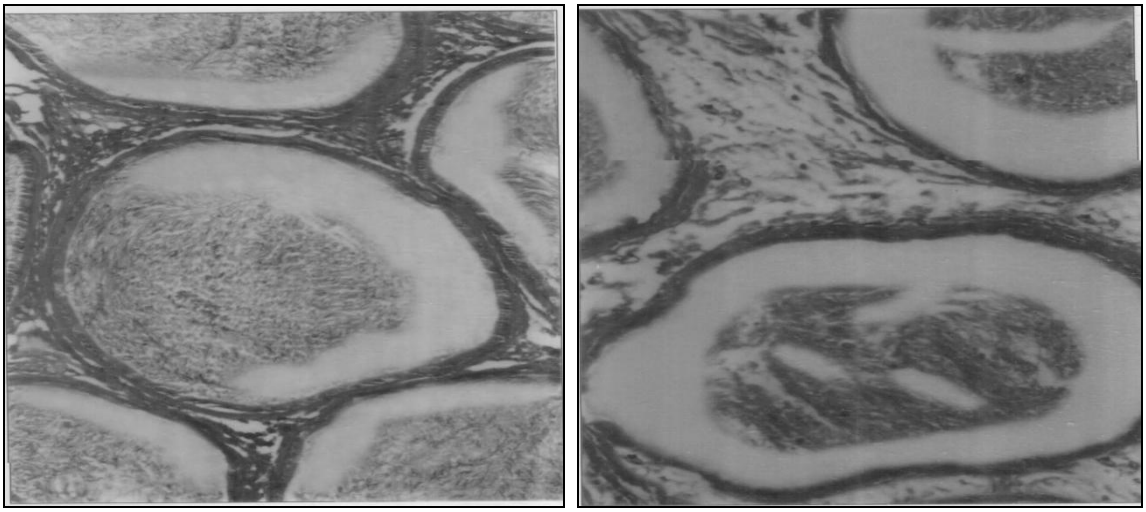


(b) **(c)**

FIG.3: HISTOPATHOLOGY OF TESTES AFTER EXPOSURE WITH METHOXYCHLOR IN RATS. (a) Testes of control rat, (b) Testes of rat treated with methoxychlor 20 mg/kg b.wt./day for 15 days, and (c) methoxychlor 20 mg/kg b.wt./day for 45 days

