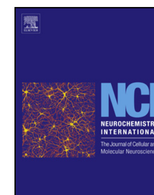
ARTICLE IN PRESS

Neurochemistry International ■■ (2014) ■■–■■

Contents lists available at ScienceDirect

Neurochemistry International

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



Evaluation of imidacloprid-induced neurotoxicity in male rats: A protective effect of curcumin

Milindmitra Lonare [a,*], Manoj Kumar [a], Sachin Raut [b], Prarabdha Badgujar [a], Sagar Doltade [a], Avinash Telang [c]

[a] Division of Veterinary Pharmacology and Toxicology, Indian Veterinary Research Institute, Izatnagar-243 122, Bareilly, UP, India
[b] Division of Veterinary Pathology, Indian Veterinary Research Institute, Izatnagar-243 122, Bareilly, UP, India
[c] CADRAD, Indian Veterinary Research Institute, Izatnagar-243 122, Bareilly, UP, India

ARTICLE INFO

Article history:
Received 31 March 2014
Received in revised form 29 August 2014
Accepted 19 September 2014
Available online

Keywords:
Imidacloprid
Curcumin
Neurotoxicity
Biochemical
Antioxidant enzyme

ABSTRACT

The present study was carried out to evaluate the neurotoxic effect and biochemical alteration as a result of imidacloprid (IMI) exposure and potential protective role of curcumin (Cur) against it in rats. Rats were administered with IMI (45 and 90 mg/kg body weight; orally) and Cur (100 mg/kg body weight; orally) alone and in combinations for the period of 28 days. Significant decrease in spontaneous locomotor activity (SLA) and pain threshold were observed in animals treated with the IMI while the effect was attenuated by the Cur co-treatment. Acetylcholinestaerase, ATPase and serum biochemicals such as creatine kinase, lactate dehydrogenase, sorbitol dehydrogenase and alkaline phosphatase levels were significantly decreased ($p < 0.05$) as result of IMI exposure and these enzyme levels were reversed in groups treated with the Cur in IMI treatments. Also, IMI caused a significant decrease ($p < 0.05$) in antioxidant enzymes activity and non-enzymes level with increase in lipid peroxidation (LPO), while, Cur administration in IMI treatments restored the altered activity of antioxidant system with decrease in LPO. The IMI induced brain damage was minimized as result of Cur co-administration in rats. In conclusion, Cur restores the altered functions of biochemical markers and neurotoxicity in IMI exposed rats.

© 2014 Published by Elsevier Ltd.

1. Introduction

The extensive use of pesticides in agro-vet practices for the management of variety of pests resulted into environmental contamination (Arnaud et al., 2005) and their residues may remain in food stuff in a significant amount causing potential health effects such as respiratory diseases, neurological dysfunctions, cancers and reproductive disorders (Flower et al., 2004; Kumar, 2004). This problem is being viewed seriously by many of the international organizations such as Codex Alimenterious Commission, USEPA, WHO and FAO of the United Nations (Cao et al., 2005). However, many of the studies have shown that environmental contaminants (pesticides and heavy metals) can alter behavioral changes in non-targeted animal species through oxidative stress and inflammation in central nervous system of animals (Duzguner and Erdogan, 2010; Yadav et al., 2009).

Neonicotinoid, a newer group of pesticides with one of the fastest growing insecticides for its applications in veterinary and agriculture (Ferrer et al., 2005). Imidacloprid (IMI), a chlorinated analogue of nicotine belongs to neonicotinoid insecticides. It act as selective agonists at the insect nicotinic acetylcholine receptors (nAChRs) and categorized under the category of "moderately toxic" compound by WHO and United States Environmental Protection Agency (Matsuda et al., 2001). It has low mammalian toxicity but exposure may cause health hazard such as neurotoxic effect and gastrointestinal disturbances (Duzguner and Erdogan, 2010), besides this, prolonged exposure may have teratogenic, mutagenic, immunotoxic and reproductive toxic effect (Bhardwaj et al., 2010; Najafi et al., 2010; Gawade et al., 2013). A number of pesticides kill insects by targeting their nervous system but may have neurotoxic effect in mammals as well. Insecticides act by interfering with chemical neurotransmission or ion channels etc. causing reversible neurotoxic effect that could be lethal (Costa et al., 2008). A pesticide with different chemical classes induces oxidative stress (EL-Gendy et al., 1990), generation of free radicals, alteration in antioxidant system and lipid peroxidation resulted into the tissue damage (Jin et al., 2011; Saulsbury et al., 2009). However, pesticide induced oxidative stress has also been a focus of toxicological research for the last few decade as a possible mechanism of neurotoxicity (Banerjee et al., 2001).

