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Physiological and biological abnormal changes in testes of male rat by the activity of DDT pesticide

P M Ravi Kumar[1], Gnana Prakasam Pattem[2], Anusha N.[3]

[1]Associate Professor, Department of Biotechnology, SGS Arts College, T.T.D., Sri Venkateswara University, Tirupati, A.P., India.

[2]Research scholar, Department of Biotechnology, Vikrama Simhapuri University, Nellore, A.P., India.

[3]Research scholar, Department of Biotechnology, PRIST University, Pondicherry (campus), India.

Email - [3] nedunchezhiyananusha@gmail.com

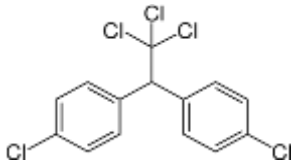
Abstract: *Endocrine disrupting chemicals (EDC) are exogenous compounds that alter the normal functioning of the endocrine system of both wildlife and humans. The number of chemicals including organochlorines pesticides has been identified as endocrine disruptors. Pesticides are used to kill unwanted organisms in crops, public areas, homes and gardens, and parasites in medicine. Human are exposed to pesticides due to their occupations or through dietary and environmental exposure (water, soil, air). For several years, there have been enquiries about the impact of environmental factors on the occurrence of human pathologies. OC, OP is known to produce reproductive toxicity resulting in a decrease in the fertility levels of humans and animals. This paper reviews mainly focused on toxicity of organochlorine such as DDT especially dealing with reproductive toxicity in males.*

Key Words: *Endocrine disrupting chemicals, Pesticides, DDT, Reproductive toxicity.*

1. INTRODUCTION:

Organochlorines (OC) are a set of chlorinated compounds widely used as pesticides. These chemicals belong to the category of persistent organic pollutants (POPs) with high persistence in the atmosphere OC insecticides were earlier successfully used in successive management of malaria and typhus, yet these are banned in most of the countries. The review statistics on the utilization of various pesticides shows that 40% of all pesticides used belong to the organochlorine category of chemicals (Gupta, 2004; FAO, 2005). Because of their low cost value and also works against varies pests, organochlorine insecticides like DDT, hexachlorocyclohexane (HCH), aldrin and dieldrin are widely used pesticides in Asia

DDT is a pesticide that initially used throughout World War II for management of lice and mosquitoes to combat typhus and malaria infection severally [5]. It is extremely hydrophobic in nature and nearly insoluble in water however has high solubility with most organic solvents, fats, and oils. DDT doesn't occur naturally and is synthesized by consecutive Friedel–Crafts reactions between chloral (CCl_3CHO) and 2 equivalents of hydrocarbon (C_6H_5Cl), within the presence of an acidic catalyst.



The World Health Organization has estimated that the use of DDT against malaria save greater than 5 million peoples life [1]. DDT became extensively overused, particularly in agriculture and forestry, and consequently its environmental awareness and it starts to affect the reproductive system of birds. Production and use of DDT peaked inside the United States for the duration of the early 1960s [2] and became banned by the Environmental Protection Agency (U.S.) in 1972[3]. During 1980s and 1990s many Third World international countries banned the usage of DDT in agriculture [2]. The most prevelant breakdown product of DDT is the dichloro diphenyldichloro ethylene (DDE). DDE have similar properties with those of DDT.

2. REVIEW OF LITERATURE:

The reproductive role of the male is to produce and deliver sperm to impregnate the female. A male has internal and external sexual organs to carry out these functions. These structures include the testes, several tubules that carry sperm out of the testes, various glands, and the penis. In most mammalian species, including human, the male's external reproductive organs are the scrotum and penis. The internal reproductive organs consist of gonads that produce gametes

(sperm cells) and hormones, accessory glands that secrete products essential to sperm movement, and ducts that carry out the sperm and glandular secretions (Campbell and Reece, 2005). Inside the testis is a network of fine-diameter tubes called seminiferous tubules. Sertoli cells nourish, support, and protect developing germ cells, which undergo cell division to form spermatozoa (immature sperm) by meiosis. Prostate secretions are rich in zinc, citric acid, antibiotic like molecules, and enzymes important for sperm function. The bulbourethral glands produce a droplet of alkaline fluid that neutralizes residual urine in the urethra during sexual excitation, protecting the sperm from its acidity.

