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Evaluation of cytogenetic effects of lambda-cyhalothrin on Wistar rat bone marrow by gavage administration

Ayla Çelik[a,*], Birgül Mazmanci[a], Yusuf Çamlica[a], Ülkü Çömelekoğlu[b], Ali Aşkin[a]

[a]*Department of Biology, Faculty of Science and Letters, Mersin University, 33342 Mersin, Turkey*
[b]*Department of Biophysics, Faculty of Medicine, Mersin University, Mersin, Turkey*

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Abstract

In this study, a synthetic pyrethroid insecticide, lambda-cyhalothrin (LCT), was administered to adult female albino rats (Wistar rats) by gavage dose of 6.12, 3.06, 0.8 mg/kg b.w. repeated for 13 days at 48 h intervals. The cytotoxic and genotoxic effects of LCT were investigated in bone marrow cells, using the structural chromosomal aberration (SCA) and micronucleus (MN) test systems. Mitomycin C (MMC) was also used as positive control (2 mg/kg b.w.). All the doses of LCT increased the number of SCAs and the frequency of micronucleated erythrocytes, with respect to the control group. Only the highest dose of LCT significantly increased the MN frequency compared with control ($P<0.01$). It was also observed that LCT caused a significant decrease in the number of polychromatic erythrocytes compared with controls ($p<0.001$). These observations indicate the in vivo suspectibility of mammals to the genetic toxicity and cytotoxicity potential of LCT.

Keywords: Lambda-cyhalothrin; Structural chromosome aberrations; Pyrethroid insecticide; Micronucleus; Polychromatic erythrocytes; Wistar rat

1. Introduction

According to 1997 market estimates, approximately 5684 million pounds of active pesticide ingredients are applied annually throughout the world (USEPA, 2001). The World Health Organization (WHO) (WHO, 1992) reported that roughly three million pesticide poisonings occur annually and result in 220,000 deaths worldwide. Many of these chemicals are mutagenic (Galloway et al., 1987; Garaj-Vrhovac and Zeljezic, 2000), linked to the development of cancers (Leiss and Savitz, 1995) or may lead to developmental deficits (Arbuckel and Server, 1998). Since several studies have shown that exposure to pesticides may induce genotoxic effects in occupationally exposed human populations (Börzsönyi et al., 1984; Dulot et al., 1985; Nehéz et al., 1988), the evaluation of the genotoxicity of pesticides in use is of immediate concern.

The synthetic pyrethroid insecticides are analogs of naturally occuring pyrethrins and have been developed with the aim to improve the specificity and activity of natural insecticide pyrethrum (Sogorb and Vilanova, 2002). Synthetic pyrethroids are a group of potent insecticides that are environmentally compatible by virtue of their moderate persistence, low volality, and poor aqueous mobility in soil. The favorable properties of this class of insecticides have promoted widespread application in virtually all sectors of food protection and pest control. With regard to effectiveness and toxicity, synthetic pyrethroids appear to be the first-choice insecticides for this type of use pattern because pyrethroids are much more effective against a wide spectrum of pests than the other insecticides particularly, organochlorine, organophosphate, and carbamate insecticides (Pauluhn, 1999). With the use of pyrethroids steadily rising, there may be an urgent need to identify

*Corresponding author. Fax: +90-324-3610047.
E-mail address: a.celik@mersin.edu.tr (A. Çelik).

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the adverse effects that may be associated with their use. Genotoxic potentials of some pyrethroid insecticides were shown in previous studies (Carbonell et al., 1989; Puig et al., 1989; Surralles et al., 1990). The carcinogenic potential of pyrethroids has been discussed in a review by Litchfield (1985). Lambda-chyalothrin (LCT) is a newer pyrethroid insecticide used all over the world. The cytogenetic effects of LCT were investigated in human and different animal species using different endpoints such as micronucleus (MN), chromosomal aberrations, sister chromatid exchange (Agarwal et al., 1994; Campana et al., 1999; Fahmy and Abdalla, 2001).

