Chemosphere 187 (2017) 163–172

Contents lists available at ScienceDirect

Chemosphere

journal homepage: www.elsevier.com/locate/chemosphere

Mutagenic, recombinogenic and carcinogenic potential of thiamethoxam insecticide and formulated product in somatic cells of *Drosophila melanogaster*

Cássio Resende de Morais [a], Stephan Malfitano Carvalho [b], Maria Paula Carvalho Naves [a], Galber Araujo [a, c], Alexandre Azenha Alves de Rezende [a], Ana Maria Bonetti [a], Mário Antônio Spanó [a, *]

[a] Institute of Genetics and Biochemistry, Federal University of Uberlândia, Campus Umuarama, 38900-402, Uberlândia, Minas Gerais, Brazil
[b] Department of Entomology, Federal University of Lavras, PO Box 3037, 37200-000, Lavras, Minas Gerais, Brazil
[c] Department of Molecular Biology, University of Salzburg, 5020, Salzburg, Austria

HIGHLIGHTS

- The mutagenic, recombinogenic and carcinogenic potential of Thiametoxam and Actara were studied *in vivo*.
- Thiametoxam and Actara are mutagenic after bioactivation.
- Increasing the metabolic capacity decreases the toxic effect of Thiametoxam and Actara.
- Inert ingredients present in Actara may interfere with the repair mechanism by homologous recombination.

ARTICLE INFO

Article history:
Received 25 May 2017
Received in revised form
18 August 2017
Accepted 19 August 2017
Available online 19 August 2017

Handling Editor: Jim Lazorchak

Keywords:
Actara
Insecticide
Neonicotinoid
SMART
Warts

ABSTRACT

Thiamethoxam (TMX) belongs to a class of neuro-active insecticides referred as neonicotinoids, while actara® (AC) is one of the most popular TMX-based products in Brazil. The aim of this study was to evaluate the mutagenic, recombinogenic and carcinogenic potential of TMX and AC insecticides. The mutagenic and recombinogenic effect of TMX and AC were evaluated *in vivo* by the Somatic Mutation and Recombination Test (SMART) while carcinogenic effects were evaluated through the Test for Detection of Epithelial Tumor Clones (wts test), both in somatic cells of *Drosophila melanogaster*. In the SMART, third instar larvae from standard (ST) and high bioactivation (HB) crosses were treated with different concentrations of TMX and AC (2.4; 4.8; 9.7×10^{-4} mM and 1.9×10^{-3} mM). The results revealed mutagenic effects at the highest concentrations tested in the HB cross. In the test for the detection of epithelial tumor, third instar larvae resulting from the cross between *wts/TM3, Sb*^{1} virgin females and *mwh/mwh* males were treated with the same concentrations of TMX and AC used in the SMART. No carcinogenic effect was observed at any of the concentrations tested. In this work, the inhibition of the mechanism of repair by homologous recombination was observed in flies exposed to 9.7×10^{-4} and 1.9×10^{-3} mM of AC. In conclusion, TMX and AC demonstrated to be a promutagen in the highest concentrations tested.
© 2017 Elsevier Ltd. All rights reserved.

1. Introduction

Pesticides are either substances or mix of substances whose function is to kill, repel or control organisms considered as pests. Pesticides may also lead to negative effects on non-target organisms apart from pests, depending on the physicochemical characteristics, mechanism of action, dose and persistence in the environment (Farooqui, 2013). Despite the satisfactory results in the agriculture, pesticides can, in a long scale, be harmful to human and other species. The main concern is related to the chronic exposure to the residues of the active principles and its metabolites (Houk, 1992), which generates negative effects such as biochemical pathway dysfunctions and genetic instability (Çelik et al., 2014).

Chronic exposure to pesticides may result in genotoxic, mutagenic, recombinogenic and carcinogenic events (Morais et al., 2016a), as well as chronic diseases at the beginning of embryonic

* Corresponding author.
E-mail address: maspano@ufu.br (M.A. Spanó).

http://dx.doi.org/10.1016/j.chemosphere.2017.08.108
0045-6535/© 2017 Elsevier Ltd. All rights reserved.

development, such as congenital malformations and degenerative diseases (Bolognesi, 2003; Bhalli et al., 2009; Mehid and Qamar, 2013; Guanggang et al., 2013; Bolognesi and Moretto, 2014; Goujon et al., 2014; Çelik et al., 2014).

Neonicotinoids are neurotoxic insecticides used in agriculture to control pests such as ants, aphids, whiteflies, beetles and some lepidopterans (Goulson, 2013) and are currently the most commercialized insecticides worldwide (Sparks and Nauen, 2015). Neonicotinoids act on the nervous system of insects and they are agonists of the nicotinic receptors, opening and excessively stimulating the sodium channels, resulting in severe insect paralysis and further death (Tomizawa and Yamamoto, 1993; Goulson, 2013).

The groups of neonicotinoid insecticides are constituted by the main molecules *N*-nitroguanidine, nitromethylene and *N*-cyanoamidin (Jeschke et al., 2011). The efficiency of these molecules is associated with their systemic activity in plants, protecting crops from a wide spectrum of pests (Goulson, 2013). Since their market introduction in 1990 (Kollmeyer et al., 1999), neonicotinoids have achieved notoriety, increasingly replacing traditional insecticides such as carbamate, pyrethroid, organophosphate and other neurotoxic insecticides (Stivaktakis et al., 2016).

