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LAMBDA CYHALOTHRIN INDUCED OXIDATIVE STRESS ON BRAIN TISSUES OF *RATTUS NORVEGICUS* AND ITS AMELIORATION BY GREEN TEA EXTRACT

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Abstract: Lambda cyhalothrin is one of the most important agricultural pesticides extensively used around the world. Pyrethroids are specially recommended insecticides as they have low mammalian toxicity, but they are known to cause an alteration in biochemical parameters and affect the oxidative status of the body through producing free radicals. However, it has been found that some herbal extracts can ameliorate the toxicity induced by the pesticides and other chemicals but the search for such compounds will always be an urgent need to achieve the optimum degree of amelioration. For this purpose, the present study was designed to evaluate the oxidative stress produced by lambda cyhalothrin, a synthetic type-II pyrethroid and ameliorating effect of green tea extract in albino rats.

Keywords: ATPase activity, Catalase, Green tea extract, Lambda cyhalothrin.

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INTRODUCTION

Synthetic pyrethroids, a group of neurotoxic insecticides have emerged as a new class of agricultural pesticides showing high toxicity to a wide range of insects including resistance strains and low toxicity to mammals and rapid biodegradability (Ali, 2012). Based on the structural differences, pyrethroids are broadly classified into two types. Type I class of pyrethroids do not contain α-cyano group and type II pyrethroid with the cyano group. Type I pyrethroids generally affects the peripheral nerves, while type II pyrethroids affects the entire nervous system and they are preferred for large scale uses due to their higher potency (Ansari *et al*., 2012). Large-scale application of pyrethroids to crops may contribute to the presence of toxic substances in the environment. These chemical compounds can find their way into the water reservoirs, streams and rivers, thus producing an adverse impact on the aquatic biota, animals and human health. Human exposure to pesticides is reported to occur mainly occupationally during application or through pyrethroids residues such as those detected in milk and blood of dairy cows and cattle meat as well as vegetables and fruits (Turgut *et al*., 2011).

Lambda cyhalothrin, a type II synthetic pyrethroid is the most widely used pyrethroid due to its effectiveness and toxicity. Lambda cyhalothrin has extensively used as an agro-pesticide in the cotton plantation, in vegetable production and to control a wide range of insect pests in a variety of crops and also used for the control of vectors and pests of public health importance (WHO, 1990). Lambda cyhalothrin is rapidly metabolized in the liver via hydrolytic ester cleavage and oxidative pathways by the cytochrome P450 (CYP450) enzymes yield reactive oxygen species (ROS) (Sankar *et al.*, 2012). The over production of ROS exceeds the capacity of the cell's endogenous systems to neutralize them result in oxidative stress. Cells had several biological defence mechanisms against intracellular oxidative stress, out of which enzymatic antioxidant defence system includes superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GR) and glutathione transferase (GST) etc. These mechanisms cooperate with each other to defend against reactive species that induced cellular damage (Shukla and Prakash, 2022).

Green tea obtained from the plant *Camellia sinensis* (L.) has been the most consumed beverages in the world. It shows many beneficial effects on diseases including cancer, obesity, diabetes, inflammatory and neurodegenerative diseases (Chacko *et al.*, 2010). During the last decades, the beneficial health effects of green tea have been demonstrated in several studies. The health-promoting effects of green tea are mainly attributed to its polyphenol content (Naghma and Hasan, 2007), which represent 30% of fresh leaf dry weight (McKay and Bloomberg, 2002). Polyphenols are the most biologically active compound of tea, which have antioxidative, antimutagenic and anticarcinogenic effects (Higdon and Frei, 2003).

A number of researchers did a lot on the effects of different pesticides in different fishes (Prakash and Verma, 2014, 2020, 2021; Verma and Prakash, 2018; Kaur and Mishra, 2019; Masih, 2021) but as far as the mammals are concerned, it is explored little. The objective of present study was to evaluate the status of oxidative stress biomarkers in rat brain, under the stress of lambda cyhalothrin, a type II pyrethroid as well as the possible protective role of green tea.

MATERIALS AND METHODS

Experiments were carried on healthy adult *Rattus norvegicus* (Berkenhout) of almost equal size and weight from either sex selected from inbred colony under controlled conditions of temperature (25 ± 50^{O}C), and humidity (60 ± 5%). They were given pellet food and drinking water *ad libitum*.

