

Original Research Article

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## Toxic Effect of Lindane on Male Reproductive Cells in Mammals

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### ABSTRACT

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Present investigation gives the effects of lindane in steroidogenesis and testis tissues of adult male albino rat. Adult male rats were orally administered with lindane at a dose of 6.0mg/kg body weight per day for 30 days, the rat were operated to remove one testis from each, for histopathological studies. Male albino rats were treated with lindane, decreased the testes parameters, protein, cholesterol and total lipid. A histopathological analysis of testicular tissue from treated rats showed cell disorganization. Cells were irregularly shaped, with marked intercellular space between the spermatogenic cells were observed. Our results imply that organochlorine insecticides like lindane can cause reproductive disorders, and therefore more attention should be directed towards understanding the affects of persistent pesticide residues on reproductive outcomes.

### Introduction

Lindane, also known as *gamma*-hexachloro-cyclohexane, ( $\gamma$ -HCH), gammaxene, Gammallin and benzene hexachloride (BHC). It is an organochlorine chemical variant of hexachlorocyclohexane that has been used to treat food crops and to forestry products, as a seed treatment, a soil treatment, and to treat livestock and pets. It has also been used as pharmaceutical treatment for lice and scabies, formulated as a shampoo or lotion(12,13,14) Lindane is a neurotoxin that interferes with GABA neurotransmitter function by interacting with the GABA<sub>A</sub> receptor-chloride channel complex at the picrotoxin binding site.

In humans, lindane affects the nervous system, liver and kidneys, and may well be

acarcinogen (5,6). It is unclear whether lindane is an endocrine disruptor(7,8,9). The lindane is widely used as a pesticide in many countries (7). Lindane ( $\gamma$  hexachlorocyclohexane) is an organochlorine insecticide that is still employed for various purposes, including both human and veterinary medicine and as agriculture and horticulture pesticide (1). Lindane may be taken up cutaneously (2) or orally from contaminated food (3,4) Even though the symptoms of chlorinated hydrocarbon toxicity convulsion and other (5) are evidence that chlorinated hydrocarbons exert physiological effects by their interaction with components of the nervous system, the mechanism of action of the insecticide lindane is still poorly

understood. Lindane has been reported to induce reproductive abnormalities in male rat and induction of stress to play an important role in the toxicity. Lindane and other pesticide are released into the environment intentionally and exposure to such pesticide interacts with the mammalian endocrine system and may cause adverse effect on reproductive function in mammals and human (6). Lindane posses lipophilic character and enter into the food chain resulting in bioaccumulation in the body tissue (9) blood and breast milk of human and animal. Lindane alter the activity of some membrane bound protein (10, 11). Lindanes interfere with peripheral and central nerve conduction inducing neurotoxic effect (12, 13). Lindane has been shown to decrease rodent sexual receptive (14) and a possible activity at the level of steroid hormone balance in female rats has been described (15). Lindane is a lipophilic compound that can be accommodated in lipid bilayers (19) and this accommodation could induce a variation in membrane fluidity by modifying the cholesterol content. Biological events such as transformation, growth, cell cycle and differentiation (20) as well as modification in the accessibility to some hormone receptor (21) or the activities of certain enzymes (22, 23) have been shown to be accompanied by alteration in membrane fluidity. Lindane has been reported to cause impairment to many biological functions, including reproduction in humans and animals. It has adverse effects on various hormone dependent reactions in the male reproductive system. The testes have been found to be highly sensitive target organs for lindane, which has been shown to disrupt testicular morphology (26,27,28,29)and induce epididymal cellular degeneration (30). It causes alterations in Leydig and Sertoli cells and impairs their functions (31,32). Investigations have revealed that exogenous

lindane treatment diminishes serum testosterone level, and it has been confirmed that lindane acts as an inhibitor on testicular steroidogenesis (33, 34). This study was conducted to examine the effects of lindane on male reproductive parameters related to hormones and lipid profile of testis and plasma.

## **Materials and Methods**

Animals Male albino rat (10-12 weeks of age) were obtained from Indian Veterinary Research Institute Bareilly (U.P). The rats were reared in plastic cages and maintained under a well regulated light and dark (12h–12h) schedule with normal room temperature during whole work. The food and water were *ad libitum*.

## **Experimental Design**

The rats are divided into two groups:

1st group: Served as a control which received normal food and water.

2nd group: is treated with lindane at a dose of 6mg/kg.

After 30 days of treatment animals were operated and testes was kept at -20c for biochemical study(40, 41, 42, 43). For Histopathological studies, testis of each rat was fixed in Bouins fluid passed through xylene and embedded in paraffin wax tissues were sectioned at the thickness of 5  $\mu$ m and stained with haematoxyline and eosin. Spermatogenesis was observed in 100 x.