Human exposure to DDT substances might occur in many ways, as well as inhalation of air, ingestion of food and water and skin absorption [5]. The foremost route of exposure to these substances is via food (and not drinking water) because of the bioaccumulation of organo chlorines in fish and different animals that humans consume [7]. It is calculable that over 90% of Organochlorines intake is through food [6]. As a result of DDT are fat soluble, fish, meat and farm product have the very best levels of them. Another route of exposure is through the long term and regular skin absorption of cosmetic products that contain organochlorines or other endocrine disrupters [8,9].The regular application of a spread of cosmetics with steroid hormone activity to the underarm and higher breast space might cause the continual direct dermal exposure and consequently to the absorption and accumulation in underlying tissues[10]. DDT compounds are lipid soluble and degrade slowly is expected to be bioaccumulated in human body and to be found in adipose tissue, breast milk and blood. In general, the levels of organochlorine substances are about the identical at distinct human tissues (adipose tissue, breast milk, muscle, blood). Long time exposure to noticeably small number of organochlorines like DDT leads to the accumulation of those substances in human tissues. It has been observed that vegetarians (i.e. consume all vegetables, fruits, and grain with no animal products) have much lower concentration of organochlorines compared to persons consume animal- primarily based products [4].

3. ABNORMAL ACTIVITIES OF TESTES EXPOSURE TO DDT:

DDT an organochlorine pesticide having endocrine disrupting effects and testicular induced oxidative stress apoptosis inducer. According to several researches, DDT, and some organic solvents lead to decreased fertility, altered sperm counts and induce oxidative apoptosis. The reproductive toxicity, oxidative apoptosis 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, in other side induce oxidative apoptosis. Administration of DDT led to a dose-dependent activity.

According to Marouani et al 2017 (13) an increase in LPO level and H2O2 production occurred, while MTs level, SOD and CAT activities were decreased. Also, the Gpx, GR, GST, and GSH activities were decreased, whereas GSSG activity was increased. Testicular tissues of treated rats showed pronounced degradation of the DNA into oligonucleotides as seen in the typical electrophoretic DNA ladder pattern. Intense apoptosis was observed in germinal cells of DDT-exposed rats. In addition, the apoptotic index was significantly increased in testis of DDT- treated rats. In other hand as per (K Ben Rhouma et al 2001 and Dalvie *et al*) (11,12) Exposure of rats to DDT reduced 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. whereas serum LH and FSH increased after pesticide exposure. This increase of gonadotrophin levels may be related to an impairment of the negative feedback exerted by the steroid on the hypothalamic--pituitary axis. It is concluded that DDT induced adverse effects on male rat fertility by acting directly on the testes and altering the neuroendocrine function.

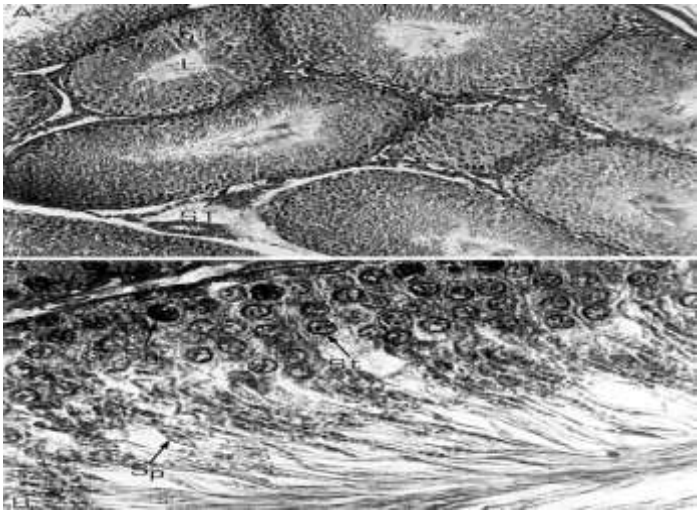


Figure 1: Photomicrographs of sections of from control rats.