The test compound chosen for this study was λ-cyhalothrin, which is type–II synthetic pyrethroids (Fig. 1) obtained from Bayer India Ltd. Mumbai. The acute oral Ld_{50} of λ-cyhalothrin was calculated as 86.40 mg/kg b wt. (Kumar and Yadav, 2021). Aqueous solution of Green Tea Extract equivalent to 1.5% (w/v) was used for experiment. Approximately 15 g of GT leaves was soaked in 1 L of boiled distilled water for 5 min with occasional swirling to prepare the green tea extract.

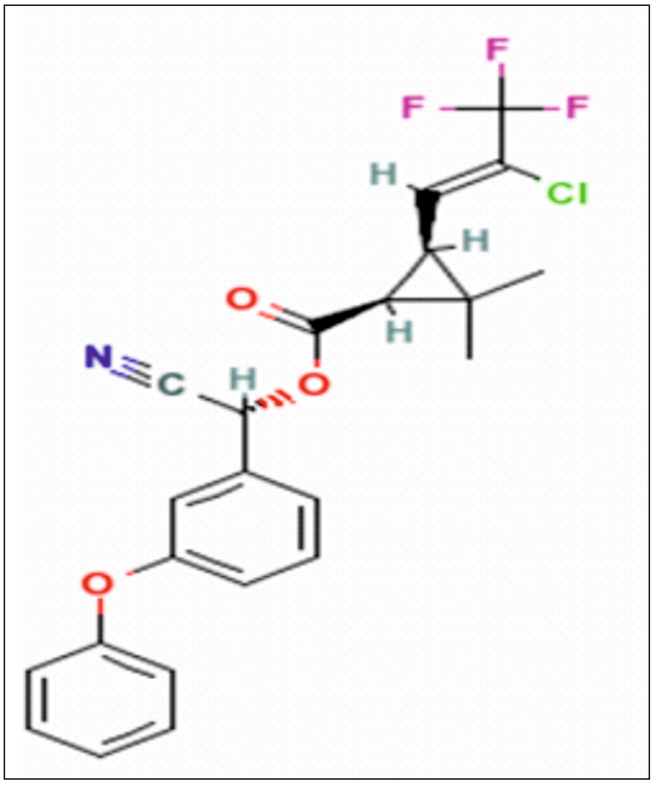

Fig. 1: Structure of lambda cyhalothrin.

The albino rats were divided into three groups (Control, λ-cyhalothrin and λ-cyhalothrin+green tea extract), which were further divided into five subgroups including one set of 5 albino rats for acute treatment (1d) for each treatment group and four sets for sub-acute treatment (7, 14, 21, 28 days). In this manner there are 3 sets for acute treatment and twelve sets for sub-acute treatment. The control sets were kept in identical

conditions. The acute doses were estimated as 1/10th of LD50 while sub-acute doses were obtained by dividing the acute dose by the number of treatment days.

Rats of all groups were sacrificed by cervical dislocation 24 hr after the last treatment, tissues were collected, washed with normal saline and used for estimations. The estimation of brain total ATPase activity was done by the method of Seth and Tangari (1966). Catalase activity in brain tissue was estimated by Kit method (Callaway, 1998). Superoxide dismutase (SOD) activity was assayed by estimating inhibition of auto oxidation of epinephrine (Mishra and Fridovich, 1972).

The results were presented as the mean ± SEM. Comparisons were made between control and treatment groups using one way analysis of variance (ANOVA). Values of p £ 0.05 were regarded as statistically significant.

RESULTS AND DISCUSSION

ATPase activity has been decreased significantly after acute and subacute treatment of lambda cyhalothrin alone as compared to control set. Further, in second set the ATPase activity has been found to be increased after acute and subacute combined treatment of lambda cyhalothrin and green tea extract as compared to lambda cyhalothrin treated set (Table-1). The Catalase activity inhibited significantly ($P<0.05$) in lambda cyhalothrin treated set as compared to control set, while significant ($P<0.05$) enhancement after combined treatment with lambda cyhalothrin + green tea extract when compared to lambda cyhalothrin treated set (Table-2). There is a highly significant ($P<0.01$) decline has been observed in SOD activity in brain tissues after acute and subacute treatment of lambda cyhalothrin as compared to control set, while significant ($P<0.05$) enhancement after combined treatment with lambda cyhalothrin + green tea extract when compared to lambda cyhalothrin treated set (Table-3). The results have been found in accordance with Tukhtaev *et al.* (2012), Ansari *et al.* (2012), Pawar *et al.* (2017) and Narayan Rao *et al.* (2022).

