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Studies on the behavioral and clinical manifestation due to toxicity of some pyrethroid insecticides in male albino Rat, *Rattus norvegicus* (Berkenhout)

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Abstract

The current study was designed to evaluate the effects of some frequently used pyrethroid insecticides (Cypermethrin@ 0, 130,150 and 200mg/kg, Deltamethrin @0, 20, 25 and 30mg/kg, Permethrin@0, 150, 250 and 350mg/kg and Lambda Cyhalothrin @0, 30, 50 and 70mg/kg) on the behavior and clinical signs in albino rats, *Rattus norvegicus* underLab conditions. Feed intake, hind limb jerking, breathing problem, salivation, eye discharge, loss in body weight, lesion (internal organs), oedema, startle response, death were recorded at 7, 14 and 28 days of post application interval including a control (0-application of pyrethroid). The results revealed a reduction in feed intake and body weight against tested pyrethroid insecticides at all dose rates and post treatment intervals.

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Introduction

Environment Pollution has become a global factor and is being multiplied with the advent of technology. Chemicals in agriculture sector are referred to as pesticides; are most frequently used to protect crops against pests, weeds and diseases, and are the main agents for this pollution Singh (2013). These chemicals have been reported as hazardous to environment and pose risks to human and animal health. The speedy and most certain way of pest controlling is insect destruction with the help of artificial chemicals. The most important gain of this insect control is observed in the situation when there is substantial insect outburst against biological and cultural control practices which are effective for working over a longer period of time. The pesticides that are used may assimilate into the tissues of plants and food ingredients and may become the part of food chain and may gather at all trophic levels generation after generation by bio intensification Sharma (2010). These pesticides are considered as a threat because they may become a part of the body of the mammals and can cause serious changes in various cytological, biochemical and physiological processes causing acute problems. With over dependence on these harmful chemicals, severe environmental and ecological problems are confronting day by day. The continual addition of insecticides in the food chains and the expansion of resistance towards these insecticides are the two stern problems that are come across these days.

During the last few decades the toxicity of the pyrethroids as insecticides has gained significant consideration due to traditional efficacy and value, and the extensive use of these chemicals for the expansion of agricultural productivity and control of pathogenic vectors. There is a widespread data that is existing on the toxicity of the stimulated pyrethroids to animals, however evidence concerning to cytogenetic effects of pyrethroids is insufficient Singh (2013). Toxicology is concerned with toxicity by any harmful chemical or compound by unintentional or unplanned acquaintance to living beings. The excess of any compound will be considered injurious to life and is taken under the umbrella of studies of toxicity Paliwal (2009). Pesticides have severe toxicity through the dermal and breathing passages and are not a skin sensitizer. Through oral passage, they are considered more fatal.

Pyrethroids are not likely to be of stern toxicity for occupationally bare issues retaining good work practices and protection insurances. Though, about two hundred cases of acute occupational pyrethroid poisoning causing from unsuitable management were first stated in China in 1982. In spite of occupational exposure, the internal presentation of pyrethroids directed to their continuing acquaintance to ignorant persons. Adsorption of pyrethroids by trivial dirt units and several other surfaces marks them prospective indoor toxicants (website). The marketing of assortments of pyrethroids insecticides has developed very common in evolving countries and has given rise to intensification in the predominance of toxicity. The scientific quality is comparatively great and the toxicity profile of pyrethroids can be considered for all properties, comprising prospective developing, generative and neurotoxin properties.

Cypermethrin is observed in several domestic ant and cockroach killers, comprising Raid and ant chalk. The insecticide cypermethrin is one of abundant synthetic pyrethroids used globally to control insect vermin. It is a frequently used pesticide in city and rural atmospheres. Cypermethrin is a recognized neuro toxicant. It is member of the pyrethroid class of insecticides, which are well-known to persuade medical symbols of neurotoxicity in the mammals, however do not usually persuade neuro pathologic abrasions. Deltamethrin, a kind II artificial pyrethroid, has headed to a extensive apprehension above the probable opposing effects on the health of human beings and display neurological Souderlund (2002) and behavior variations similar to Attention-Deficit/ Hyperactivity Disorder (ADHD) in human beings. Toxicity in form of extreme salivation, damaged limb function, ataxia, damage of rectifying reflex, lethality, paraesthesias, choreoathetosis, shocks, hardly paralysis and spasms has been stated

on mice, rat, rabbit and guinea pig via dermal, oral and inhalational paths. Professional dangers realized in human beings are momentary cutaneous and mucous membrane exasperation, irritating, faintness, irregular facial feelings, anaphylaxis, bronchospasm, eosinophilia, fever, hypersensitivity, pneumonia, sweltering, and unexpected edema of the face, eyelids, lips, mucous membrane and tachycardia Souderlund *et al*., (2002) and O' Mallay (1997).

