

# Adverse Effects Of Cypermethrin: A Review

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**Abstract :** Synthetic pyrethroids are most widely used pesticides for pest eradication all over the world rather than organochloride, organophosphorous and carbamate because of their high effectiveness, easy to degrade and low toxicity to human and other organisms. Cypermethrin is actively used synthetic pyrethroid which belongs to class 2 of synthetic pyrethroids. It most frequently used in agriculture, household and veterinary application to control ectoparasites such as moths, fleas, cotton and vegetables pest, cockroaches and ticks etc. But unconsciously increase in production and consumption of pesticides in agriculture to meet the rising demands of population has crossed the tolerance level and creating imbalance in the system. Cypermethrin not only affect those organisms which come in its exposure directly but also indirectly effect the development of foetus in the womb of mother by crossing placenta barrier. The incomplete development of enzyme in newly born child makes them more sensitivity towards the exposure of pyrethroids than adults. Cypermethrin exposure cause many adverse effects related to morphology, histology, physiology and biochemical parameters. Toxic symptoms regarding to cypermethrin exposure are oxidative stress, vomiting, headache, dizziness, nausea, allergic reaction, irritation to skin and eyes, blood disorder, infertility and some other harmful effects are also observed. Along with these bad effect on health, there must be some other parameters are here which are equally facing risk of damage because of these pesticides. This review will fall flash light on this context.

**Index terms:** Adverse effects, exposure, Cypermethrin, synthetic pyrethroids

## 1. INTRODUCTION

In many countries there is a broad use of pesticides in food production system and public health because human population are increasing day by day so to fulfill the needs of rapidly growing human population and also their protection from disease, pesticides are used most abundantly all over the world (Bhaskar, et al, 2014; Gabr, et al, 2015). Extensively use of pesticides put up many questions about their harmful effects on health of human and other animals. When pesticides are introduced in environment, they takes various routes to enter into the body of humans and domestic animals and then they changes the proper working of internal endocrinology of human and wild life organism. Human population exposure to insecticides is very difficult to be limited on a particular chemical because in their routine life they daily exposed to different types of chemicals in foods, beverages, cosmetic products, inside and outside pollutants (Marinovich, et al, 1996). At present, synthetic pyrethroids are contributes about 30% of insecticides used globally (Prasanth and Rajini, 2005). Due to their great effectivity at low concentrations, increased stability to photochemicals, easily degrade by microorganisms and relatively low human and animal toxicity, these insecticides were chosen over organochlorine, organophosphorus and carbamate insecticides (Oda, et al, 2012). Pyrethroids are synthetic (man- made) form of pyrethrins, they are modified derivatives of pyrethrins, natural substance obtained from the flowers of pyrethrum species (chrysanthemum flower) (Luty, et al, 2000). Pyrethroids are two types based on the difference in their chemical structure, different target site, exposure symptoms and different profiles of toxicity (Saka, et al, 2011). Type I pyrethroids containing no cyano group (Noncyanopyrethroids) and their aim is to inactivate sodium channels in a very short period.

