Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 2 (7) June 2013: 43- 47

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com

ORIGINAL ARTICLE

Deltamethrin induced Changes in the Testicular Adenosine Triphosphatases (ATPases) activities in the Adult rats

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ABSTRACT
Deltamethrin (DM), a synthetic pyrethroid type II is used extensively in agriculture, forestry, horticulture, public health and households throughout the world. The present investigation was undertaken to study the effect of DM on the specific activities of Adenosine Triphosphatases (ATPases) in the testis of adult rats. Adult male rats (90 days old) of Wistar strain were exposed to DM at the dose of 1mg/kg body weight, orally for 60 days. The control group received corn oil alone as vehicle. Another group of rats were treated with DM and the same was withdrawn for a further period of 60days. After the treatment period rats were euthanized and the testes were immediately removed and used for estimating the enzyme activities. Administration of DM significantly decreased the activities of Na^+ K^+ dependent ATPase, Mg^{++} dependent ATPase and Ca^{++} dependent ATPase. However, the parameters from the animals after withdrawal of DM treatment were similar to those of control groups. Thus, the present study suggests that chronic low dose of treatment of DM is capable of inducing testicular toxicity.
Keywords: *Deltamethrin, Adenosine Triphosphatase, Testis.*

Received 22.04.2013 Accepted 07.06.2013

INTRODUCTION

Pesticides constitute the major potential environmental hazards to humans and animals as these are present and concentrated in the food chain [1]. Synthetic pyrethroids are modified derivatives of pyrethrins, natural substances obtained from flowers of *Pyrethrum* species [2]. Pyrethroids are a group of highly potent lipophilic insecticides with relatively low mammalian toxicity and one of the least acutely toxic insecticides to mammals because they are quickly deactivated by metabolic processes. They are widely used in agriculture, forestry, horticulture, public health and households throughout the world.

Pyrethroids are a class of agents which mainly act on the central nervous system, although significant effects on peripheral nerves and muscle are also known. Their capacity to interact reversibly with a wide range of ion channels, possibly via their phosphorylation state, is a key property of pyrethroids and sodium channels are their major targets [3-5].

Deltamethrin (DM) is a synthetic pyrethroid with strong insecticidal properties. The technical grade DM is composed of eight stereomeric esters (four cis and four trans isomers) of the dibromo analogue of chrysanthemic acid, 2, 2 - dimethyl - 3 - cyclopropanecarboxylic acids. Evidences support the deleterious effects of DM on various aspects of male reproduction in rats and mice. The effects include decreased weight of testes and accessory sex organs, sperm count, motility and increased incidence of sperm abnormalities [6-10], decreased level of gonadotrophins, testosterone, induced oxidative stress [11], degenerative changes in the seminiferous tubules, germ cell depletion, alterations in the structure of sertoli and interstitial cells [12,13].

ATPases are the enzymes which hydrolyse ATP. ATPases exist in all cell membranes and regulate the ionic concentrations inside the cells and these ions play a significant role in many metabolic pathways and a crucial role in a variety of pathological and toxicological processes. Recent reports suggest that the activities of ATPases were inhibited by DM in human erythrocytes [14] and in Channa punctatus [15]. In the present paper, we report the effect of DM invivo on the specific activities of ATPases in the testis of adult rats.

MATERIALS AND METHODS

Chemical:

Deltamethrin (98.1% purity) was a gift from the BR Agrotech Ltd. Kathua (J &K), India.

Animals

Male Wistar rats (90 days old were obtained from Sri Raghavendra Enterprises, Bangalore. They were maintained in a separate animal house with a 12:12 light dark cycle. Then the animals were housed in polypropylene cages with a paddy husk bedding at a temperature of 28 ± 2^0C and 50 ± 5% humidity. The rats were fed on laboratory chow and water adlibitum. The body weight and growth rate of the experimental animals were registered on alternate days. All experimental procedures and animal maintained and handled as per the guidelines of the Committee for the Purpose of Control and Supervision of Experimental on Animals (CPCSEA) Government of India and Institutional Animal Ethics Committee (IAEC) (845/ac/04/2004).

Experimental Design:

Animals were divided into **three** groups and each group consists of six animals

Group I – Control: Rats were given corn oil as vehicle orally for 60 days.

Group II – Deltamethrin (DM) treatment: Rats were treated with Deltamethrin dissolved in corn oil at a dose of 1 mg/kg body weight daily for 60 days, orally.

Group III – Deltamethrin Withdrawal treatment (DM-W): Rats were treated with Deltamethrin dissolved in corn oil at a dose of 1mg/kg body weight, orally for 60 days and left untreated for another 60 days to observe the withdrawal effects.