The data reported on the genotoxicity of synthetic pyrethroids, including LCT, are rather controversial. The aim of the present work was, therefore, to authenticate the in vivo potential genotoxic effects of LCT in bone marrow cells of laboratory female rats using chromosomal aberrations and MN assays as genetic endpoints. The ratio of PCEs to normochromatic erythrocytes (NCEs) was also calculated to evaluate cytotoxic effects of LCT in bone marrow.

2. Materials and methods

2.1. Chemical (substance)

LCT is a synthetic pyrethroid insecticide with the trade name "Karate". Cas, chemical name (R + S) α-cyano-3-(phenoxyphenyl)methyl-(1S + 1R)-*cis*-3(2-2chloro-3,3,3-trifluoroprop-1-enyl)-2-2-dimethylcyclopropane carboxylate, CASRN 91465-08-06, was from Zeneca Agrochemicals, England (2.5%).

2.2. Animal and treatment

Healthy adult female Swiss albino rats (Wistar rat) (6–8 weeks of age and average body weight (b.w.) 180–200 g) were used in this study. Rats were obtained from the Experimental Animal Center, University of Gaziantep, Turkey. The study was approved by the research and ethical committee at the University of Mersin. The rats were randomly selected and housed in polycarbonate boxes (three or four rats per box) with steel wire tops and rice husk bedding. They were maintained in a controlled atmosphere of 12 h dark/light cycle, 22 ± 2 °C temperature, and 50–70% humidity, with free access to pelleted feed and fresh tap water. The animals were supplied with dry food pellets commercially available. For each dose group, the animals were allowed to acclimate for 5 days before treatment. LCT was suitably diluted with isotonic saline. The animals received by gavage an aqueous solution of LCT at three different doses (0.8 mg/kg b.w., 3.06 mg/kg b.w., 6.12 mg/kg b.w.) per 48 h for 13 days. Three animals were used in each group/assay. The animals received a total of seven injection of LCT during the present study.

2.3. Doses

The animals tolerated the highest dose with minimal toxic symptoms. The toxic symptoms were mostly neurological. However, the animals recovered within 2 h of the treatment. It has been determined that the LCT LD_{50} dose was 612 mg/kg for mammals. Therefore, the highest dose was determined as 6.12 mg/kg b.w., 1% of the LD_{50}. The lowest dose was determined as 0.8 mg/kg b.w. because this dose did not neurologically affect the rats. Groups of three rats each were treated with three doses of LCT, 6.12 mg/kg b.w., 3.06 mg/kg b.w., and 0.8 mg/kg b.w. per 48 h for 13 days, to investigate genotoxic and cytotoxic effects on rat bone marrow cells. Therefore, the cumulative doses of LCT given to rats were 42.84 mg/kg b.w., 21.42 mg/kg b.w., and 5.6 mg/kg b.w.

Mitomycin C (MMC) (2 mg/kg) was used as a positive control. Positive control and untreated control rats were identically treated with equal volumes of normal saline only via gavage (per os). It is acceptable that a positive control may be administered by a different route or the same route as the test agent sampled at only a single time (Hayashi et al., 1994). MMC was given as a single dose. Same-dose regimes were used in both chromosomal aberration and MN assays.

2.4. Chromosome aberrations assay

The rats were sacrificed 24 h after last dose administration for a chromosome aberration assay. Cytogenetic analysis was performed on bone marrow cells according to the recommendations of Adler (Adler, 1984), with slight modifications. Experimental animals were injected (i.p.) with colchicine (4 mg/kg) 1.5 h prior to sacrifice. Both femurs were dissected out and cleaned of any adhering muscle. Bone marrow cells were collected from both the femurs by flushing in KCl (0.075 M, at 37 °C) incubated at 37 °C for 25 min. Material was centrifuged at 2000 rpm for 10 min, fixed in acetomethanol (acetic acid:methanol, 1:3, v/v). Centrifugation and fixation (in cold) were repeated five times at an interval of 20 min. The material resuspended in a small volume of the fixative, was dropped onto chilled slides, flame-dried, and stained on the following day in 5% buffered Giemsa (pH 6.8). At least 75 good metaphases containing 42 ± 2 chromosomes were examined per animal to score different types of aberrations.

2.5. Micronucleus test

Rats were killed by cervical dislocation 30 h after treatment. The frequency of micronucleated erythrocytes