Type II pyrethroids have alpha-cyano group and they open sodium channel for a longer duration which leads to constant depolarization of the nerve membrane (soderland, et al, 2002). Cypermethrin is a type II synthetic pyrethroid and also a broad spectrum pesticide which used in household, veterinary and farming application due to its high rate of degradation. It has been widely used to control ectoparasite including moth pests, cockroaches, fleas, and termites of cotton, fruit and vegetable and also a main component of cockroach killer products (lal hit, baygon). In West Africa mosquito bed nets are impregnated with cypermethrin for protection of malaria (Lim, et al, 2011; Guessan, et al, 2014). Population which are more prone to high dose exposure are manufacturers, hygienic and pesticide workers, and small field owners which applying cypermethrin for the safety of their plants, low dose of pesticides generally used in domestic activity, some food products and water are also contaminated during the exposure of pesticides (Gorell, et al, 1998). There are so many studies which states that the people who work in agricultural field are more prone to organ toxicity like defect in reproductive organs, blood disorders, damage in nervous system, paralysis, jaundice and hepatic fibrosis, hypersensitivity, respiratory disorder, kidney problems, genetic disorders, birth defects, miscarriage, impotence, and infertility or sterility. The pregnant females which exposed to pesticides during working in industrial and agricultural area are indirectly affects the development of fetus. CYP cause oxidative stress by producing oxygen reactive species in the body (Huang, et al, 2016). ROS production is the main reason of cell death because it damages the biomolecules such as carbohydrates, triglycerides, proteins and DNA of cells (Ferrari, 2000). Cypermethrin is lipophilic in nature, it can easily cross the cellular membrane and alter its internal structure and cause seepage of cytoplasmic enzymes (Manna, et al, 2004; Hussien, et al, 2013). Its hydrophobic nature also help in the storage of pesticide in body fat, skin, liver, kidneys, adrenal glands, ovaries and brain of an organism (Tao, et al, 2008). Cypermethrin, can cross the placenta barrier, that's why it affects the physiological functioning and neurological development of fetus (Dewailly, et al, 2014). Cypermethrin is basically neurotoxin and its main site of action is central nervous system of insect (Ray,

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2001). Its exposure caused sodium channels to open for a longer duration resulting prolonged membrane depolarization, neurotransmitter are released at higher concentration which increased neuronal activity and ultimately leading to depletion of the neurotransmitter (Right and Palermo, 2003). Additionally, it also blocks voltage-sensitive chloride channels and inhibit the activity of monoamine oxidase enzyme that breakdowns neurotransmitters ((Miyamoto, et al, 1995). Due to extensively use of cypermethrin, a wide range of disorder has been reported in insect, animal, birds, and fishes even human. Symptoms of severe toxicity including abnormal facial sensations, faintness, headache, nausea, anorexia and tiredness, vomiting and increased stomach secretion, irritant to skin and eye, persistently muscular spasm, coma and convulsive attacks.

## 2. EFFECT OF SYNTHETIC PYRETHROID (CYPERMETHRIN) ON ALBINO RATS

### 2.1 Biochemical changes

In a study by (Abdou, et al, 2012) in which albino rats were treated with CYP (12mg/kg b.wt) for 30 days. In this study it has been observed that CYP cause oxidative stress which leads to lipid peroxidation and cellular damage. The main center of this damage is liver because liver play a major role in detoxification process, along with it kidney also possess the risk to maximum exposure of xenobiotics and their metabolic by products which is released by the liver. The balance between the oxidative stress and antioxidant efficacy is due to the susceptibility of liver and tissue to this stress. This study shows that CYP exposure cause reduction in the activity of liver enzyme such as aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) but the activity of these enzymes increased in plasma which confirmed histological damage in liver. Elevation in plasma urea and creatinine level considered destruction in kidney structure. Increase level of malondialdehyde (MDA) cause liver necrosis. The primary defence which prevent biological macromolecule from oxidative damage are antioxidant enzymes. But CYP exposure decreased the activity of antioxidants such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx). Increase amount of oxidant enzymes (ALT, AST, ALP and MDA) and decrease value of antioxidant enzymes (SOD, CAT and GPx) indicates liver toxicity, lipid peroxidation and oxidative stress (Hamdani, et al, 2017). According to (Sayim, et al, 2005) cypermethrin exposure has no major effect on the brain of albino rats. There were no changed in total protein of plasma and brain and also plasma cholinesterase (ChE) and brain acetyl cholinesterase (AChE) in rats after treatment with cypermethrin. Whereas increased AChE activity in rat brain was recorded in group which received 150 and 300mg/kg CYP. Biochemical study of female reproductive organs showed that pyrethroid cause degenerative effect in the ovary of female rats which is characterized by increased degeneration of follicles and decreased level of protein (38%), lipid (20%), phospholipids (18%) and cholesterol (37%). In addition, cypermethrin exposed female rat showed enhance activity of acid (49.2%) and alkaline phosphatase (41%) while decreased level of lactate dehydrogenase (37%) and 3 $\beta$ - hydroxysteroid