Statistical Analysis: SD for six rats $\pm$ Values were expressed as mean in the each group and statistical significant differences between mean values were determined by one way analysis of variance (ANOVA). The results were statistically analyzed by

Graphpad Instat Software version 3 was used and  $p < 0.05$  was considered to be significant.

### Results and Discussion

Abnormal spermatogenesis due to Lindane: Seminiferous tubules are cleaved, Sertoli cells are affected as a result spermatogenesis is affected. Junction between the tubules is affected (29, 30, 31) Histopathology of albino rat testis Sertoli cells are normal Junction between tubules are normal Seminiferous tubules are normal (Fig 1). Sertoli cells are affected due to lindane effect in testis. There is breakage in junction between tubules seminiferous tubules are cleaved due to toxicity of lindane (Fig 2).

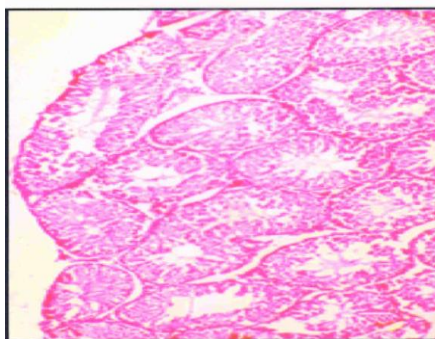
Treatment of lindane at 6mg/kg for 30days cause the decreased level of lipid, & protein

in testes. It may be due to the lipid peroxidative damage caused by lindane. Cholesterol is the precursor for synthesis of steroid hormones and its decreased level in testes indicates the direct effect of lindane on Leutinizing hormone (LH) and testosterone. Many chemicals, such as pesticides, industrial chemicals, plastics, plasticizers, pharmaceuticals and others present in the environment, have been shown to cause disruptive endocrine effects, yet currently, for many of them, there is no known structure/ function relationship (24). Like other persistent organic pollutants, lindane can enter the food chain and lipophilicity facilitates its accumulation in the various tissues of living organisms where, after absorption and distribution, it can easily reach the essential tissues of the reproductive system (25).

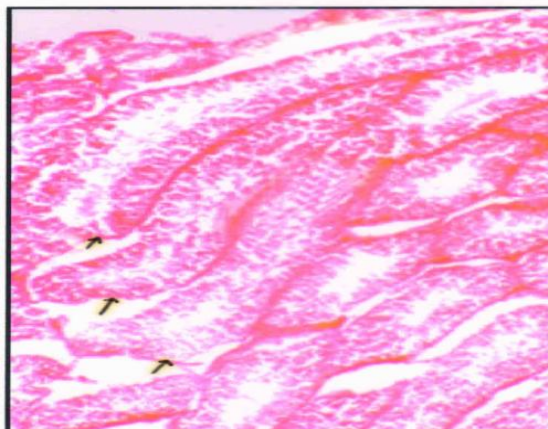
**Table.1** Effect of Lindane on Testis Parameters of Experimental Rats

| S.No. | PARAMETERS         | CONTROL      | LINDANE TREATED |
|-------|--------------------|--------------|-----------------|
| 1     | Protein (mg/g)     | 123.55±0.45  | 116.25±0.28*    |
| 2     | Cholestrol (mg/g)  | 14.806±0.073 | 14.892±0.33*    |
| 3     | Total lipid (mg/g) | 166.38±0.42  | 140.85±0.43*    |

**Fig.1** Showing Normal Testes



**Fig.2 Shows Lindane Exposed Testes**



It is generally accepted that testosterone is converted into  $5\alpha$ -reduced metabolites, which interact with their specific receptors to become fully active (35, 36). Both in vitro and in vivo lindane exposure interfere with androgen metabolism and with the formation of a  $5\alpha$ -dihydrotestosterone receptor complex in the prostate of rats (37, 38) as the consequences of exposure to lindane. Seminiferous tubules and Leydig cells degenerated during treatment with doses of 5 mg kg<sup>-1</sup> daily, over a 30-day period (54). The atrophy of seminiferous tubules carrying necrosis spermatogenic cells was observed after lindane-treatment. Testicular tissue was analyzed morphologically by light microscopy (Fig. 1). In the lindane-treated rats, the cells were irregularly shaped and there was marked intercellular space between the spermatogenic cells. Spermatogenesis was still present, but cell disorganization was found. According to the present results and previously published reports (49, 29) much more attention should be paid to the possible effects of environmentally persistent pesticides, even if they are banned in most developed countries, in view of the fact that they may induce changes at the cellular level to crucial stages in the reproductive processes.

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