Permethrin belongs to kind I pyrethroid broadly used as an insecticide Yuan *et al*., (2010). The marketable permethrin-containing pesticides are extensively used wood preservers and its efficiency in the control of termites, beats and parasites Patrick *et al*., (2016). It is also used topically in the medicinal cure of scabies and ailments related with parasites and ticks. Very regularly, it is used in numerous domestic, in its powdered form, in killing pests, like cockroaches. It is also used on agricul-tural crops, chiefly fruits and vegetables Kotil (2015). Lambda cyhalothrin being a third generation insecticide comprises of cyno group and is existing in a number of designs Meister (1992). Because to its quick metabolism and secretion its poisonousness for mammal at present is fairly small, on the other hand it might produce harms in non-target species in future if applied indiscriminately Sharm (2004). Lambda cyhalothrin is used in vector control such as mosquito by straight spraying over water bodies Velmurugan *et al*., (2007). Contact to Lambda-cyhalothrin postures both severe and long-lasting dangers. Severe effects comprise skin and eye exasperation, edema, cardiovascular toxicity, coma, tremors and stark muscle fasciculation Elhalwagy *et al*., (2015) and Iqbal *et al*., (2007). Long-lasting effects in rats comprise reduced body weights, organ weight variations (liver, kidney, brain, heart and lung), abridged brain size, cell injury (neoplastic and histopathological lesions), tumors and endocrine toxicity Kothari *et al*., (2002) and Lee *et al*., (2006).

The albino rats are vertebrates and thus, extensively used as a model organism in the field of pharmacology, toxicology, general physiology and the biology and pathophysiology of disease Sayim (2007). Toxicological studies on the albino rat to locally or regionally used pyrethroids would not only benefit us to defend the atmosphere as a whole. However, it also offers toxicological data which can be used for the controlling matters of such chemicals in the area or elsewhere. With this interpretation, the current study was designed to study the effect of some pyrethroid insecticides; cypermethrin, deltamethrin, permethrin and Lambda cyhalothrin to evaluate the behavioral and clinical changes in albino rat, *Rattus norvegicus* at different doses and post treatment intervals

Materials and methods

The present study was designed to evaluate the toxicological effects of some pyrethroids (Cypermethrin, Deltamethrin, Permethrin and Lambda cyhalothrin) on albino rats. All experimental work was performed in research Laboratory at Department of Zoology, Government College University, Faisalabad.

The Pyrethroids formulations

Commercial formulation of pyrethroids was used. The emulsion was adequately diluted in distilled water in order to reach different concentrations (mg/kg).

The test concentrations of pyrethroids were calculated from the percentage of active ingredient of commercial formulation of pesticides. Solutions were freshly made immediately before usage. The tested pesticide insecticides and the formulations are shown in Table 1.

Table 1. The tested Pyrethroid insecticides and formulations along with their trader names.

SN	Pyrethroids	Formulations	Trader Name
1	Cypermethrin	10 %EC	FMC United (Pvt.) Limited, Pakistan
2	Deltamethrin	15 % EC	Starlet International, Pakistan
3	Permethrin	1.0 % W/V	Fauji insecticide, Corporation, Pakistan
4	Lambda cyhalothrin	2.5 % EC	Four Agri Services, Pakistan

Animal Model

Total 120 healthy Albino rats of 3-4 weeks (weighing 100g-190g) procured from animal house of Govt. College University Faisalabad.

Rats were reared in animal house in ventilated cages under standard lighting condition and natural day/night cycles after approval from the local ethical committee.

Experimental Design

The present study to evaluate the toxic effect of pyrethroids was conducted for 28 days on albino rats. Data were collected at every 7, 14 and 28 day. Before starting the experiment, body weight of all the albino rats were measured. Diet including poultry feed was mixed with olive oil and pyrethroid was given to albino rats on alternate days. Pyrethroids mix doses prepared is shown in Table 2. One hundred and twenty albino rats were divided into five main and subgroups, in which each group contained eight (n=12) albino rats. These groups are following as.

