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Popular Article

Pyrethroid Pesticides – As an Endocrine Disrupting Substances

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Introduction

After the prohibition of Organochlorine and Organophosphorus pesticides usage of Synthetic Pyrethroids such as cypermethrin, deltamethrin, fenvalerate, fenpropathrin, bifenthrin λ-cyhalothrin etc., has been widely acknowledged. This group of pesticides are utilized on wide-scale in agriculture farm lands, forestry, and fish ponds as they offer may advantages such as broad spectrum, low toxicity, high efficiency, and biodegradability. The market share of these synthetic pyrethroids is 38% in the year 2015 and is reported to be escalating in the subsequent years. These pesticides could enter water bodies through agriculture farmland drainage, surface runoff, sewage outfalls, atmospheric deposition. Synthetic pyrethroids being highly hydrophobic in nature they may persist on the suspended particles or aquatic organisms, damaging the harmony of aquatic ecosystem and posing risk to public health through the food chain (Farina et al 2018). The major route of exposure of these compounds might be through oral ingestion through dietary components and dermal absorption. 3-Phenoxbenzoic acid is considered as a non-specific metabolite of nearly 18 pyrethroids and act as biomarker of pyrethroid exposure.

Many reports suggest that pyrethroids even at environmentally relevant concentrations can act as endocrine disrupting substances which can affect the synthesis, metabolism, function of hormone which can impair homeostasis. They can exhibit reproductive and developmental toxicity by disrupting the function of nuclear receptor genes.

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Effects on Hypothalamus-pituitary-thyroid axis

In vertebrates, thyroid hormones play a crucial role in the growth, development, metabolism and reproduction. Many studies have documented that a correlation between pyrethroid pesticide exposure and interference in the thyroid hormonal status. Both in vertebrates as well as in aquatic organisms' thyroid endocrine function is primarily controlled by hypothalamus-pituitary-thyroid (HPT) axis. Hypothalamus secretes corticotropin releasing hormone which coordinates the HPT axis by regulating the release of thyroid stimulating hormone from the pituitary which stimulates the release of thyroid hormone T_4 and T_3. Thyroid hormone T_4 is converted into biologically active T_3 by the action of deiodinase enzymes such as Dio1 and Dio2. T_3 acts on thyroid receptors and mediates the action on target organs (Shi et al 2009). For instance, studies conducted on rats with oral administration of permethrin (400 mg/kg); deltamethrin (12.5 and 25 mg/kg) lead to significant decrease in thyroid hormone levels whereas, fenvalerate (100 and 200 mg/kg) caused significant elevation of T_3 and T_4 levels.

Effects on Hypothalamus-pituitary-gonadal axis

Similarly, exposure to the pyrethroids can also affects the reproductive-endocrine health. Endocrine disrupting properties of pyrethroids also includes toxic effects on hypothalamus-pituitary-gonadal (HPG) axis both in aquatic organisms and humans. HPG axis is regulated by the pulsatile release of gonadotropin-releasing hormone from the hypothalamus which stimulates the HPG axis and triggers the release of luteinizing hormone (LH) and follicle stimulating hormone (FSH) from pituitary by interacting with GnRH receptor located on the gonadotropic cell membrane in pituitary. These hormones subsequently act on the ovaries/testis to release sex steroids such as estrogen, progesterone, and testosterone. Further the release of these hormones also has feedback effect over the secretion GnRH from the hypothalamus. The secretion and feedback mechanism of gonadosteroidal hormones have a pivotal role on growth, development and reproduction (Bliss et al 2010).

Studies indicated that exposure to the pyrethroids while spraying resulted in decrease in ovarian reserve (Whitworth et al 2015), increase in risk of primary ovarian insufficiency in women (Li et al 2018). Usually, the effect of pyrethroids on the pituitary gonadotropins depends on the dose, exposure duration and physiological stage of the animal. Studies in male rodents upon exposure to various pyrethroids suggested a significant increase in the levels of FSH and LH (Pascotto et al 2015), whereas decrease in serum levels were observed upon exposure to

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cypermethrin at postnatal day 5 to 10 at various doses ranging from 5, 10 15mg/kg and deltamethrin at a dose of 300µ/kg/day. Exposure to pyrethroids can also effect the production of estrogen and progesterone hormones from the ovarian granulosa cells and can also down regulate the expression of steroidogenic acute regulator protein and cytochromeP450 side chain cleavage enzyme genes which are important in steroid synthesis regulation.

Pyrethroid such as cypermethrin, fenvalerate, permethrin exposure not only inhibited the release of pituitary FSH but also restrained the FSH dependent ovarian follicle growth, increased the follicular atresia percentage and decrease in follicular diameter (Pascotto et al 2015; Sangha et al 2013) further they also induced gross and histopathological changes corpus luteum along with decreased formation in female offspring.

Similarly, exposure to these compounds has got significant alterations in the functions of testicles, seminiferous tubules, Sertoli and Leydig cells effecting spermatogenesis and disruption in the synthesis and release of testosterone.

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