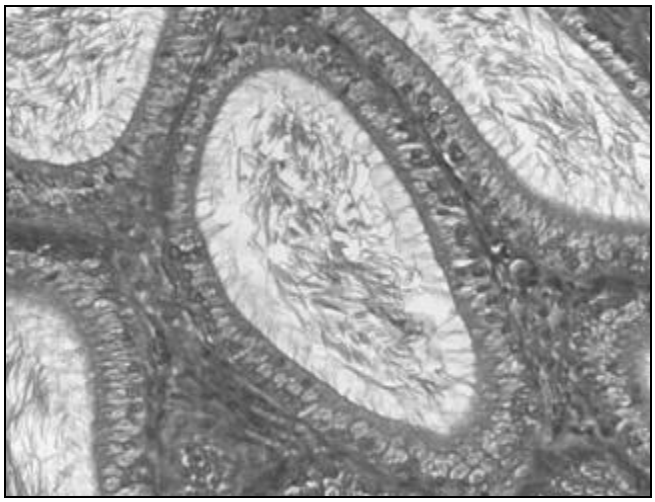


(**a)**

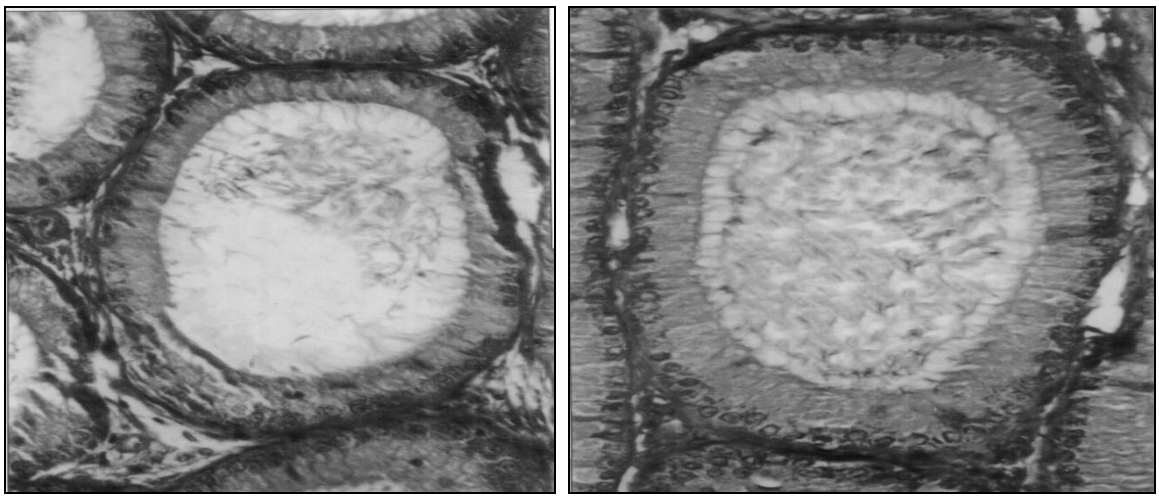


(b) **(c)**

FIG.5: HISTOPATHOLOGY OF CAUDA EPIDIDYMIS AFTER EXPOSURE WITH METHOXYCHLOR IN RATS. (a) Cauda epididymis of control rat, (b) Cauda epididymis of rat treated with methoxychlor 20 mg/kg b.wt./day for 15 days, and (c) methoxychlor 20 mg/kg b.wt./day for 45 days



(a)



(b) **(c)**

FIG.6: HISTOPATHOLOGY OF CAPUT EPIDIDYMIS AFTER EXPOSURE WITH METHOXYCHLOR IN RATS.
(a) Caput epididymis of control rat, (b) Caput epididymis of rat treated with methoxychlor 20 mg/kg b.wt./day for 15 days, and (c) methoxychlor 20 mg/kg b.wt./day for 45 days

TABLE 2: SPERM DYNAMICS, FERTILITY ANALYSIS AND TESTOSTERONE LEVEL AFTER EXPOSURE TO METHOXYCHLOR

Treatment	Sperm motility (%)	Sperm density (million/ml)	Sperm density (million/ml)	Fertility (%)	Testosterone
	Cauda epididymis	Cauda epididymis	Testes		
Group I (Control: vehicle treated)	67.64 ± 1.17	20.80 ± 1.90	4.30 ± 0.13	100%(+)ve	2.72 ± 0.03
Group II (20 mg/kg b.wt./day for 15 days)	60.22* ± 3.97	15.81* ± 0.55	3.64 ns ± 0.25	20%(-)ve	2.51 ns ± 0.05
Group III (20 mg/kg b.wt./day for 45 days)	36.16** ± 8.69	8.35** ± 1.26	1.46** ± 0.30	50%(-)ve	1.33** ± 0.04

(Mean ±SEM of 10 Animals), Group II and III compared with group I, ns = non-significant, * = significant (P<0.01)
** = highly significant (P<0.001)

CONCLUSION: It can be concluded that organochlorine pesticides induced abnormalities in reproductive system which may be as a result of disturbance in the androgen-estrogen balance, as well as oxidative stress and impairment in testicular functions. All these events cannot be linked

together but it is assumed that their collective impact leads to a perceptible change in sex hormone balance and spermatogenesis arrest. Thus, application of organochlorine pesticides should be limited to a designed program with special care in handling to limit or minimize hazards to both wild life and humans. Thus, the people need to be educated for vigilant use of these pesticides. The risk assessment to the human is absolutely necessary for the pesticides that have already proven to be toxic to the reproductive system in animal studies.

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