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Toxicological impact of Lambda Cyhalothrin in brain of Albino rats

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Abstract: *The man started leading comfortable life using natural resources in favour of him. After some time there was a wide gap between the rate of food grain production and the rate of increase in population. To meet the requirement, steps were taken to increase the food production, i.e. using high-yielding variety seeds which are prone to infection. To overcome that infection, the usage of pesticides especially pyrethroid based ones was increased. But toxicity of pesticides show its impact on non-targeted species including mammals, besides insects resulting physical, mental, neuro disorders. So the focus of study is on the impact of Lambda Cyhalothrin belonging to pesticide pyrethroid on nervous system, behavior, cholinergic activities, detoxification mechanism, histological changes of male Albino rat. So finding of this study help us to observe the impact of toxicity of pyrethroid substance Lambda Cyhalothrin(LCT) on non-targeted species.*

Keywords: *Pyrethroids, Lambda Cyhalothrin, Cholinergic activities, Detoxification, Albino rat.*

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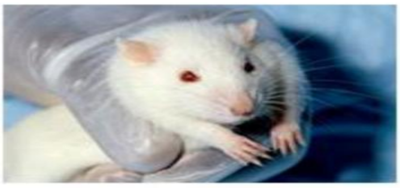
I. Introduction

In nature, there are no pests. We label as “pests” any plants or animals that endanger our food supply, health or comfort. To manage these pests we have pesticides. These are products intended for preventing, destroying, repelling or mitigating any pest.Increase in population demands an increase in food production and therefore the demand for pesticides are growing day by day.All types of pesticides are poisonous and extremely risk. Life without the usage of pesticides is not even remotely possible because of the benefits of the pesticides. There are two types of toxicity in pesticides. They are: 1)Acute toxicity 2)chronic toxicity. To help to understand the toxicity of a substance, a measure termed as LD (Lethal Dose) is used.Based on their chemical structure, pesticides may be classified as : 1)Organo-chloride 2)Organo-phosphates3)Carbonates4)Pyrethroids. Pyrethroid exposure include cerebro-organic disorders, sensomotor-polyneuropathy in the lower extremities and nervous disorders like peroxisomal tachycardia.Lambda cyhalothrin(LCT) is a synthetic type –II pyrethroid insecticide acaricide used to control a wide range of pests in a number of agricultural crops.LCT accumulates in biological membranes leading to the oxidative damage and as a result altering the anti-oxidant enzyme activities.

II. Experimental Methods

Research pertaining to the effect of LCT(Lambda cyhalothrin) in general and mice in particular are sparse. Hence the study is about the sub-lethal effect(1/5th of LD 50) of LCT on neuro toxicity, behavior cholinergic Neuro transmitter ,detoxification-enzymes, histological aspects in mice.Present study was carried out on the male albino rat, Rattus norvegicus, weighing 160(+/-) 20 grams. Rat was chosen an experimental model for the present study.

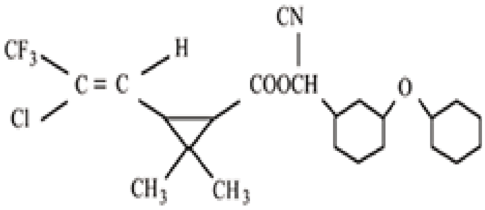
Pesticide Selected: Lambdacyhalothrin(LCT98% purity)



Oral route of administration. Tissue is selected at the brain in the region of Cerebral cortex, Hippocampus, Cerebellum and Medulla oblongata.

IUPACName:3-(2- chloro -3,3,3,-trifloro-1-propenyl)-2,2-dimethyl-cyno(3-phenoxyphenyl)methylcyclopropanecarboxylate.

S.No	Parameter	Method
1.	Toxicity Evaluation	Probit analysis method of finney(1971)
2.	Behavioral Aspects	Morris water maze experiment(1984)
3.	Cholinergic neuro transmittors a)Total Protiens b)Acetylcholine(Ach) c)Acetylcholinesterase(AchE)	 Lowryetal(1951) Metcalf(1951) as given by Augustinson(1957) Ellmanetal(1961)
4.	Anti oxidantdefence system a) Lipid Peroxidation b) Super oxide dismutase c) Catalase d) Gluthathione Peroxidase e) Gluthathione Reductase	Ohkawa et al(1979) Beachamp and Fedowich(1971) Modified version of Aebi(1984) Flohi and Gunzler(1984) Carlberg and Mannevik(1985)
5.	Histological Studies	Humanson(1972)



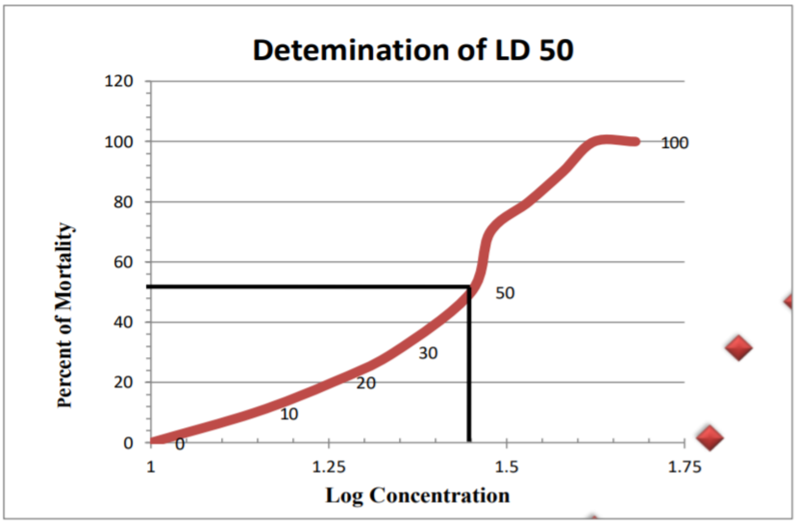
III.Results and discussion

1.Toxicity Evaluation:

Toxicity is defined as inherent capacity of a toxicant that affects any biological activity of an organism.The term dose is used to specify the amount of chemical administered and is usually expressed as mg/kg per bodyweight.The most commonly used methods of calculation of LD50 are the graphical method, regression analysis and estimation of confidence limits as proposed by Finney(1971).

