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Prospective Effect of Zinc Oxide Nanoparticles against Some Pesticides Toxicity in Rats

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ABSTRACT

Widespread use of insecticides for public health and agriculture has caused severe environmental pollution and potential health hazards. Nanotechnology is a powerful new technology for reconstructing nature at the atomic and molecular level. This study was conducted to determine the efficacy of nanoparticles Zinc Oxide (ZnO-NPs) to reduce the toxic effects of Chlorpyrifos (CPF) or Fipronil (FIP) on the immunity and fertility of adult male rats for 9 weeks. Animals were divided into a control and five experimental groups (20 each). The first experimental group received water contained 75mg/L CPF. The second group received water contained 75 mg/L CPF and 200 mg/L ZnO-NPs. Rats of the third experimental group received 30 mg/L FIP. While, the fourth group received 30 mg/L FIP and 200 mg/L ZnO-NPs. The fifth group received water contained 200 mg/L ZnO-NPs. Result showed that CPF or FIP induced toxicological effects, they markedly reduced body weight gain and water consumption and induced pathologic changes in the liver, spleen and testis as showed on postmortem inspection and histopathological examination. The level of serum ALT and oxidative stress biomarkers including CAT, MDA and reduced GSH showed significant changes. DNA fragmentation of liver spleen and testis was severely increased by CPF or FIP. The immune response was reduced as determined by assessment of the phagocytic activity of neutrophils, comet assay on lymphocytes, macrophages activity, the levels of serum lysozyme activity, IL-2 and IL-6, and total protein and its profile as estimated by dendrogram bands of SDS-PAGE electrophoresis. In addition, fertility of male rats was decreased as evaluated through estimation of sperm motility, morphology and concentration by CPF or FIP. On the other hand, all these deleterious effects of CPF or FIP were alleviated in the groups that received water containing CPF or FIP and ZnO nanoparticles. These findings suggested that nanoparticles of ZnO have high affinity to adsorb CPF or FIP and can effectively modulate their toxicity in rats; this may offer a novel approach to the preventive management of pesticides in animals.

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INTRODUCTION

Modern agriculture requires million tons of pesticides worldwide to protect plants and products from pests and insects. Because of indiscriminate and extensive use of pesticides, they persist in soil, ground, surface waters, air, and agricultural products. Pesticides are the only toxic chemicals deliberately released into the environment in large amounts. Their potential to cause adverse effects to human and wildlife populations has been the subject of intense study and has led to the development of increasingly stringent and encompassing regulations for the risk assessment of novel formulations and to control the use of existing compound. Precautionary measures to minimize the release of chemicals into the environment are recommended. While waste avoidance and proper management of waste streams would be among the most sustainable practices, the high prevalence of contaminated waters and soils requires the development of new strategies for environmental mangment. **(Oerke and Dehne, 2004)**.

Organophosphorus pesticides are used for many years throughout the world **(Antonio et al., 2014)**. They are basically target the nervous system; sometime it affects non-target group of organisms also **(Cavieres et al., 2002)**. It is highly toxic for aquatic organisms even in low concentration. Chlorpyrifos is a well-known organophosphorothioate wide spectrum insecticide that is used in agricultural and nonagricultural areas **(Kamel et al., 2009)**. Chlorpyrifos inhibits the acetyl cholinesterase enzyme associated with the functioning of nervous system. It is thoroughly used to kill wide range of insects in agriculture worldwide **(Tang et al., 2015)**. Symptom associated with the Chlorpyrifos poisoning including nausea, vomiting, diarrhea, headache, convulsions, coma and death in severe conditions **(Fenner-Crisp, 2000)**. Exposure to Chlorpyrifos for long periods results in serious harm to the nervous system, respiratory tract, and

cardiovascular systems **(Benachour and Gilles-Eric, 2009)**. The effects of Chlorpyrifos have been observed about 24 km away from the place of application; **t**herefore, the degradation of Chlorpyrifos present in environment has become a public concern. Chlorpyrifos can be oxidized by various oxidizing agents, such as ozone, dinitrogen tetroxide, peracid, and chlorine, which give Chlorpyrifos Oxon after the replacement of "S" by oxygen in the thiophosphoryl bond **(Duirk et al., 2008)**. Chlorpyrifos Oxon is substantially more toxic compared to its parent compound, as it inhibits acetyl cholinesterase which is necessary for proper function of the nervous system **(Wu and Laird, 2003)**.

