



Research paper

Effect of oral administration of a mixture of pyrethroids at doses relevant to human exposure on the general and male reproductive physiology in the rat

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ABSTRACT

Studies on the effects of unintentional intake of pyrethroid pesticides that are akin to actual human exposure settings are very rare. Such an exposure is primarily by consuming the food products as routine diet that contain residual levels of pyrethroids. In this study, rats were orally administered for 15 months with a mixture of pyrethroids at a dose that is one-fifth (high dose; HD) or one-twenty fifth (low dose; LD) of the residual levels commonly present in the average amount of rice and vegetables consumed by Indian population. Lipid profile, kidney and liver function were assessed. Lipid peroxidation, nitric oxide, antioxidant enzyme activities and histopathological changes were analyzed in the liver, lung, kidney, pancreas, testes, caput, cauda and prostate. The effect on the male reproductive system as a function of sperm count, enzyme activity of 3 β -HSD and 17 β -HSD and the expression profile of genes involved in spermatogenesis, steroidogenesis, genetic reprogramming and apoptosis of male gametes were evaluated. Significant increase in the relative organ weight, perturbations in the activities of antioxidant enzymes, lipid profile and liver function were observed in both LD and HD groups. Damage to the anatomical architecture was evident in all the tissues due to pyrethroid toxicity. Exposure to LD and HD of pyrethroid mixture resulted in decreased sperm count, activities of 3 β -HSD and 17 β -HSD, impaired capacitation and acrosome reaction and perturbations in the expression of genes that govern male gamete production. Results of our study indicate that exposure to pyrethroids for longer durations even at doses that are far below the residual levels present in the food consumed will result in severe damage to general physiological processes as well as reproductive function.

1. Introduction

Pesticide usage to increase agriculture production resulted in the percolation of these chemicals into water bodies, landscape and the food chain thereby posing a threat to all life forms. Further, use of pesticides in households for pest management compounded the exposure in humans. Among the pesticides used, pyrethroid based ones are more popular because of their low toxicity on mammals, high toxicity to insects and biodegradability. Hence, pyrethroid based ones constitute to one fourth of the global pesticide market (Saillenfait et al., 2015). The primary mechanism of action of pyrethroids is based on their ability to target the voltage gated channels of the nervous system (Field et al., 2017). Other effects of pyrethroids that were recently reported include toxicity to the immune and respiratory systems and carcinogenicity (Alavanja et al., 2014; Ambwani et al., 2018; Kawamoto et al., 2020; Pauluhn, 2018; Yamada et al., 2019). Defective liver and kidney function, alterations in the hematological and lipid profile and imbalance in

the oxidant-antioxidant status have been recently reported to be associated with pyrethroid toxicity (Feriani et al., 2020; Jaremek et al., 2020; Martínez et al., 2018). Evaluation of the biochemical parameters that define these functions is crucial, especially in studies that involve long term exposure settings. Hence, in this study, we determined the effect of a mixture of pyrethroids on liver, kidney and hematological biochemical parameters along with the status of oxidative stress and the antioxidant enzymes.

Reproductive toxicity of pyrethroid based insecticides continues to be an active area of investigation. It is being recognized globally that increased risk of reproductive cancers and falling fertility rates is associated with pesticide exposure. Germ cell production in the males (spermatogenesis) is a continuous process that is tightly articulated by androgens and testicular factors. Differential gene expression of factors that contribute to spermatogenesis, steroidogenesis, genetic reprogramming via epigenetic modifications (DNA methylation, histone methylation and acetylation) and apoptotic pathways occur in a

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