Toxicity Results:

Animals which were exposed to different concentrations of LCT showed no mortality up to 10mg per kg per body weight.A sigmoid curve was obtained and the LD50 value was 26 mg per kg per body weight. After the exposure to LCT, behavioral changes such as salvation, nausea, blinking of eyes, stretching of limbs, erect tails etc., were observed indicating that LCT is toxic to rats.

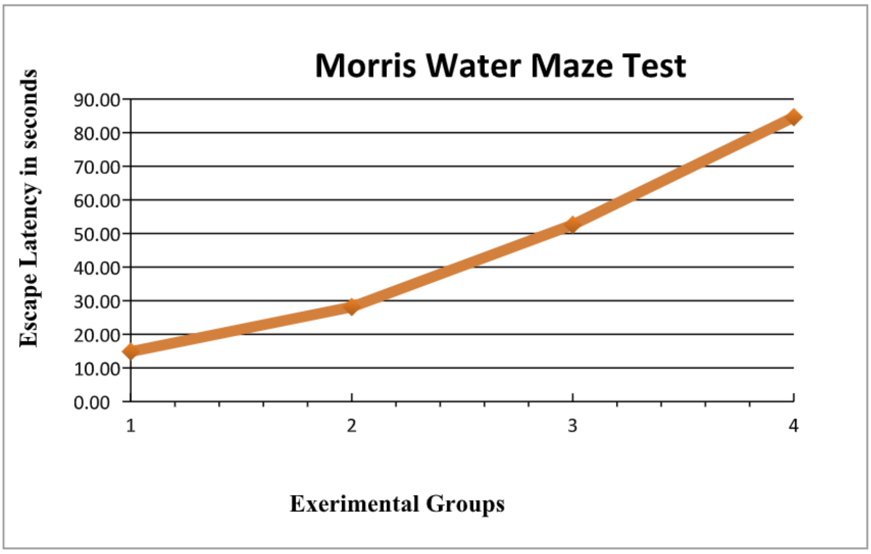


2. Behavioral Studies:

Behavioral observations can provide information regarding the appearance of both overt and neurological abnormalities such as Convulsions, Paralysis and Ataxia.

Results:In the present study the morris water maze task was used to assess the cognitive skills spatial learning and memory ability in control and LCT expressed to rats.In experiment rats expressed to long periods showed increased in latency time on controlled rats (15 seconds) 15th day(28 seconds), 30th day(52 seconds) and 45th day(84 seconds) to reach hidden platform .

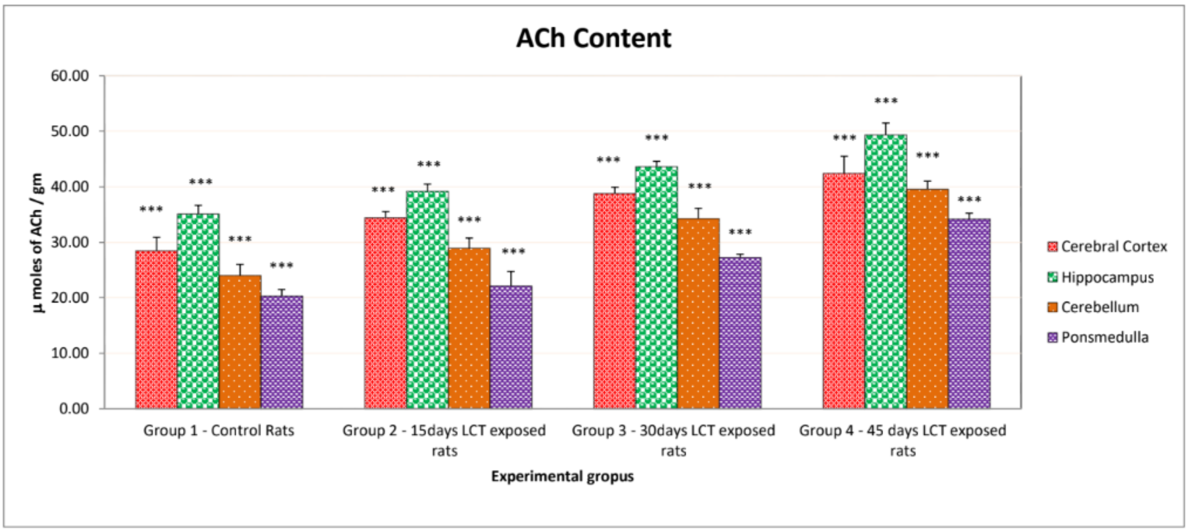
Graph-3: Graphical representation of differences in **Escape latency** between control and experimental groups of rats test on selected days of experimentation by **Morris water maze test**.