Collection of tissue:

The Rats were weighed and sacrificed twenty four hours after the last treatment, by anaesthetic ether. The testes, epididymis, seminal vesicles, ventral prostate were removed and cleaned of fat and adhering tissue, washed in cold physiological saline repeatedly and were weighed and kept on ice at 4^0C for further analysis .

Biochemical analysis:

The tissue was homogenized in Teflon homogenizer (Potter Ekvehjem) in 0.32M sucrose solution and the homogenate was centrifuged at 10000 x g for 30 mins at 4ºC. The supernatant was used for enzyme assays. Protein was determined by the method of Lowry et al.,[16]. The activities of Sodium and Potassium (Na^+ $K^{+)}$ dependent ATPase, Calcium (Ca^{++}) dependent ATPase and Magnesium (Mg^{++}) dependent ATPase were estimated according to the method of Takeo and Sakanashhi [17].

Satistical analysis

Single way Analaysis of Variance (ANOVA) was followed to analyse the data according to Zar [18]. If the 'F' ratio was significant, Student – Neumann – Keul's (SNK) test was followed.

RESULTS AND DISCUSSION

Like in all other systems, development and function of the reproductive system (Hypothalamic – pituitary- gonadal axis) are influenced by a large array of environmental factors; spermatogenesis and steroidogenesis are affected by chemicals (Heavy metals, Nitrofurans, Pesticides, alkylating drugs) and physical agents (heat, irradiation). [19]

The effect of DM at the dose of 1 mg/kg body weight orally for 60 days on the body weight, testicular, epididymal, seminal vesicular and prostate gland weight in adult rats has been shown in Fig. 1 and 2.Organ weight is a fundamental bench mark for the toxicological studies.[20] Deltamethrin treatment reduced the body weight, testicular, epididymal, seminal vesicular and prostatic weight significantly ($P<0.05$) in male adult rats. The present study is consistent with the earlier report of Oda et al., [13] who observed mild to severe degenerative changes in seminiferous tubules at the dose of 6 mg/kg body weight of DM for 60 days and decreased testes weight in rats. The reduction in the weight of the testis of deltamethrin treated animals indicates impaired testicular growth. The weight of testes is largely dependent on the mass of differentiated spermatogenic cells and the reduction in the weight of testes may be due to reduced tubular size, decreased number of germ cells and elongated spermatids. [21]

In our study DM caused a significant reduction in the reproductive organ weights which might be due to reduced bioavailability of androgen. Our results are in agreement with the findings by Abd El-Aziz et al [8] and Anderson et al [7], who mentioned that testicular weight of wistar rats treated by DM was reduced at the dose of 4.0 mg/kg body weight from day 1 of pregnancy to day 21 of lactation. The weight of the testis is basically dependent on the mass of the differentiated spermatogenic cells; the reduction in the weight of the testis may be due to decreased number of germ cells, inhibition of spermatogenesis and steroidogenic enzyme activity [22].

ATPases are the lipid dependent membrane bound enzymes. Any alteration in membrane lipids leads to change in membrane fluidity, which in turn alters the ATPase activities and cellular function [23]. A certain degree of membrane fluidity is essential for Na^+ K^+ dependent ATPase; the fluidity of membrane is determined by the fatty acids [14, 15]. They play a vital role in the maintenance of ionic gradients and the release and uptake of biogenic amines in CNS [24, 25].

Fig 3. Shows the effect of DM on the specific activites of Na^+ K^+ dependent ATPase, Ca^{++} dependent ATPase and Mg^{++} dependent ATPase in the testis of adult rats. It has also been shown that the inhibition of these ATPases by synthetic Deltamethrin. [14, 15, 26] Thus, ATPases are very sensitive to chemical interaction and can be used as reliable biomarker for the mechanistic toxicity studies of pesticides.[27] In the present investigation, the activities of Na^+ K^+ dependent ATPase, Ca^{++} dependent ATPase and Mg^{++} dependent ATPase were significantly ($P<0.05$) decreased in the testis of Deltamethrin treated rats.

Fig 1 : Effect of Deltamethrin on body weight and Testicular weight in adult male rats. Each value is mean ± SEM of 6 animals [a] and [b] represent statistical significance at $P<0.05$ compared with control and DM, respectively.