Table 2. The tested Pyrethroidsalongwith their LD_{50}doses.

SN	Pyrethroids	LD50 Doses	References
1	Cypermethrin	433mg/kg	Bhushan, *et al.* (2013)
2	Deltamethrin	25mg/kg	Ibiang *et al.* (2013)
3	Permethrin	430mg/kg	Patrick, (2016)
4	Lambda cyhalothrin	80mg/kg	Omotoso, (2014)

Group I: Control group

Rats of this group were received water and food only during the whole study. No treatment was given to this group.

Group II: Treated with Cypermethrin

Three subgroups made for 100mg (1/4th of LD50) as low dose CG1 , 150mg as medium dose CG2, 200mg (two fold of low dose) CG3 as high dose were selected which was given by adding in feed.

Group II: Treated with Deltamethrin

In this group, three subgroups was made for the dosage which was contained 20mg (1/4th of LD50) as low dose DG1, 25mg as medium dose DG2, 30mg DG3 as high dose selected by feeding.

Group IV: Treated with Permethrin

In this group, three subgroups was made for the dosage which was contained 150mg (1/4th of LD50) as low dose PG1, 250mg as medium dose PG2, 350mg as high dose PG3 selected by feeding.

Group V: Treated with Lambda Cyhalothrin

In this group, three subgroups was made for the dosage which was contained 30mg (1/4th of LD50) as low dose LG1, 50 mg as medium dose LG2, 70mg as high dose LG3 selected by feeding.

Results

Behavioral and Clinical Manifestation

Control albino rats were remained highly energetic with voracious appetite and furry throughout the experiment. Decrease in feed intake and the loss in body weight were observed at all the doses at post treatments intervals. Breathing problem occurred at 14 and 28 days at higher dose rate. Hind limb jerking was found at 28 days at all the doses and it also found at 14 days post treatment intervals on high dose rate.

Cypermethrin

The application of Cypermethrin resulted in no salivation and death of rats at all the doses and post treatment intervals. Notably, eye discharge, oedema, lesion and startle response were recorded at all the post treatment intervals in high dose rate (Table 3). Cypermethrin toxicities elicit a host of clinical and behavioral changes in rats. Thus oral and inhalation exposure of this insecticide in rodents were indicative of an action on the central nervous system that consisted of salivation, ataxia, splayed gait and hyper-excitability to auditory stimuli, tremors, convulsions and choreoathetos is Agriphar (2010). An oral dose of cypermethrin in male albino rats, *Rattus norvegicus* induced intermittent diarrhea, whereas a higher dose of displayed mild to moderate toxicosis with diarrhea. Other clinical manifestations were in accordance to the studies of Islam and Hoque (2015). In addition, nervous signs, gross lesions, bloat, congestion of lungs, heart, brain, pulmonary haemorrhage and degenerative changes in the liver and kidneys; loss of body weight, hind limb extensor tone followed by recovery, burrowing behavior, abnormal jerking of the hind limbs, increased startle response, salivation, somnolence and seizures, labored breathing, gasping and death at higher doses were recorded in Sprague Dawley rats Nair *et al.*, (2011). Loss of body weight, soft faeces, frequent diarrhoea and occasional death were the most prominent clinical signs of cypermethrin poisoning in Wister rats Adjrah *et al.*, (2013).

In contrast, oral administration of cypermethrin at 103.72mgkg-1 body weight had no significant changes in behavior of Wister rats Raj *et al.*, (2013). The aforesaid findings corroborate nicely with the present results in terms of decreased feed intake, limb jerking, labored breathing, lesions on various organs, loss in body weight, necrosis and startle response, haemorrhages, eye discharge and eodema, although the used doses did not elicit death, salivation and seizures in the experimental rats (Table 1).

Table 3. Behavioral and Clinical manifestation in albino rats under exposure of Cypermethrin.