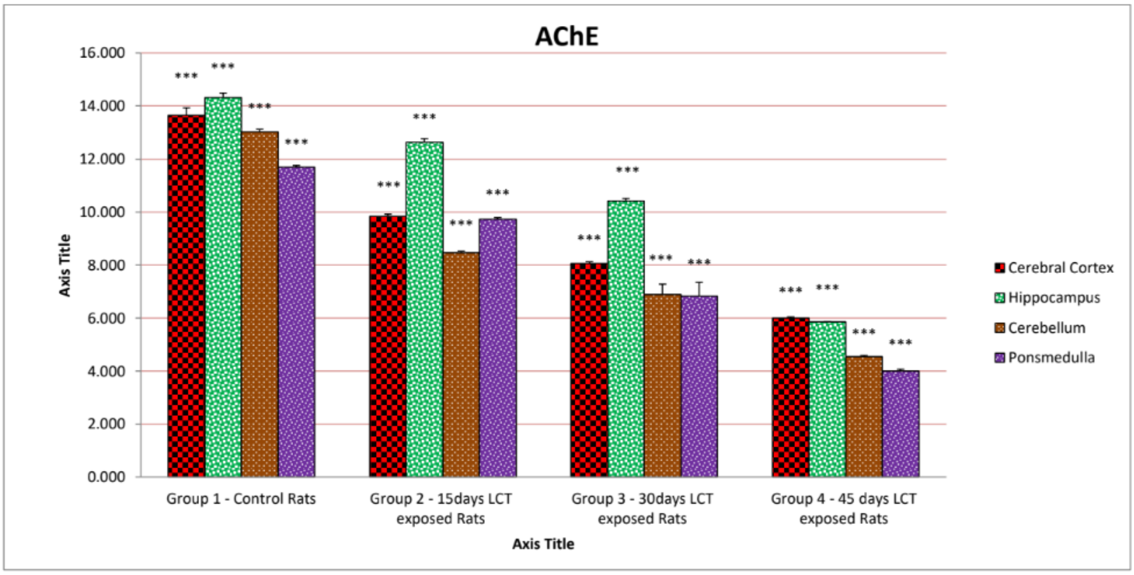
3. Cholinergic Mechanism:

Choline acetyl transferase is the enzyme that is responsible for biosynthesis of acetyl choline. It is the most specific indicator that monitors the functional state of cholinergic neurons.The choice of mice was based on the fact that most of research pertaining to toxicity studies is confined to rats and it is possible that pyrethroids may disturb cholinergic mechanism in mice as well.Hence in the present investigation cholinergic mechanism of pyrethroids pesticide LCT was studies in different regions of brain of mice.

Results:
The increment in the Ach content in different regions is as follows :



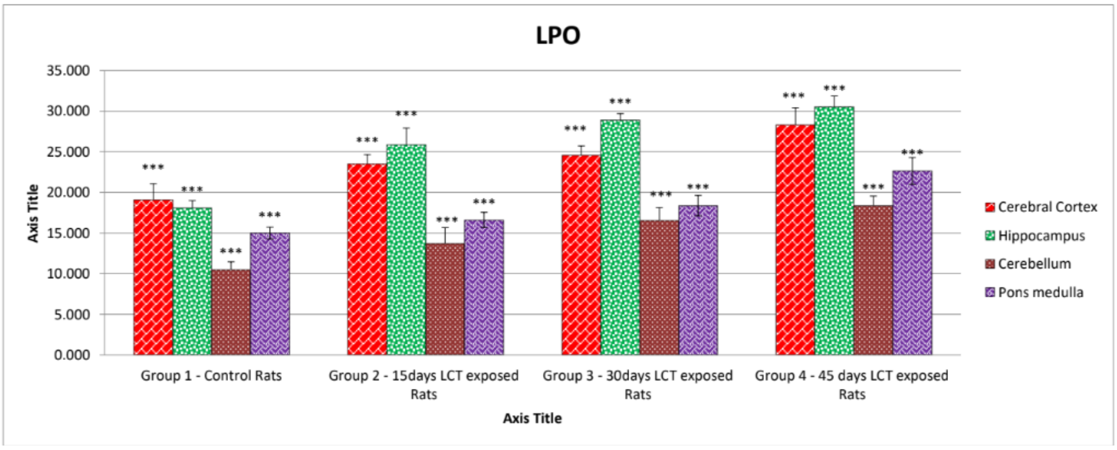
The decrement in the Ach content in different regions is as follows :

