



Toxicological outcome of exposure to psychoactive drugs carbamazepine and diazepam on non-target insect *Nauphoeta cinerea*



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HIGHLIGHTS

- Impact of co-exposure to psychoactive drugs on insects' behavior was investigated.
- Diazepam (DZP) alone did not alter behavioral and biochemical indices in insects.
- Carbamazepine (CBZ) alone-induced behavioral and biochemical deficits in insects.
- Binary mixtures of CBZ and DZP disrupt behavioral and biochemical responses in insects.
- Toxicity of CBZ alone and binary mixtures is associated with oxido-inflammatory stress.

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ABSTRACT

The continuous detection of human pharmaceuticals during environmental biomonitoring is a global concern because of the menaces they may exert on non-target organisms. Carbamazepine (CBZ) and diazepam (DZP) are commonly prescribed psychotropic drugs which have been reported to coexist in the environment globally. *Nauphoeta cinerea* is a common insect with high ecological impact. This study elucidated the influence of co-exposure to DZP (0.5 and 1.0 $\mu\text{g kg}^{-1}$ diet) and CBZ (1.5 and 3.0 $\mu\text{g kg}^{-1}$ diet) for 42 days on the behavior and biochemical responses in *Nauphoeta cinerea*. Results showed that DZP alone did not induce adverse effect on the behavior and antioxidant status in the exposed insects. However, exposure to CBZ alone and binary mixtures of DZP and CBZ significantly decreased locomotor and exploratory accomplishments evidenced by decreased mobile episodes, total mobile time, maximum speed, total distance traveled, absolute turn angle, body rotation and path efficiency in comparison with control. The decline observed in the exploratory activities of insects fed with CBZ alone and the mixtures was confirmed by track plots and heat maps. Further, acetylcholinesterase and antioxidant enzyme activities decreased significantly whereas reactive oxygen and nitrogen species, nitric oxide and lipid peroxidation levels increased significantly in the hemolymph, head and midgut of insects exposed to CBZ alone and the mixtures. Collectively, CBZ alone and binary mixtures of CBZ and DZP caused neurotoxicity via induction of inflammatory and oxidative stress in insects. *Nauphoeta cinerea* may be a potential non-target insect model for monitoring ecotoxicological hazard of pharmaceuticals.

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1. Introduction

Contaminants of emerging concern are chemical compounds that are not enumerated in environmental monitoring programs

but are frequently introduced into water, air and soil where they elicit harmful effects on non-target organisms (Petrie et al., 2015; Fontes et al., 2020). Pharmaceuticals are considered as contaminants of great concern to both regulatory authorities and scientific community largely because of the inability of wastewater treatment plants to effectively degrade and remove them before their discharge to the environment. The major sources of soil pollution with pharmaceuticals includes discharge of expired or unwanted drugs into landfills, the usage of recovered wastewater for

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