The plant based drugs might be helpful in ameliorating oxidative stress induced by environmental neurotoxicants. Evidence showed that consumption of natural antioxidants of plant origin leads to a decrease in various pro-inflammatory and/or oxidative

* Corresponding author. Tel.: +91 9356654258; fax: +91 161 2400822.
E-mail address: drmilind12@rediffmail.com (M. Lonare).

http://dx.doi.org/10.1016/j.neuint.2014.09.004
0197-0186/© 2014 Published by Elsevier Ltd.

Please cite this article in press as: Milindmitra Lonare, et al., Evaluation of imidacloprid-induced neurotoxicity in male rats: A protective effect of curcumin, Neurochemistry International (2014), doi: 10.1016/j.neuint.2014.09.004

UNCORRECTED PROOF

ARTICLE IN PRESS

stress biomarkers (Vouldoukis et al., 2004). In the line of plant based natural remedies, curcumin (Cur) is the active constituent of ground rhizome *Curcuma longa* Linn (turmeric), an Indian spice and herbal medicine (Maheshwari et al., 2006). Cur is a potent inhibitor of free radical formation (Biswas et al., 2005) in conditions like myocardial ischemia (Manikandan et al., 2004); paraquat induced lung injury (Venkatesan, 2000), aflatoxin-induced testicular toxicity (Mathuria and Verma, 2008). Cur decreases the lipid peroxidation induced by fluoride and oxidative stress induced by sodium nitroprusside in brain (Nazari et al., 2014; Sharma et al., 2014). Cur administration has been reported to prevent the arsenic, gentamicin and acetaminophen-induced oxidative stress (Cekmen et al., 2009; Fatma et al., 2009). Recently, Cur has attracted special attention due to its pharmacological activities, such as potential protectant in neutotoxicity, neuro-degenerative diseases and as a anticancer agent (Ali and Arafa, 2011; Duan et al., 2014; Kim et al., 2014; Thapa et al., 2013; Vishvakarma et al., 2011).

In view of the above, continued exposure of IMI to humans and animals with extensive application procedure, there is a lot of interest in investigating its neurotoxicity if any that could be prevented. Therefore, the present study was planned to investigate the effect of IMI after sub-acute exposure on neurotoxicity and biochemical alterations in rats and to study the possible role of curcumin (Cur) to overcome these alterations, if administered with exposure to IMI.

2. Materials and methods

2.1. Materials

Curcumin (Sigma Aldrich, St. Louis, MO, USA), Imidacloprid (Indofil Chemical Company, Division of Indofil Organic Industries Ltd., Mumbai, India). Standard commercial kits such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), sorbitol dehydrogenase (SDH), creatine kinase (CK, CK-BB), total serum protein (Span Diagnostic Ltd.), lactate dehydrogenase (LDH) (Crest Biosystems, Goa, India). Bovine serum albumin (Spectrochem Pvt. Ltd., Mumbai, India). All other the chemicals used were of analytical grade and purchased from standard manufacturers.

2.2. Animals

The protocol for the study was approved by the Institutional Animal Ethics Committee of Indian Veterinary Research Institute (IVRI), Izatnagar, India and all experiments have been carried out in accordance with the guidelines laid down by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), New Delhi, India. Male rats of Wistar strain weighing 100–120 g obtained from the Laboratory Animal Resource Section, IVRI, Izatnagar, Bareilly were used for the study. Rats were housed in an air conditioned room at 25 ± 2 °C with a 12 h light/dark cycle under standard hygiene conditions and standard rat feed and water ad libitum.