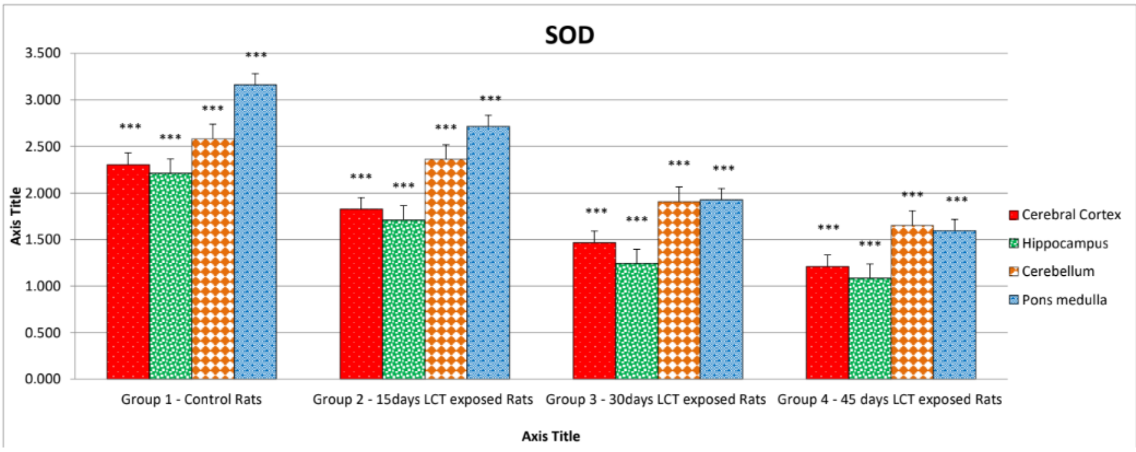


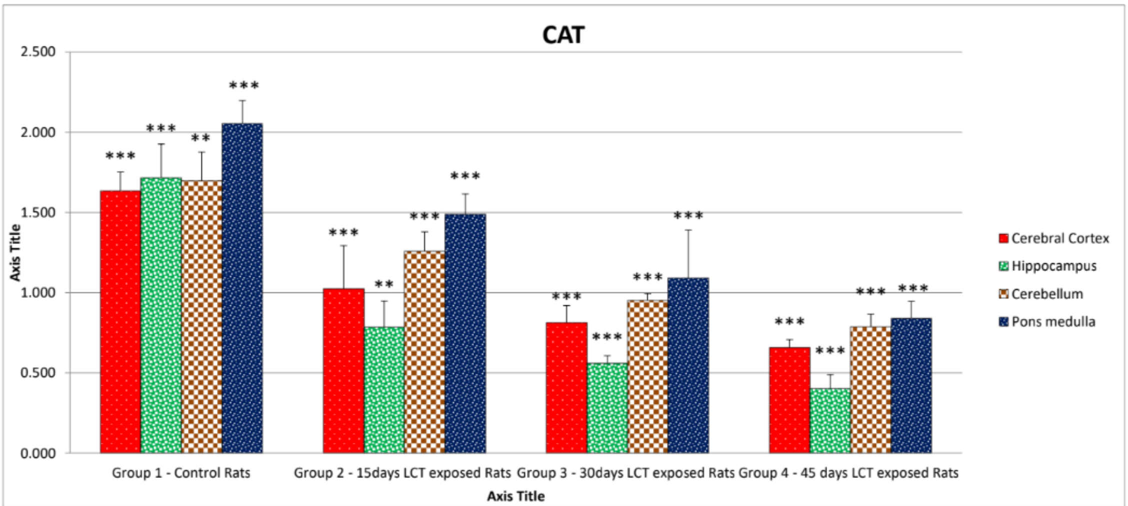
4. Detoxification Mechanism:

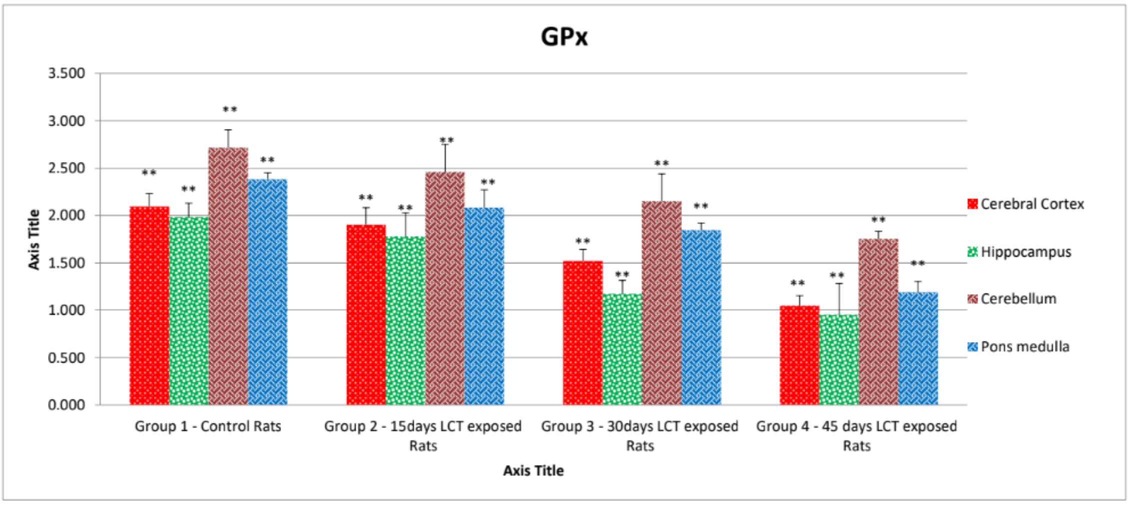
Oxidative stress is the imbalance between biochemical processes leading to the production of the reactive oxygen species(ROS). The antioxidant cascade constitutes the enzymes and other metabolites responsible for the removal of ROS.LCT is found to accumulate in biological membranes leading to oxidative damage and alterations in the anti-oxidative enzymes in mammals are also reported(EI – Demerdash, 2007; Fetoui et al..,2008,2009).LCT induces neuro toxicity and oxidative damage to the rats. The present chapterdeals with the effect of LCT on the markers of oxidative stress in different regions of the Brain.