Behavioral and Clinical Signs	Doses (mg/kg)	Day 0 (Control)	Day 7	Day 14	Day 28
Decrease in feed intake	130	×	✓	✓	✓
	150	×	✓	✓	✓
	200	×	✓	✓	✓
Hind limb jerking	130	×	×	×	✓
	150	×	×	×	✓
	200	×	×	✓	✓
Breathing Problem	130	×	×	✓	✓
	150	×	✓	✓	✓
	200	×	✓	✓	✓
Salivation	130	×	×	×	×
	150	×	×	×	×
	200	×	×	×	×
Eye discharge	130	×	×	×	×
	150	×	×	×	×
	200	×	✓	✓	✓
Loss in body weight	130	×	✓	✓	✓
	150	×	✓	✓	✓
	200	×	✓	✓	✓
Lesion (internal organs)	130	×	×	×	×
	150	×	×	×	✓
	200	×	✓	✓	✓
Oedema	130	×	×	×	×
	150	×	×	×	×
	200	×	×	×	×
Startle response	130	×	×	×	
	150	×	×	✓	✓
	200	×	✓	✓	✓
Death	130	×	×	×	×
	150	×	×	×	×
	200	×	×	×	×

Deltamethrin

Similarly, reduction in feed intake, loss in body weight and startle response were observed against deltamethrin at all the doses and post treatments intervals. Breathing problem, eye discharge and lesion was occurred at 14 and 28 days of post treatment intervals at higher dose rate. Hind limb jerking and oedema was found at 28 days of post treatment intervals at the high dose rate. No salivation and death of animal found at all the doses and post treatment intervals.

Eye discharge till blindness and oedema were also observed at higher doses of deltamethrin (Table 4). The weakness, ataxia and paralysis of hind limbs against deltamethrin treatment are typical manifestations of the pesticide and also noticed by Macan *et al.*, (2006) and Tiwari *et al.*, (2008). Deltamethrin led to dullness, oversleep and faster breathing rate sometimes which indicates stress and heightened metabolism during pesticide poisoning USEPA (1999) which could be due to the effect of insecticides on gastrointestinal tract resulting in decreased appetite. However, it might be due to the toxicity of deltamethrin Sankar (2010). Chronic administration of pesticides has been reported to lead to significant reduction in body weight of animals Ibiang *et al.*, (2013). Consistently, in the present study, significant decrease in body weight was observed at the end of experimental trial period.

Table 4. Behavioral and Clinical manifestation in albino rats under exposure of Deltamethrin.

Behavioral and Clinical Signs	Doses (mg/kg)	Day 0 (Control)	Day 7	Day 14	Day 28
Decrease in feed intake	20	×	✓	✓	✓
	25	×	✓	✓	✓
	30	×	✓	✓	✓
Hind limb jerking	20	×	×	×	✓
	25	×	×	×	✓
	30	×	×	✓	✓
Breathing Problem	20	×	×	✓	✓
	25	×	×	✓	✓
	30	×	✓	✓	✓
Salivation	20	×	×	×	×
	25	×	×	×	×
	30	×	×	×	×
Eye discharge	20	×	×	×	✓
	25	×	×	✓	✓
	30	×	✓	✓ (Blindness)	✓ (Blindness)
Loss in body weight	20	×	✓	✓	✓
	25	×	✓	✓	✓
	30	×	✓	✓	✓
Lesion (internal organs)	20	×	×	×	✓
	25	×	×	✓	✓
	30	×	✓	✓	✓
Oedema	20	×	×	×	×
	25	×	×	×	✓
	30	×	×	✓	✓
Startle response	20	×	×	✓	✓
	25	×	✓	✓	✓
	30	×	✓	✓	✓
Death	20	×	×	×	×
	25	×	×	×	×
	30	×	×	×	×

Permethrin

Permethrin caused decrease in the feed intake, laboured breathing, lesions, loss in body weight and startle response. It also produced death and salivation in the experimental albino rats. Additionally, breathing problem, salivation, lesion and oedema was found at 14 and 28 days of post treatment intervals. Eye discharge, hind limb jerking and death were occurred at 28 days at high dose of post treatment intervals (Table 5).

Table 5. Behavioral and Clinical manifestation in albino rats under exposure of Permethrin.

Behavioral and Clinical Signs	Doses (mg/kg)	Day 0 (Control)	Day 7	Day 14	Day 28
Decrease in feed intake	150	×	✓	✓	✓
	250	×	✓	✓	✓
	350	×	✓	✓	✓
Hind limb jerking	150	×	×	×	✓
	250	×	×	×	✓
	350	×	✓	✓	✓
Breathing Problem	150	×	×	×	✓
	250	×	×	✓	✓
	350	×	✓	✓	✓
Salivation	150	×	×	×	✓
	250	×	×	✓	✓
	350	×	✓	✓	✓
Eye discharge	150	×	×	×	✓
	250	×	×	×	✓
	350	×	×	✓	✓
Loss in body weight	150	×	✓	✓	✓
	250	×	✓	✓	✓
	350	×	✓	✓	✓
Lesion (internal organs)	150	×	×	×	✓
	250	×	×	✓	✓
	350	×	✓	✓	✓
Oedema	150	×	×	×	✓
	250	×	×	✓	✓
	350	×	×	✓	✓
Startle response	150	×	✓	✓	✓
	250	×	✓	✓	✓
	350	×	✓	✓	✓
Death	150	×	×	×	×
	250	×	×	×	✓
	350	×	×	✓	✓