2.3. Experimental design

The animals were randomly divided into seven groups comprise of six animals in each. Cur and IMI were suspended in corn oil and administered by oral gavage for the period of 28 days.

Group I: Rats provided with normal feed and deionized water serve as control.
Group II: Rats treated with corn oil (1 mL/kg body weight) serve as vehicle control.
Group III: Rats treated with Cur (100 mg/kg body weight daily for 28 days).
Group IV: Rats treated with IMI-I (45 mg/kg body weight daily for 28 days).
Group V: Rats treated with IMI-II (90 mg/kg body weight daily for 28 days).
Group VI: Rats treated with IMI-I plus Cur identically as in groups III and IV.
Group VII: Rats treated with IMI-II plus Cur identically as in groups III and V.

At end of the 28 days of last dosing, rats were necropsied. Blood was collected in EDTA containing tubes for various biochemical estimations. Pack cell was prepared and used for preparation of 10% hemolysate for estimation of membrane enzymes. Brain and liver were removed, washed in ice-cold saline and preserved in –80 °C until processed for biochemical estimation and part of the brain was preserved in 10% formal neutral saline for histopathological examination.

2.4. Evaluation of neurotoxicity indicators

Signs and symptoms of toxicity (salivation, lacrymation, piloerection diarrhea, dyspnea, tremor, convulsion, paralysis) and death, if any, were observed twice daily throughout the period of exposure.

2.4.1. Measurement of spontaneous locomotor activity

Spontaneous locomotor activity (SLA) was evaluated after last dosing. Animals were individually placed in photosensitive cages by using automated photoactometer animal activity monitors (UGO Basile, Comerio, VA, Italy). The activity was monitored for horizontal as well as vertical movements for the duration of 5 min.

2.4.2. Measurement of pain threshold

Pain threshold was measured through mechanical stimulation and radiant heat latency. Mechanical stimulation: pressure in grams in rats was recorded as pain threshold by Randall–Selitto assay method (Randall and Selitto, 1957) using Randall–Selitto analgesiometer (UGO Basile). The test consisted of the progressive application of an increasing point-pressure over the hind paw, which evokes a pain reaction characterized by a fighting reaction (struggle) and a vocalization as manifestations of the pain sensation. Radiant heat latency: paw-flick latency in seconds was recorded as paw withdrawal latency to infrared radiant heat (UGO Basile) and expressed in seconds.

2.5. Assessment of oxidative stress

Brain samples were weighed and 10% tissue homogenate was prepared in ice-cold 100 mM potassium phosphate buffer (pH 7.4). For estimation of reduced glutathione (GSH), organ samples were taken separately in solution containing 0.02 M EDTA. The homogenates were prepared under cold conditions. The homogenates were centrifuged for 10 min at 3000 rpm at 4 °C. The supernatant was collected and stored in –80 °C and used for different biochemical estimations. Lipid peroxidation (LPO) was measured in terms of malondialdehyde (MDA) production (Shafiq-Ur-Rehman, 1984). GSH content was measured by the method of Sedlak and Lindsay (1968). Catalase (CAT) activity was assayed by the method as described by Bergmeyer (1983). The activity of superoxide dismutase (SOD) was assayed as per the method described by Madesh and Balasubramanian (1998). Glutathione peroxidase (GPx) activity was determined by the method of Paglia and Valentine (1967). Glutathione-S-transferase (GST) activity was determined by the method of Habig et al. (1974). The protein content of brain was estimated by the method of Lowry et al. (1951) using bovine serum albumin as standard.

Please cite this article in press as: Milindmitra Lonare, et al., Evaluation of imidacloprid-induced neurotoxicity in male rats: A protective effect of curcumin, Neurochemistry International (2014), doi: 10.1016/j.neuint.2014.09.004

Download English Version:

https://daneshyari.com/en/article/8479209

Download Persian Version:

https://daneshyari.com/article/8479209

Daneshyari.com