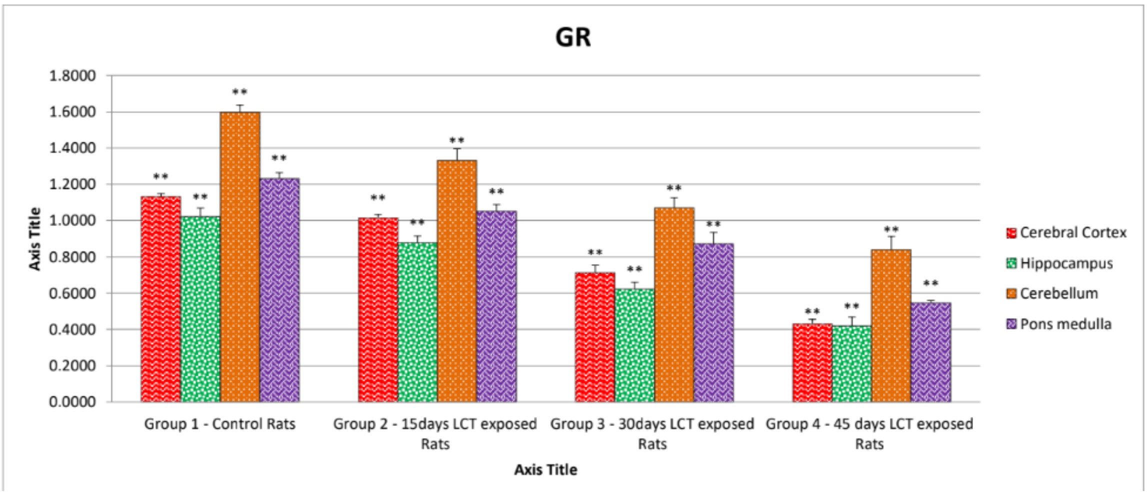
Results:The result of the present study clearly indicates that oral administration of LCT caused a significant elevation in LPO,Asharp decline was noticed in SOD, CAT,GPXand GR in LCT exposed rats.


LPO
35.000
30.000
25.000
20.000
15.000
10.000
5.000
0.000
Axis Title
Group 1 - Control Rats
Group 2 - 15days LCT exposed Rats
Group 3 - 30days LCT exposed Rats
Group 4 - 45 days LCT exposed Rats
Axis Title
Cerebral Cortex
Hippocampus
Cerebellum
Pons medulla


SOD
3.500
3.000
2.500
2.000
1.500
1.000
0.500
0.000
Axis Title
Group 1 - Control Rats
Group 2 - 15days LCT exposed Rats
Group 3 - 30days LCT exposed Rats
Group 4 - 45 days LCT exposed Rats
Axis Title
Cerebral Cortex
Hippocampus
Cerebellum
Pons medulla


CAT
2.500
2.000
1.500
1.000
0.500
0.000
Axis Title
Group 1 - Control Rats
Group 2 - 15days LCT exposed Rats
Group 3 - 30days LCT exposed Rats
Group 4 - 45 days LCT exposed Rats
Axis Title
Cerebral Cortex
Hippocampus
Cerebellum
Pons medulla





5. Histological Studies:

Histology is the study of the tissue sectioned as a thin slice using a microtome. It can also be described as microscopic anatomy.

Histology of rat cerebral cortex under LCT toxicity:

Pyknosis of neurons, moderate congestion of blood vessel (MCBV), loss of neurons (LON), loss of neuronal process (LNP), Virchow robin space (VRS) and vacuolation around outer pyramidal layer.

Histology of rat Hippocampus under LCT toxicity:

Neuro fibrillar network around the glial cells and degenerative changes in glial cells, dilated blood vessels.

Histology of rat cerebellum under LCT toxicity:

Loss of granular layer, neurotic changes in molecular layer, severe congestion of blood vessels etc.,

Histology of rat Medulla Oblongata under LCT toxicity:

Moderate congestion blood vessel (MCBV) and Architectural neuronal process (ANP), severe hemorrhagic areas etc.,

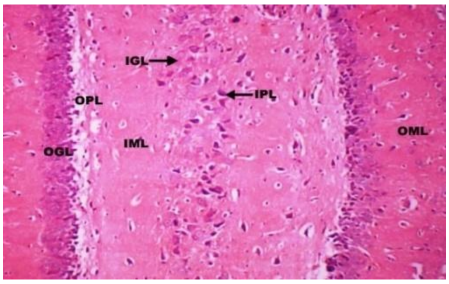
Results:

Ultra-structure of rat Cerebral cortex:

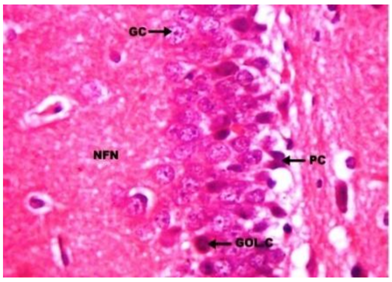
Normal nucleus, nuclear membrane, nucleolus and mitochondria were observed in the control rat Cerebral cortex.Multiple dose treated rat Cerebral cortex showed degenerated nuclear membranes and pyknosis nucleus.