Fipronil is polychlorinated biphenyls pesticides; exposure to Fipronil associated with increased predisposition to cancer, diabetes, obesity, infertility and other endocrine disorders **(Soto and Sonnenschein, 2010 and Magdalena et al., 2011)**. Although the precise impact of this chemical on the prevalence of diseases is still unknown **(Rappaport and Smith, 2010)**.

Nanotechnology may offer fast and effective solutions for environmental clean-up **(Shannon, 2008)**. For example, nanostructured membranes with size-selective pores may provide efficient ways of separating solutes from water **(Yang, 2013)**. Besides filtration, which is generally energy-intensive, the removal of contaminants by sequestration (adsorptive remediation) or degradation to less toxic products (reactive remediation) may represent an effective alternative. Nanomaterials possess a very large surface-to-volume ratio that favors interaction with their environment. For example, nanomaterials have the potential to effectively adsorb molecules or catalyse chemical reactions at their interface **(Yuan, 2008)**.

Shahram et al., (2014) showed that nanoparticles ZnO beads was effective adsorbing agent for pesticide in water system, and the amount of reduction is related to pesticide concentration**.**

No study has been reported, in vivo system, on the role of ZnO in nano particles form as a binder for Chlorpyrifos or Fipronil to decrease their toxic effects on animals. Therefore, this study aims to show the potential effects of this formulation to relive the toxic effect of Chlorpyrifos or Fipronil on immunity and fertility hopping that its applications industrially and medically to remove pesticides from animal's water. In addition to prove that nanoparticles have no any negative harmful effects when it is added to the drinking water for animals.

LITERATURE REVIEW

Immune system plays a crucial role in maintaining health and accumulating evidence indicates that this system can be the target for immunotoxic effects caused by a variety of chemicals including the environmental pollutants, such as polychlorinated biphenyls, chlorinated dibenzo-p-dioxins, pesticides and heavy metals **(Krzystyniak, 2005).** It is often difficult to predict how a given chemical will interact with the immune system since there are numerous factors that influence toxicity. For instance, external factors such as housing of the animals, stress, exercise and intrinsic factors such as hormonal status or genetic disposition make each case unique. Also feedback or compensatory mechanisms associated with immune regulation could further complicate these predictions. In many instances, it is these compensatory mechanisms that trigger immune mediated diseases and cellular dysfunction. The susceptibility of the immune system to toxic damage can result from many factors. Host resistance to infectious agents and spontaneous neoplasms depends on immune competent cells, which are subject to continuous proliferation and differentiation and because of that they become excessively susceptible to variety of agents. The immune system is known for highly organized co-operation and regulation of various cells, which is ensured on one hand by soluble mediators (immunoglobulins, immune hormones and cytokines) and on other hand by intercellular interactions on the level of membrane receptors and anti-receptors. All agents that affect the fine balance mechanisms mentioned can cause agent specific or species specific immunity damage which in majority of cases results in immunosuppression **(Kacmar et al., 1999).**

Exposure of animals to the residual concentration of pesticides can lead to immunosuppression either directly or with participation of stress mechanisms and that of the neuroendocrine system. Immunosuppression leads to change in length

of life span, increased susceptibility to infectious diseases and decreased immune response to vaccination. Thus there is an urgent need to obtain more information regarding the manner in which various pesticides alter the immune system. Modulation of immune response through stimulation or suppression may help in maintaining a disease free state.

In recent years, the effects of pesticides on immune response have received great attention. **Luster et al., (1994)** have indicated immune system as sensitive indicator of toxicity assay especially for environmental contaminants and pollutants, which may have residual effects in the ecosystem. Considering the importance of immunotoxicity, **Moore et al., (1982)** suggested that all newly introduced compounds should be tested for immunotoxicity before they are introduced in the market. It is now clear that important changes in host immunity may occur after pesticide ingestion. Many pesticide chemicals like pyrethroids **(Prater et al., 2002),** organophosphates **(Galloway and Handy, 2003),** organochlorines **(Kumar et al., 2014)** are known to cause suppression of the immune system. Moreover, immunomodulation by agrochemicals is gaining significance in toxicity evaluation as low level dietary intake through food residues might decrease the resistance to infectious agents and cause breakdown to protection by vaccination **(Rodgers, 1996).**

Oxidative stress has been identified as one of the major factor for immunomodulation in any species of animal. Oxygen is essential to sustain life; conversely, breakdown products of oxygen such as reactive oxygen species (ROS) can be detrimental to cell function and survival.

There are several studies on immunotoxicity of most groups of pesticides, Organochlorine, organophosphates to which chlorpyrifos belong , carbamates, pyrethroids, however reports are lacking on detailed immunotoxicity of