Although neonicotinoids present selective toxicity in insects when compared to vertebrates (Tomizawa and Casida, 2003, 2005), several studies have demonstrated the relationship between neonicotinoid insecticides and events resulting in DNA damage (Karabay and Oguz, 2005; Demsia et al., 2007; Bhinder et al., 2012; Perez-Iglesias et al., 2014; Arcaute et al., 2014; Rodriguez et al., 2015; Stivaktakis et al., 2016). In addition, some neonicotinoid insecticides have been directly or indirectly related to the colony collapse disorder (CCD) (Iwasa et al., 2004; Farooqui, 2013), which is implicated in the large-scale disappearance of honey bees (Johnson, 2010).

The 3-(2-Chloro-thiazol-5-ylmethyl)-5-methyl-(1,3,5)oxadiazinan-4-yldene-*N*-nitroamine compound known as thiamethoxam (TMX), is a second-generation class III (moderately toxic) neonicotinoid insecticide (Maienfisch et al., 2001; Nauen et al., 2003). Thiamethoxam has low affinity to nicotinic receptors when compared to imidacloprid, another neonicotinoid insecticide. While imidacloprid is effective at nanomolar concentrations, thiamethoxam acts in millimolar ones (Wiesner and Kayser, 2000).

In Brazil, Actara® (AC) is one of the most popular TMX-based products in dispersible granules and it is applied in different crops such as rice, potato, coffee, sugarcane and wheat (MAPA, 2017).

Although several studies have demonstrated the mutagenic effect of neonicotinoid insecticides (Bagri et al., 2014; Çavas et al., 2014; Stivaktakis et al., 2016), few data are available in the literature about the TMX effect (Green et al., 2005; Bhinder et al., 2012; Sinha and Thaker, 2013).

Changes in the DNA may lead to mutation retentions which, if unrepaired, can be accumulated and trigger cancerous processes (Hernandez et al., 2013). Thus, to evaluate the *in vivo* effects of insecticides, as well as prevent diseases associated with genetic instability, it is important to know the toxicokinetics of the molecule.

Among the different tests based on toxicological genetics, the Somatic Mutation and Recombination Test (SMART) and the Test for Detection of Epithelial Tumor Clones (wts test), both performed in *Drosophila melanogaster*, stand out for their sensitivity to the evaluation of chemicals with mutagenic and carcinogenic properties (Morais et al., 2016a,b).

SMART is based on the analysis and identification of fly wings by mutants that result from the loss of heterozygosity of the marker genes, *mwh* and *flr*^{3}. By means of this test it is possible to detect single spots (produced by point mutation, chromosome breakage or mitotic recombination) and twin spots (produced exclusively by mitotic recombination) (Graf et al., 1990) and to detect mutagens and pro-mutagens (Graf et al., 1984; Graf and van Schaik, 1992; Graf and Würgler, 1996).

The wts test is used to identify tumors in the fly epithelium caused by potential xenobiotics (Orsolin and Nepomuceno, 2009; Silva and Nepomuceno, 2011; Costa et al., 2011; Furtado and Nepomuceno, 2012; Orsolin et al., 2012; Nepomuceno, 2015; Morais et al., 2016a,b; Vasconcelos et al., 2017). This test is performed in a lineage of *D. melanogaster* that possesses the warts (*wts*) marker which, when expressed in the wild condition, acts as a tumor suppressor gene (Xu et al., 1995). The deletion of the *wts* wild-type gene and the consequent expression of the mutant allele leads to the formation of cell clones that are considered highly invasive, resulting in the manifestation of epithelial tumor in the body and appendages of the fly (Nishiyama et al., 1999).

Considering that industrialized pesticides may present higher toxicity when compared to the active component (Mesnage et al., 2014), the present study aimed to evaluate *in vivo* the mutagenic, recombinogenic and carcinogenic effects of the insecticide TMX (active component) and its formulated product (AC) in somatic cells of *D. melanogaster*.

2. Material and methods

2.1. Chemical agents

Thiametoxam (99.9%) (CAS 153719-23-4) was obtained from Sigma-Aldrich and Thiametoxam Actara® 250 WG (25%) from BASF AS (São Paulo, Brazil). The chemical structure of the TMX is shown in Fig. 1A. Ethyl carbamate-Urethane (CAS 51-79-6) (Fig. 1B) was obtained from Fluka AG (Buchs, Switzerland). Mitomycin C (Fig. 1C) was manufactured by Kyowa Hakko Kirin Co. Ltd. (Shizuoka, Japan), packaged by Bristol-Myers Squibb S.r.1. Sermoneta-Latin-Italy and imported by Bristol-Myers Squibb S.A.

2.2. Somatic Mutation and Recombination Test (SMART) in somatic cells of Drosophila melanogaster

2.2.1. Strains, crosses and treatments

Three strains of *D. melanogaster* were used in this study: [1]

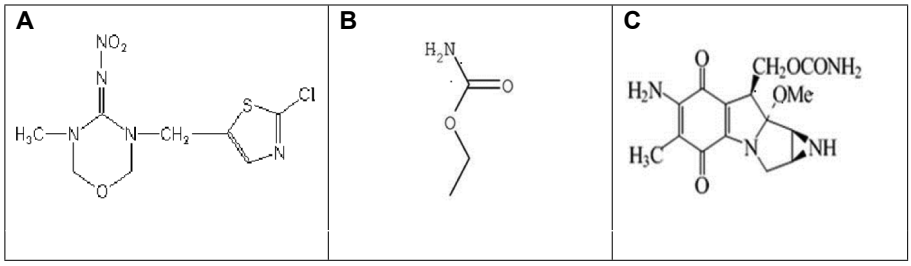

Fig. 1. Structural formula of compounds. A. Thiamethoxam (TMX); B. Ethyl carbamate - Urethane (URE); C. Mitomycin-C (MMC).

Download English Version:

https://daneshyari.com/en/article/5746436

Download Persian Version:

https://daneshyari.com/article/5746436

Daneshyari.com