Brain Region :Cerebral Cortex

Control :



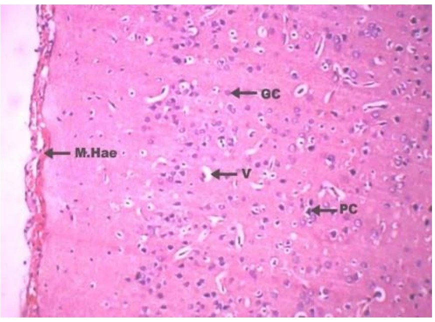
A



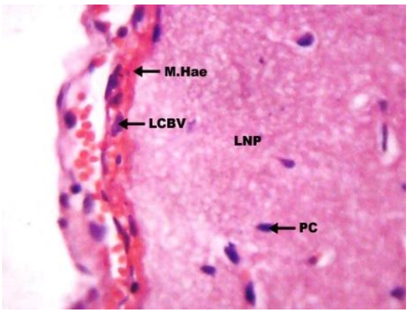
A-1

Control Rat cerebral cortex showing mild haemorrage (M.Hae), vaculation (V), with loss of neuronal process and light congestion of blood vessel– H & E X 400

Experimental (15 days)



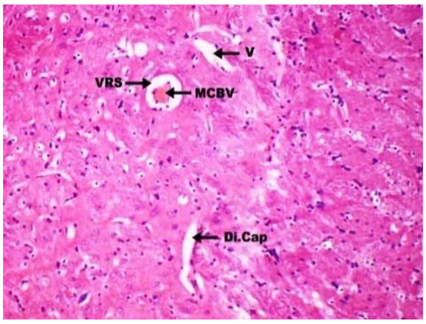
B



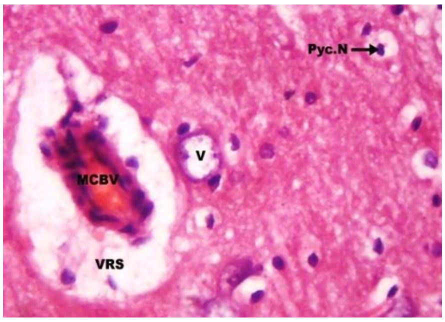
B-1

Experimental Rat cerebral cortex exposed to LCT hydrochloride showing mild haemorrage (M.Hae), vaculation (V), with higher magnification with loss of neuronal process and mild congestion of blood vessel (MC BV) and vacuolation .

Experimental (45 days)



C



C-1

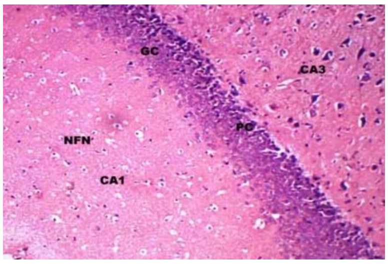
Experimental rat cerebral cortex Longer period exposed to LCT showing pyknosis of neurons (Pyc.N) and moderate congestion of blood vessel (MC BV) under higher magnification Vacuolation (V) Virchow robin space (VRS) and dilated blood capillary (DiBCap), loss of neurons (LON), loss of neuronal processes (LNP) moderate congestion of blood vessel (MCBV) , virchow robins space (VRS) and vaculation are present in outer pyramidal layer

Ultra-structure of rat Hippocampus:

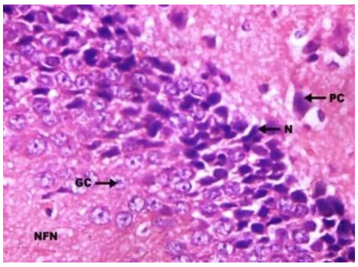
Granular cells with normal, thick and intact membranes were observed in control rat hippocampus.Degenerated changes in neuronal membranes and thinning of membranes were observed in Acephate intoxicated rat Hippocampus.

Brain Region : Hippocampus

Control :



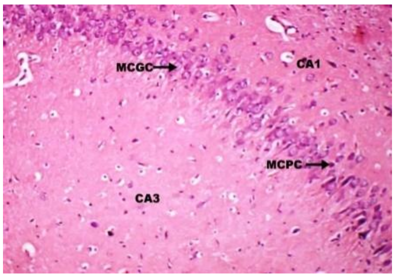
D



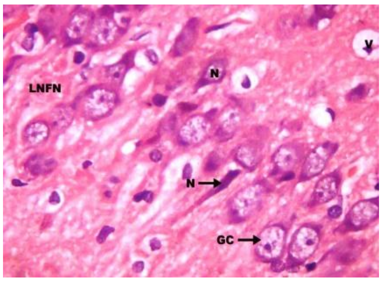
D-1

Control rat hippocampus showing Cornu Ammonis-1, and Cornu Ammonis-3 (CA1 & CA3) layers. Between these two layers glial cells (GC) and pyramidal cells are concentrated, in higher magnification the CA1 area shows glial cells (GC), neurons with neuronal processes (NP), and neuro fibrillar network (NFN) between the nerve cell bodies

Experimental (15 days)



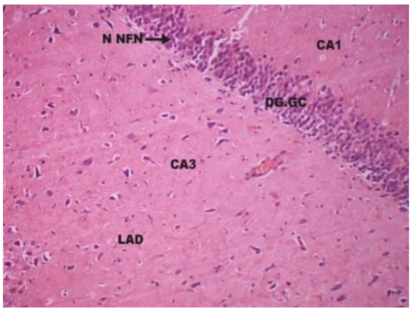
E

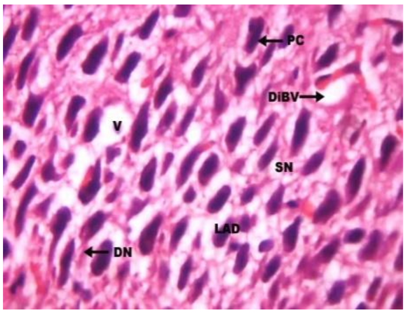


E-1

Experimental Rat rat hippocampus exposed to LCT hydrochloride mild changes in glial cells (MC GC) and in neuro fibrillar network (MCNFN at higher magnification of rat hippocampus showing vacuolation and mild changes in neurofibrillar network (MC NFN)