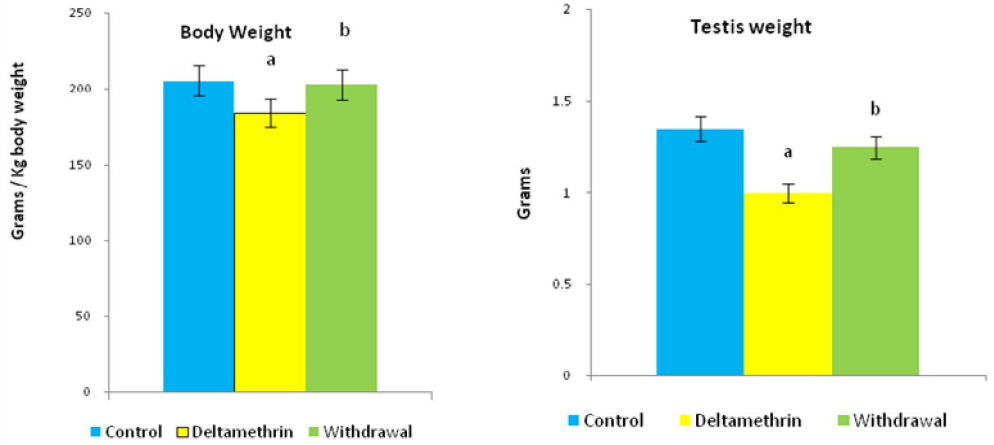
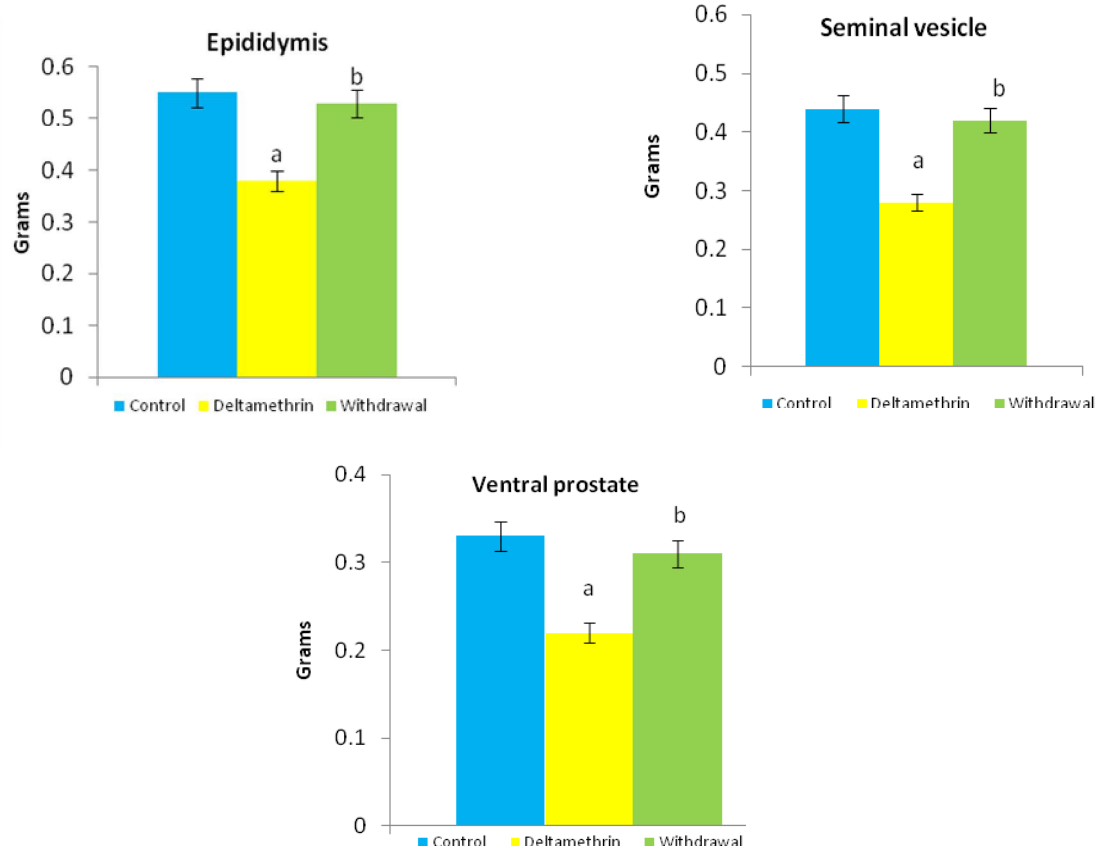
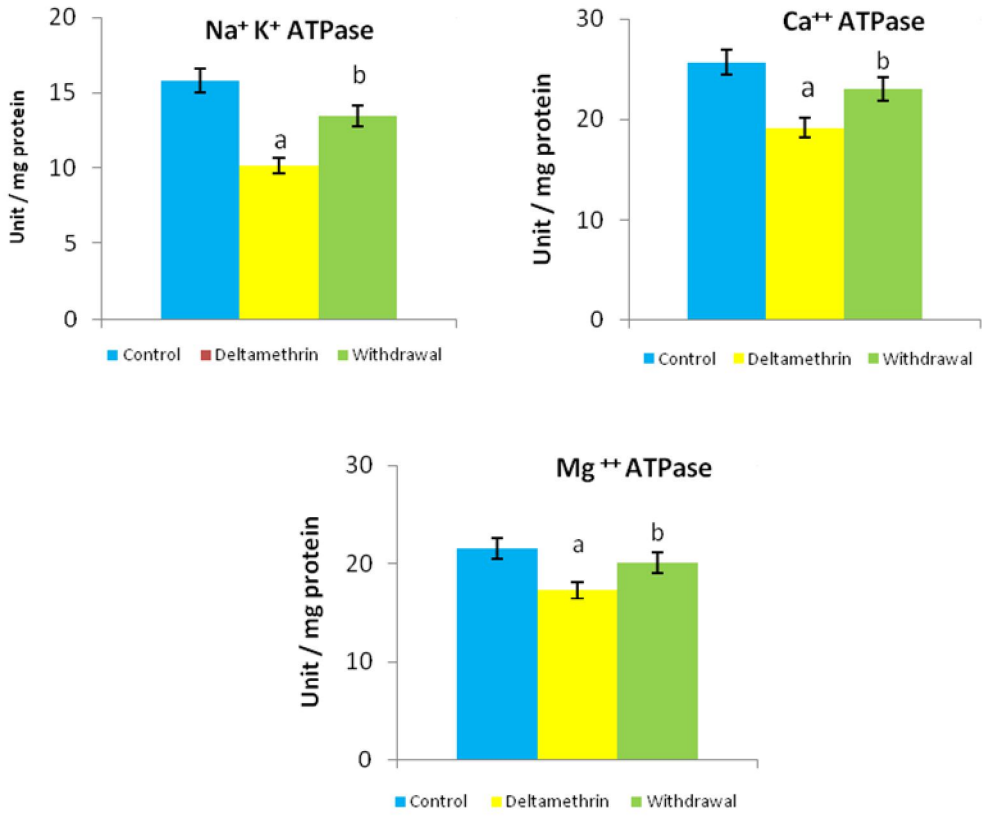