dehydrogenase (31.3%). Reduction in 3 $\beta$ - HSDH activity in ovary of treated rats indicates altered level of reproduction hormone in female rats. Progesterone level was also decreased in cypermethrin treated rats. Irregular concentration of these biomolecules in cypermethrin treated animals affect the normal development of gametogenesis (Sangha, et al, 2013). CYP exposure also affects the biochemical parameters in offspring through their mothers because cypermethrin can cross the placenta barrier easily. CYP exposure at dose of 0.02 mg/kg b.wt which is considered as acceptable daily intake (ADI) for human being can also affect the level of macromolecules in pregnant rats and their newborns but it cause no major effect on the development of neonates. Slight fluctuation occurs in the concentration of biomolecules after exposure of CYP on pregnant females and their pups but their level remains in normal range, because they were treated with low dose. But these slight alterations were enough to disturb biochemical concentration of fetus (Hocine, et al, 2016). Joshi, et al, 2011 reported that CYP treated male albino rats show decrease in glycogen level and testicular saillc acid content and increase in total protein, cholesterol, alkaline phosphatase and acid phosphatase activity. Glycogen is source of energy, which supply glucose continuously for the normal functioning of testis. Pyrethroid treatment also affects biosynthesis of testosterone. CYP exposure in male albino rats induce decrease in testicular enzymes 17  $\beta$  – hydroxysteroid dehydrogenase (17 $\beta$ - HSD) and glucose - 6 – P – dehydrogenase (G-6-P-DH) which are required for testosterone (T) biosynthesis. The direct action of synthetic pyrethroid on testis affects the androgen biosynthesis pathway which reduced pituitary gonadotrophin (FSH and LH) secretion. Reduction in LH hormone level ultimately affects T production because LH stimulates leydig cells to produce testosterone. Reduction in FSH affects the spermatogenesis and development of seminiferous tubule. Due to reduction or low production of androgenic hormone after exposed to CYP affects the fertility of male albino rats.

### 2.2 Hematological changes

According to Sayim, et al, 2005 rats were orally treated with cypermethrin at doses (60, 150, 300mg/kg) for 28 days for hematological study. It has been observed that CYP treatment cause a dose and time dependent changes in hematological parameters. The level of (RBC) counts, Hematocrit (Ht), thrombocyte and mean corpuscular hemoglobin (MCH) were found declined in rats treated with 150 and 300 mg/kg CYP and number of WBC, lymphocyte and monocyte was found high in 300 mg/kg CYP treated rats. Cypermethrin treatment also caused damage in D1- and D2- like receptors of renal dopamine.

### 2.3 Behavioral changes

Behavioral study of CYP on rats proved that no significant changes occur in the memory, movement coordination and locomotion on rats when intraperitoneal injection of CYP given to them (Lwanicko, 2008). Cypermethrin treatment did not produce any apparent behavioral changes but some sign of toxicity were observed in these rats. Animals exposed to CYP at the lower dose 5mg/kg/day produced toxic symptoms such as diarrhea, reduced feed intake and thick eye discharge. One female died during last days of

treatment. Mild to moderate sign of toxicity were produced by the rats which taken higher dose characterized by diarrhea, reduction in body weight, dyspnea, eye discharge and salivation. In higher dose treated group 2 female and 1 male rat were found died (Grewal, 2010).

