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Effect of long-term treatment with a mixture of pyrethroids on the expression of genes that govern male germ cell production in rats

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Abstract

Humans are exposed to pyrethroid-based pesticides through agricultural produce. In this study, male Wistar rats were orally treated for 9 to 12 months with a mixture of pyrethroids that is equivalent to one-fifth (high dose; HD) or one-twenty fifth (low dose; LD) of the amount of pyrethroids present in the cereals and rice consumed by an average Indian. In rats treated for 9 months, the spermatogenesis-associated genes *Abp*, *Ar*, *Cd9*, *Dax1*, *Dazap1*, *Ddx3y*, *Gdnf*, *Gfra1*, *Grth*, *Inhb*, *Ovol1*, *P1*, *Plzf*, *Pygo2*, *Scf*, *Tgfb1*, *Tp1*, *Tp2*, and *Vim1* were downregulated in both LD and HD groups. In rats treated for 12 months *Gdnf*, *Hsf2*, *Inhb*, *Tgfb1*, *Thy1*, and *Ybx2* expression was downregulated in both LD and HD groups. Steroidogenesis-associated genes *17-β-Hsd*, *Gata4*, *Hmgcr*, *Hmgcs1*, *Pde4b*, and *Tspo* gene expression were reduced in both LD- and HD-treated groups treated for 9 months. In 12-month-treated rats, *Creb1* expression decreased in both LD and HD groups. The epigenetic reprogramming-associated genes, *Dnmt1*, *Dnmt3a*, *Dnmt3b*, *Hdac10*, *Hp1bp3*, *Kat3a Kat3b*, *Mch2ta*, *Ncoa7*, and *Sirt1* were downregulated in both HD and LD groups of 9-months-treated rats. In rats treated for 12 months, *Hdac10*, *Mch2ta*, *Ncoa7*, and *Sirt1* messenger RNA levels decreased in both the HD and LD groups. Thus, we demonstrate that long-term exposure to a mixture of pyrethroids caused aberrations in the transcriptome of factors involved in sperm production and development.

KEYWORDS

genetic reprogramming, pyrethroids, spermatogenesis, steroidogenesis, testis

1 | INTRODUCTION

Pesticide usage is rampant throughout the world for domestic and agricultural purposes. Indiscriminate use of pesticides caused approximately 3 000 000 instances of poising and 220 000 deaths annually.[1] In India, the agricultural sector mainly depends on spraying pesticides to protect the crop to achieve a better yield. As per the Food and Agriculture Organization of the United Nations, 52 750 metric tons of pesticide is used in India annually with the 13th position on the global pesticide usage index.[2] The presence of residual levels of a variety of pesticides including pyrethroids in cereals, vegetables, fruits, and milk products is reported in India.[3,4]

Among the pesticides used, pyrethroid-based ones are more popular because of their high biodegradability and insecticidal activity. They primarily target the nervous system to cause malfunctioning of the voltage-sensitive sodium channels.[5] In humans, pyrethroid toxicity is implicated to induce the motor deficiency associated with the central nervous system and Parkinson's disease.[6-8] In murine models, pyrethroids cause cognitive defects,[9] alterations in the levels of GABA, 3, 4-dihydroxyphenylacetic acid, and noradrenaline[10] dopaminergic neurodegradation[11] and alterations in xenobiotic enzyme levels of the brain.[12] Pyrethroid toxicity in other organ systems is reported as well. Pyrethroids damage the immune system.[13,14] Immunotoxicity is characterized