No toxic clinical signs (abnormal muscle tonus or motility, salivation, rough fur, bloody nostrils, hunched back) and no changes in the behavior (aggressiveness) were observed during cage-side observations Institoris *et al.*, (1999). In present study, Permethrin draw out death and salivation in the experimental albino rats, characteristic symptoms such as decrease in the feed intake, laboured breathing, lesions, and startle response were manifested by different doses of the insecticide at different days. Notably, hind limb jerking, eye discharge and oedema were observed only at higher doses.

Lambda cyhalothrin

Of lambda cyhalothrin; decrease in feed intake, breathing problem, loss in body weight, lesion and startle response were manifested at all the doses and post treatments intervals. Breathing problem, salivation, lesion and oedema was found at 14 and 28 days of post treatment intervals. Death was recorded at 28 days of all the post treatment intervals at high dose rate. Notably, hind limb jerking and eye discharge were also observed (Table 6). Lambda cyhalothrin-treated rats (80mg/kg body weight) succumbed after 8 hours following exposure. Toxic manifestations included profuse salivation, mild fur erection, exophthalmia, abnormal gait and posture, hyper aesthesia, tremors, respiratory distress, death and in acute toxicity may be responsible for cardiac oedema Mate *et al.*, (2010) and Mitchell *et al.*, (2006). Similar clinical signs with slight variations have been observed in rats subjected to fenvalerate exposure Saxena and Sharma (2000) and Sarkar (1993). The reduction in body weight in rats exposed to lambda cyhalothrin could be either due to reduced daily feed intake or disturbances in level of metabolic hormones subsequently resulted into decreased feed intake ultimately leading to significant reduction in body weight Ali *et al.*, (2014).

Table 6. Behavioral and Clinical manifestation in albino rats under exposure of Lambda Cyhalothrin.

Behavioral and Clinical Signs	Doses (mg/kg)	Day 0 (Control)	Day 7	Day 14	Day 28
Decrease in feed intake	30	×	✓	✓	✓
	50	×	✓	✓	✓
	70	×	✓	✓	✓
Hind limb jerking	30	×	×	×	✓
	50	×	×	✓	✓
	70	×	✓	✓	✓
Breathing Problem	30	×	✓	✓	✓
	50	×	✓	✓	✓
	70	×	✓	✓	✓
Salivation	30	×	×	×	×
	50	×	×	×	✓
	70	×	✓	✓	✓
Eye discharge	30	×	×	×	✓
	50	×	×	✓	✓
	70	×	✓	✓	✓
Loss in body weight	30	×	✓	✓	✓
	50	×	✓	✓	✓
	70	×	✓	✓	✓
Lesion (internal organs)	30	×	✓	✓	✓
	50	×	✓	✓	✓
	70	×	✓	✓	✓
Oedema	30	×	×	×	✓

Behavioral and Clinical Signs	Doses (mg/kg)	Day 0 (Control)	Day 7	Day 14	Day 28
	50	×	×	×	✓
	70	×	✓	✓	✓
Startle response	30	×	✓	✓	✓
	50	×	✓	✓	✓
	70	×	✓	✓	✓
Death	30	×	×	×	✓
	50	×	×	×	✓
	70	×	×	✓	✓

Conclusions

The results revealed a reduction in feed intake and body weight against tested pyrethroid insecticides at all dose rates and post treatment intervals. The characteristic symptoms such as hind limb jerking, breathing problem, salivation, eye discharge, loss in body weight, lesion, oedema, startle response and death were also noticed.

Hence, direct and indirect exposure to these compounds should be reduced so as to minimize the possible health hazards. Thus, it is recommended to improving the working conditions. Further research work is needed to evaluate pyrethroids effect on large sample to obtain detailed information about the exposure route, pathways, other mechanisms of toxicity and other health hazards.

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