## 2.4 Histological study

Cypermethrin treatment cause neurotoxicity which is showed by increase in cholinesterase (ChE) activity and deformation of neural conductivity in the central and peripheral nervous system. Due to reduced blood flow (ischemia) and presence of pyknotic nuclei in cytoplasm of neurons severe impairment were observed in the CYP treated rats (Sayim, et al, 2005). Aziz, et al, 2001 showed that administration of 1 mg/kg deltamethrin increased the functioning of acetylcholinesterase (AChE) in hippocampal region of rats. Dermal exposure of chlorpyrifos and cypermethrin affects various region of brain and also increased density of cytoplasm in neurocytes of albino rats (Latuszynska, 2001, 2003). According to (Mamun, et al, 2014) CYP treated rats indicated alteration in shape and structure of liver. Data regarding effect of cypermethrin on the histology of liver showed dilation and congestion of central vein, vacuole formation in hepatocytes, enlargement of sinusoids, degeneration of hepatic cord and hemorrhage in hepatic tissue. Histological study of kidney showed inflammation in the renal tubules, enlarging renal spaces, shrinkage of glomeruli, destroyed Bowman's capsule, congestion of renal glomerulus and dilation of blood vessel in albino rats. Jaya raj, et al, 2013 showed that combined treatment of cypermethrin and endosulfan in mice produced medullary congestion in kidney. Abdou, et al, 2012 reported that orally exposure of CYP in rat showed pyknosis and necrosis in the liver. Treatment of CYP with a dose of 50 or 75mg/kg for 45 days in rats showed reduced seminiferous tubule size, blockage of spermatozoa formation and increased space between tubules with ruptured interstitial cells in the testes of males. Decreased number of sperm cells, reduction in the weight of testes, decreased fertility, formation of vacuoles in seminiferous tubule, low spermatocytes and decreased number of sertoli and leydig cells were found in testes of cypermethrin treated rats (Joshi, et al, 2010). Elbetieha, et al, 2001 observed that the females which has fertilized by cypermethrin treated rat showed decreased rate of pregnancy, number of implantation sites and also showed reduced number of viable fetuses. The sperm count decreased in testes and epididymis of cypermethrin treated rats. Daily production of sperm was also reduced. Due to CYP exposure premature spermatids were released in the lumen of seminiferous tubule. Wang, et al, 2009 reported that CYP treatment on mothers during lactation was not only effect the development of pups but also effect the development of adult male offspring. No sign of toxicity were found in the mothers treated with CYP. During the exposure of CYP body weight of pups was slightly affected but testes weight was reduced in both pups and adult male offspring. CYP treated mother during lactation caused reduction in the amount of sperm count in adult male offspring. Maternal CYP exposure caused reduction in testosterone level in pups but the level of testosterone in adult male offspring found slightly affected. In a study by Hamdani, et al, 2017 reported that orally exposure of CYP for two durations (6

&12 weeks) on female mice showed that the number of estrous cycle per month, level of estradiol in serum, total number of healthy ovarian follicles were reduced and the number of atretic follicles were increased in treated females. After 6 weeks exposure all treated groups showed 100% fertility but after 12 weeks exposure fertility were reduced about 80% in low and medium dose and 60% in high dose treated females. Yusuf, et al, 2017 reported that combined treatment of dimethoate and cypermethrin in female albino rats during gestation period showed reduced litter size, maternal organ weight and increased fetal resorption. Some sign of toxicity were also observed in animals treated with high dose of cypermethrin such as tremors, hypersalivation, nasal discharge and spasms. According to (Joya, et al, 2016) female albino rats were treated with acceptable daily intake (ADI) (0.01mg/kg) and ten times higher ADI dose of deltamethrin during gestation period. ADI dose of deltamethrin caused no adverse effect on adult rats but little effect occur on the development of pups such as reduced litter size and delayed weight gain by pups. Some weakness and less activeness observed in female rats which treated with 10 time higher ADI dose of deltamethrin and also observed fetal resorption and cysts in uterus and ovary of treated rats.

## 3. CONCLUSION

From all above studies, it has been concluded that extensively use of synthetic pyrethroid cypermethrin at higher concentration in agriculture for pest control and increase food production cause toxic effects on the health of human beings. According to literature reviewed effect of cypermethrin is dose and time dependent. It caused neurological, histopathological, behavioural, hematological, biochemical and other adverse effect in rats. All the studies related to human being are experimentally performed on model organism albino rats/mice due to their similarity with human. So, it's time to educate land owners and workers about the harmful effect of cypermethrin on the health of human being and other non-target organisms and also need to educate them for using protective equipment during working with pesticides.

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