Fig 2: Effect of Deltamethrin on Male accessory sex organs weights in adult rats



Each value is mean ± SEM of 6 animals
[a] and [b] represent statistical significance at $P<0.05$ compared with control and DM respectively

Fig 3 : Effect of Deltamethrin on the specific activities of Adenosine triphosphatases in the testis of adult rat.



Each value is mean ± SEM of 6 animals
[a]and [b] represent statistical significance at P<0.05 compared with control and DM, respectively

Pesticides are known to have a strong affinity of interaction with membrane lipids. [28] It has been shown that the cell membrane is believed to be the site of action of insecticides by altering structural and functional integrity of cell membrane and also effects membrane bound enzymes such as total ATPase, $Na^+ K^+$ ATPase and Mg^{++} ATPase [29, 30]. Javier vargas – Madraro etal [14] have reported that the Plasma membrane Ca^{++} dependent ATPase activity was partially inhibited by Deltamethrin in human erythrocytes. However, significant decrease (P<0.01) was found in $Na^+ K^+$ ATPase, Ca^{++} and Mg^{++} ATPase activities in the brain, kidney, gills, muscles and intestine of fish Channa punctatus exposed to Deltamethrin [15].

In the present study, it has been observed that the exposure of Deltamethrin at the dose of 1 mg/kg body weight for 60 days caused decreased activity of testicular ATPases in albino rats. This may be due to deltamethrin induced effect on cell membrane because of their strong affinity for interaction with membrane lipids [28] causing inhibition of membrane bound ATPase enzyme activity by affecting enzyme complex [29, 31].Thus, the results obtained in the present study indicates that the exposure of DM at the dose of 1 mg/ kg body weight for 60 days affects the testicular functions leading to physiological impairment.

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HOW TO CITE THIS ARTICLE

Sandhia.D and Kumaran.B. Deltamethrin induced Changes in the Testicular Adenosine Triphosphatases (ATPases) activities in the Adult rats *.Bull. Env. Pharmacol. Life Sci*., Vol 2 (7) June 2013: 43-47