Experimental (45 days)





Experimental rat hippocampus Longer period exposed to LCT showing necrosis of neurofibrillar network (N NFN) around the glial cells and degenerative changes in glial cells (DG GC) higher magnification vacuolation (V) in neuro fibrillar network, dilated blood *vessel (DiBV),Loss of architectural details (LAD),slight necrosis (SN), degenarated neuron(DN)*

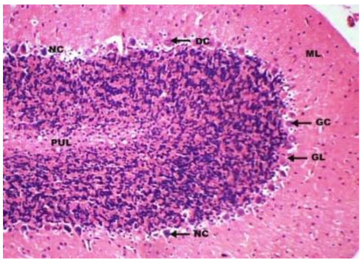
F **F-1**

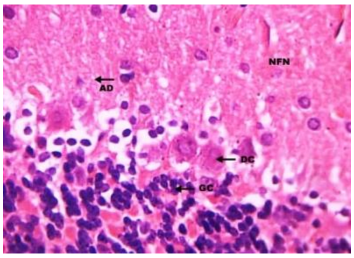
Ultra-structure of rat Cerebellum:

A clearly visible neuron with prominent cell body, axon and inter-neuronal junctions were observed in control rat cerebellum.Multiple dose treated rat Cerebellum showed vacuolative areas due to cytoplasmic shrinkage and apoptotic neurons.

Brain Region : Cerebellum

Control:

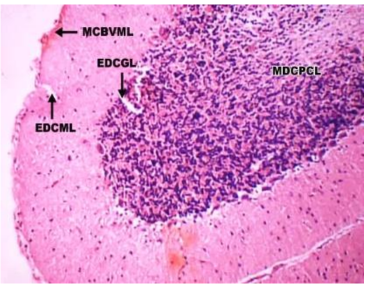


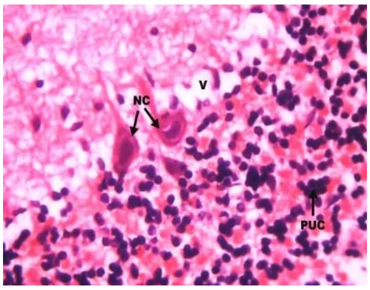


Control rat cerebellum showing molecular layer (ML), granular layer (GL), and Purkinje layer (PUL), neuronal cell (NC), glial cell (GC) and with archetectural details. Under In higher magnification with neurofibrillar network (NFN)are noticed.

G **G-1**

Experimental (15 days)

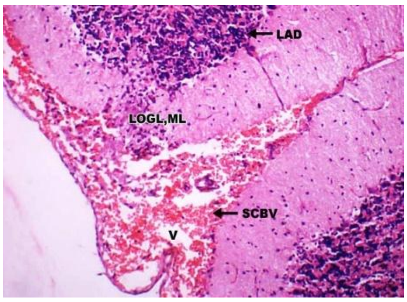


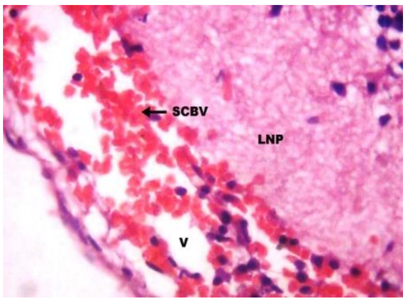


Experimental Rat cerebellum exposed to LCT early degenerated changes of granular layer (EDCGL), mild degenerated changes in purkinje cell layer (MDCPCL), mild congestion of blood vessel in molecular layer (MCBVML), early degenerated changes of molecular layer (EDCML) at higher magnification purkinjecell (PUC), neuronal cell(NC) and vacuolation(V) observed.

H **H-1**

Experimental (45 days)





Experimental rat cerebellum Longer period exposed to LCT showing severe congestion of blood vessel (SCBV) loss of archaetectural details (LAD) vacuolation (V) loss of granular layer, molecular layer. In higer magnification vacuolation(V) severe congestion of blood vessel (SCBV) loss of neuronal process(LNP) were observed.

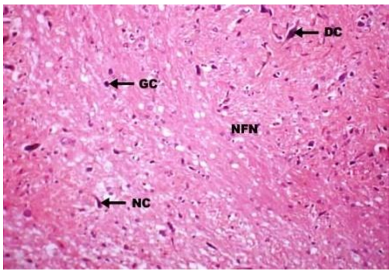
I **I-1**

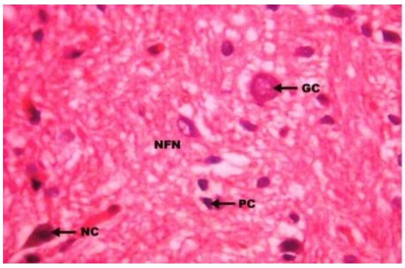
Ultra-structure of rat Medulla oblongata:

The long pyramidal neurons with prominent nuclei were observed in control rat Medulla oblongata.The cytoarchitectural changes in multiple dose treated rat Medulla oblongata include vacuolative areas, degenerated neurons, and degenerated pyramidal cells and degenerated nucleus.