Table 1: ATPase activity (U/mg of protein) after lambda cyhalothrin intoxication and amelioration by green tea extract in albino rat after acute and subacute treatment.

Treatment Group	Acute	Treatment Group				Level of Significance
	(1 day)	(7 days)	(14 days)	(21 days)	(28 days)	
Control	1.24±0.035	1.28±0.040	1.25±0.038	1.24±0.030	1.26±0.066	
Lambda cyhalothrin	1.10±0.033	1.02±0.025	0.95±0.067	0.85±0.045	0.78±0.038	P<0.01
Lambda cyhalothrin + Green tea extract	1.15±0.025	1.20±0.030	1.22±0.020	1.24±0.040	1.26±0.035	P<0.05

In the present investigation significant lowering of ATPase activity has been observed under stress of lambda cyhalothrin in brain on all treatment days may be due to the adaptive changes occurring inside the body. The decreased activity of the enzyme may lead to decrease in ATP breakdown leading to reduction in the free energy and thus creating disturbances in ion homeostasis and gains support by studies done by Forshaw *et al.* (2000) and Latuszynska *et al.* (2001).

The catalase (CAT) and superoxide dismutase (SOD) are very important enzymes of cytosol. These acts as endogenous antioxidants hence protect cells from attack of free radicals produced in various vital processes These are very important because our body regularly produces free radicals and ROS which damages the cells. These enzymes maintain the balance between

Table 2: Catalase (U/min) activity after lambda cyhalothrin intoxication and amelioration by green tea extract in albino rat after acute and subacute treatment.

Treatment Group	Acute	Treatment Group			Level of Significance
	(1 day)	(7 days)	(14 days)	(21 days)	(28 days)	
Control	11.10±0.23	11.15±0.35	11.18±0.33	11.22±0.38	11.20±0.40	
Lambda cyhalothrin	10.95±0.65	10.67±0.45	09.88±0.48	09.10±0.40	08.77±0.67	P<0.05
Lambda cyhalothrin + Green tea extract	10.99±0.28	11.05±0.33	11.10±0.35	11.14±0.42	11.18±0.40	P<0.05

Table 3: SOD (U/mg of protein) activity after lambda cyhalothrin intoxication and amelioration by green tea extract in albino rat after acute and subacute treatment.

Treatment Group	Acute	Sub-acute			Level of Significance
	(1 day)	(7 days)	(14 days)	(21 days)	(28 days)	
Control	7.15±0.67	7.20±0.60	7.18±0.33	7.00±0.35	7.22±0.66	
Lambda cyhalothrin	6.59±0.33	6.33±0.50	5.90±0.40	5.30±0.88	4.99±0.80	P<0.01
Lambda cyhalothrin + Green tea extract	6.99±0.50	7.05±0.33	7.19±0.65	7.25±0.67	7.30±0.45	P<0.05

oxidant-antioxidant. They are present in all cells of body but concentrates in brain and liver. The superoxide dismutase (SOD) and catalase (CAT) are endogenous antioxidant enzyme which protects from oxidative damage to cells and cellular parts. The lambda cyhalothrin induces production of free radicals and ROS which damage cellular membrane and injured the neuronal conduction sites. The ions of lambda cyhalothrin are responsible for free radicle production. Further it enhances other processes to induce the ROS production other than the brain. Overall, this condition is pathogenic and lead to malfunctioning of nervous system. The green tea extract is supplemented for antioxidants which neutralize the free radicals and ROS by binding action. This way green tea extract reduces the damage produced by lambda cyhalothrin and modulates its toxic effect. These findings have been supported by Walker (2000) exhibited the role of various xenobiotics in producing neurotoxicity in human, Luty *et al.* (2005) evaluated oral toxicity of alpha cypermethrin and its distribution in mice organs, Ravisekhar *et al.* (2010) assessed cypermethrin and sodium fluoride synergistic effect on oxidative enzyme in muscle and kidney of albino mice, Tukhtaev *et al.* (2012) revealed, that prolonged exposure of lambda cyhalothrin leads to the development of oxidative stress in both of pregnant females and their offspring.

CONCLUSION

This study demonstrates that green tea has a potential protective effect against lambda cyhalothrin toxicity. The ameliorative effect is due to antioxidative nature of catechins, and some flavonoid components present in the green tea. Thus, green tea extract has beneficial effects to minimize toxic effects and to limit the toxicity against pesticides exposure.

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