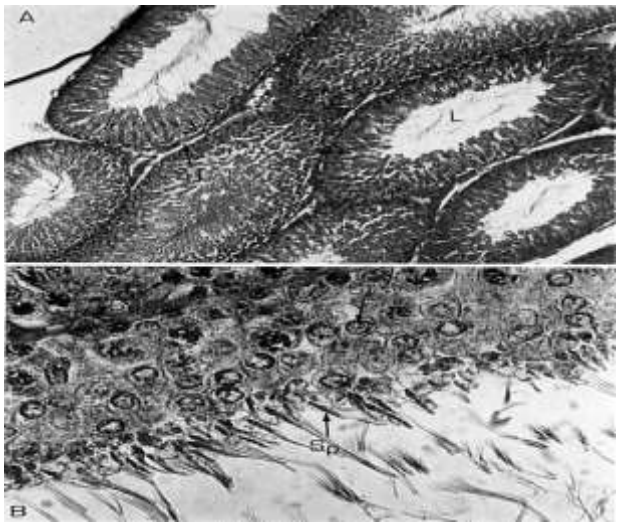


Figure 2: Photomicrographs of sections testes of testes from DDT treated rats

4. DISCUSSION AND CONCLUSION:

Most environmental chemicals are hormonally active compounds that target the endocrine system and cause reproductive anomalies (14). Arise in these environmental contaminants impair testicular functions by disturbing the pro-oxidant/antioxidant balance of testicular cells, thereby activating associated downstream pathways like apoptosis (15). For the actual functioning of the testes, physiological levels of ROS and apoptosis are required however an imbalance or pathological levels may cause deleterious effects. Spermatogenesis and steroidogenesis occur within the seminiferous tubules and interstitial of the testes. These two compartments are functionally connected however they differ morphologically. Several intra and extra testicular regulatory processes are involved within the regulation of normal spermatogenesis. Apoptosis may be a genetically regulated cellular suicide mechanism during which multiple signaling pathways are implicated [30]. Among them, oxidative stress is a crucial event which can affect different macromolecules and components of the cells, triggering the activation of several antioxidant response genes and mechanisms [30]. The oxidative stress might be related to severe damage to DNA. The study revealed that exposure to DDT induced DNA single-strand breaks [31]. Recently, it was reported that exposure to p,p'-DDE induced DNA damage in Sertoli cells, which might account for subsequent development of apoptosis [18, 19, 24]. DNA isolated from testicular tissues of DDT- treated rats show degradation into oligonucleotide fragments forming a transparent ladder pattern. additionally, histological examination of testicular tissue by the TUNEL method showed that apoptosis cells occurred within the germ cells of DDT-treated rats (34). Also, the apoptotic index was significantly increased in testis of DDT-treated rats. Moreover, it's been demonstrated that the surplus or deprivation of hormones like FSH and testosterone can cause cellular apoptosis within the testis [32] and capable of disrupting the steroidogenic capability of Leydig cells also as the capacity of the germinal epithelium to differentiate normal spermatozoa . it has been shown that both extrinsic and intrinsic apoptotic death pathways are operative within the germ cells following decrease in FSH and testosterone levels; therefore, FSH and testosterone maintain spermatogenic homeostasis by inhibiting death signals for the germ cells [33]. Serum FSH and LH levels were significantly increased, and testosterone levels were decreased in rats exposed to DDT. Decreased testosterone levels and the increased FSH levels in response to DDT exposure stimulates caspase activity and produces DNA fragmentation in germ cells. Some studies explain DDT-induced apoptosis of germ cells through mitochondria-mediated and FasL- dependent pathway (34).Reduction level of testosterone hormone resulting in the rise of serum FSH and LH as a consequence of the impairment of the negative feedback control on the hypothalamic–pituitary axis. Increase of circulating gonadotrophin remained controversial (35). the expansion and maintenance of the accessory sex glands are well known to be highly dependent on the level of circulating testosterone (36). Therefore, decrease within the weight of the seminal vesicles by exposure to DDT may be due mainly to the reduction level of testosterone. The alteration of gonadotrophin secretion may also be explained by the well-known estrogen-like effect of DDT (37) and therefore the failure within the inhibin production by Sertoli cells, since FSH secretion is modulated by inhibin (38). the autumn in plasma testosterone levels in DDT-treated rats showing alteration in Leydig cells because of oxidative stress. DDT decreased serum concentration of testosterone (39) and its metabolite inhibited the steroid production in developing Leydig cells (40). This reduced androgen production may contribute to reproduction failures DDT-related compounds exposure. However, DDT passes through the blood/testis barrier and affects both the production and the maturation of sperm in the epididymis. the weight of the seminal vesicles of rats exposed to DDT is significantly reduced. this is often due to the anti-androgenic activity of the DDT compound.

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