Brain Region : Pons medulla

Control :

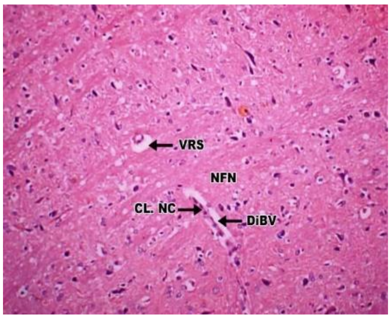


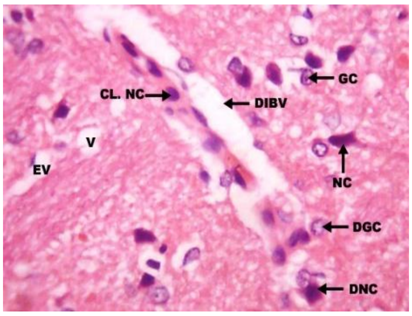


Control rat Pons medulla showing granular cell (GC) neuro fibrillar network(NFN) dendritic cell(DC) neuronal cell (NC). In higher magnification with neurofibrillar network (NFN) are noticed

J **J-1**

Experimental (15 days)

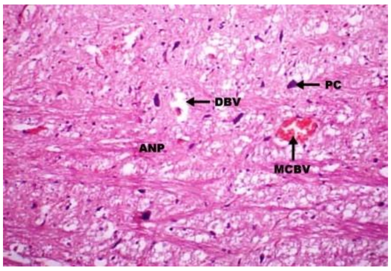


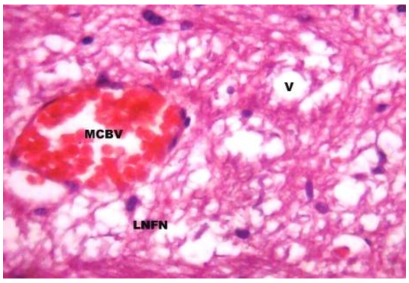


Experimental Rat Pons medulla exposed to LCTvirchows robin space (VRS) neuro fibrillar network (NFN) clumping of neuronal cells (CL. NC), and dilated blood vessel (DiBV) at higher magnification clumping of neuronal cells (CL.NC), dilated blood vessel (Di BV) granular cell (GC) neuronal cell (NC) degenerated granular cell(DGC) degenerated neuronal cell (DNC) Vaculation(V) and excessive vacuolation (EV) were observed.

K **K-1**

Experimental (45 days)





Experimental rat Pons medulla Longer period exposed to LCT showing moderate congestion blood vessel (MCBV) and architectural neuronal process(ANP). Under higer magnification vacuolation (V), moderate congestion blood vessel (MCBV), loss of neurofibrillar network (LNFN) elivated.

L *L-1*

IV. Conclusion

Albino rats due to Acephate intoxication is due to excessive production of free radicals or depletion in the activity of detoxification enzyme.Similarly the damage in mitochondria is responsible for decrement in ATPases activity, as reported in chapter-III. So the damage to normal cytoarchitecture of cells would affect the normal neurochemical processes. Thus there is a correlation between histology and neurochemical processes.

Acknowledgements

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References

[1]. Li-Ming He, John Trojano, Albert Wang and Kean Goh (2008). Environmental chemistry,ecotoxicity and fate of Lambda-cyhalothrin. Rev. Environ. Contm. Toxicol. 195: 71-98.

[2]. Bradberry, S.M., Cage, S.A., Proudfoot, A.T. and Vale, J.A. (2005). Poisoning due to pyrethroids.Toxicol Rev. 24(2): 93-106.

[3]. Casida, J.E. and Quistad, G.B. (1998). Golden Age of insecticide research: past, present or futureAnnu.Rev. Entomol. 43: 1-16.

[4]. Thatheyus, A.J.and Deborah Gnana Selvam, A. (2013). Synthetic pyrethroids: Toxicity andBiodegradation. Appl. Ecol. Environ. Sci. 1(3): 33-36.

[5]. Alzogaray, R.A., Fontan, A. and Zebra, E.N. (1997). Evaluation of hyperactivity produced by pyrethroid treatment on third instar nymphs Triatoma infestans(Hemiptera: Reduviidae). ArchInsectBiochem. Physiol. 35(3): 323-333.

[6]. Baatrup, E. and Bayley, M. (1993). Effects of the pyrethroid insecticide cypermethrin on thelocomotor activity of the wolfspiderPardosaamentata: Quantitative analysis employingcomputer-automated video tracking. Ecotoxicol. Environ. Saf. 26: 138-152.

[7]. Vais, H., Williamson, M.S., Devonshire, A.L. and Usherwood, P.N. (2001). The molecularinteractions of pyrethroid insecticides with insect and mammalian sodium channels. J. PestManag. Sci. 57(10):877-888.

[8]. Godin, S.J., Scollon, E.J., Hughes, M.F., Potter, P.M., DeVito, M.J. and Ross, M.K. (2006). Speciesdifferences in the in vitro metabolism of deltamethrin and esfenvalerate: differential oxidative andhydrolytic metabolism by humans and rats. Drug Met. Dispos. 34(10): 1764-1771.

[9]. VinayagamMagendira Mani, Sivaji Asha, Abdul Majeeth. and Mohamed Sadiq. (2013). Pyrethroiddeltamethrin-induced developmental neurodegenerative cerebral injury and ameliorating effct of dietaryglycoside naringin in male wistar rats. Biomed. Ageing Pathol. 116: 1-8.

[10]. Abdel Aziz, K.B. and Abdel Rahem, H.M. (2010). Lambda, the pyrethroid insecticide as a mutagenic agentin both somatic and germ cells. J. Am. Sci. 6(12): 317-326.

Bonu. Narayana Rao, et. al. "Toxicological impact of Lambda Cyhalothrin in brain of Albino rats." *IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)*, 15(3), (2020): pp. 30-40.