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# Imidacloprid Induced Toxicity and Oxidative Stress

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**ABSTRACT**

*Indiscriminate usage of pesticides in agriculture is leading to contamination of environment and natural resources, and thereby producing an adverse impact on animal and human health. Imidacloprid is a neonicotinoid insecticide and classified under toxicity class II /III agents by United States Environmental Protection Agency (USEPA, 1994). It is an extensively used for crop protection in the world wide from the last decade due to its low soil persistence and high insecticidal activity at low application rate (Chao and Casida, 1997). Recently imidacloprid has raised concern because of its ability to cause egg shell thinning, reduced egg production and hatching time, which are considered as signs of possible endocrine disrupters (Matsuda et al., 2001). Experimental administration of imidacloprid through various routes in animals produces multiple organ toxicity and also induces oxidative stress.*

**KEYWORDS: imidacloprid, oxidative stress, organ toxicity**

## INTRODUCTION

Imidacloprid, a neonicotinoid insecticide, is extensively used in agriculture for control of the sucking insects and coleopteran beetles (Cox, 2001) and also used as foliar treatment for soil and for seed dressing (Felsot, 2001). In Veterinary Medicine, it is used as flea control agent on dogs and cats (Hutchinson *et al.,* 2001). It is one of the fastest sold insecticide across the world because of its high selective toxicity in insects. It acts on nervous system by blocking post synaptic acetylcholine receptors (Tomizawa *et al.,* 2005). Its selective toxicity results from its high affinity to insect's nicotinic acetylcholine receptors compared to mammals (Tomizawa and Casida, 2003). A case of acute poisoning was reported in human following ingestion of a pesticide formulation containing 10% imidacloprid (Wu *et al.,* 2001) and two fatal intoxication cases have been reported recently (Proenca *et al.,* 2005). Since imidacloprid is now being considered as a replacement for other existing pesticides, therefore the relative risk and benefits of this insecticide must be compared to the existing pesticides. In this article we had tried to review few important toxic effects caused by imidacloprid.

### Imidacloprid induced hepato, nephro toxicity and oxidative stress

In a sub chronic oral toxicity study, *wistar* rats were treated with imidacloprid at concentrations of 150, 600 and 2400 ppm for a period of 13 weeks. Liver showed hypertrophy of hepatocytes and sporadic cell necrosis. The biochemical changes included elevated levels of alanine amino transferase, serum alkaline phosphatase with slight increase in blood clotting time (USEPA, 1998).

Administration of imidacloprid at the rate of 0.62 mg/kg b. wt for a period of 3 to 6 weeks via stomach tube in Japanese quail produced degenerative changes in liver including highly dilated portal spaces, large degenerated area, faintly stained cells and nuclei (Omiama, 2004).

Oral administration of imidacloprid at 1 mg/kg b. wt for 21 days in cow calves resulted in elevation of plasma ALT, AKP (Barinderjit *et al.,* 2006).

In a 90 days oral toxicity study with imidacloprid in female rats at the rate of 20 mg/kg b. wt per day resulted in an increased relative weight gain of liver and kidney at necropsy. Histopathologically liver showed a mild focal necrosis of hepatocytes with swollen nuclei, cytoplasmic lesions and kidney showed degeneration of tubules and glomerulus. Elevated levels of ALT, AST, glucose, BUN and decreased acetyl choline esterase in serum and brain were also observed (Bhardwaj *et al.,* 2010).

Imidacloprid at the rate of 10 µM through intravenous administration in rats resulted in increased nitric oxide levels and upregulated inflammatory cytokines tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), interleukin-1 beta (IL-1β) in liver. Elevated levels of xanthine oxidase, myeloperoxidase activity, depleted intracellular glutathione in liver and brain also observed (Duzguner and Erdogan, 2010).

Oral administration of imidacloprid at the rate of 139 mg/kg b. wt in chicken resulted in hepato and nephro toxicity which was evident from gross lesions like hemorrhages, paleness of kidneys and histopathological lesions like hemorrhages, degeneration of hepatocytes, congestion, mild dilation of hepatic sinusoids in liver, sub capsular hemorrhages and coagulative necrosis of tubular epithelium in kidney. Increased levels of AKP, ALT, AST and plasma glucose were also noticed (Kammon *et al.,* 2010).

Oral administration of imidacloprid in male white leg horn chicken at 1.25, 1.67 and 2.5mg/kg b. wt for 28 days resulted in increased ALT levels (Balani *et al.,*2011).

Treatment of male albino rats with imidacloprid at the rate of 0.21 mg/kg b. wt for 28 days orally produced histopathological changes in liver like homogenous cytoplasm in hepatocytes, congested central vein, leucocytic infiltration and fibroblasts around the bileduct and central vein. Eelevated levels of AST, ALT, ALP and MDA were also observed and these changes were modulated by supplementation of thymoquinone (Mohany *et al.,* 2012).

Administration of imidacloprid at 80 mg/kg body weight/day by oral gavage for 28 days in male rats resulted in hepatotoxicity which was evident from increased ALT and AST activities, decreased total protein, reduced glutathione concentration in the liver. Histologically, the liver showed marked dilation, congestion of central vein, portal vein and sinusoidal spaces, vacuolation/fatty change and degenerated hepatocytes. Ultra thin sections of the liver revealed swollen nuclei, varied size and shape of mitochondria, disrupted chromatin and rough endoplasmic reticulum (Soujanya *et al.,* 2013).

Oral administration of imidacloprid at the rate of 14.9 mg/kg b. wt. in male mice produced oxidative stress which was evident from increased levels of lipid peroxidation (LPO), activities of the antioxidant enzymes like catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), glucose-6-phosphate dehydrogenase (G6PD), glutathione-s-transferase (GST) and decreased levels of reduced glutathione (GSH) whereas Vitamin C (200 mg/kg) treated mice showed ameliorating effect documented by decreased levels of LPO (El-Gendy *et al.,* 2010).

Oral administration of imidacloprid at the rate of 20 mg/kg b. wt for 90 days in female rats resulted in decreased levels of SOD, CAT, GPx activity in liver and brain, decreased GSH levels only in liver and increased levels of MDA in liver, kidney (Kapoor *et al.,* 2010).

**Imidacloprid induced neuro toxicity**

Administration of pregnant rats with a single intraperitoneal injection of imidacloprid at the rate of 337 mg/kg b. wt produced neurobehavioral deficits, increased expression of glial fibrillary acidic protein in the motor cortex and hippocampus in offspring rats (Abou-Donia *et al.,* 2008).

In a 90 days oral toxicity study with imidacloprid in female rats at the concentration of 20 mg/kg/day evidenced decreased activity of acetyl choline esterase (AchE) in brain, spontaneous locomotor activity, histopathologically cerebellum of brain showed degenerative changes in purkinji cells and loss of granules in granular layer (Bhardwaj *et al.,* 2010).

Administration of imidacloprid at the rate of 80 mg/kg b.wt/day through oral gavage for 28 days resulted in neuro toxicity which was evident from histopathological changes in brain like marked congestion in cerebellum, degeneration of purkinje cells with loss of dendrites, vacuolation around neurons, shrunken neurons, chromatolysis and ultra structural alterations like vacuolar mitochondria, apoptotic nuclei with disrupted and margination of chromatin material (Soujanya *et al.,* 2012).

## CONCLUSION

Imidacloprid exposure leads to marked biochemical, histopathological and ultrastructural changes in various organs so imidacloprid was found to be a potent hepato, nephro and neurotoxic agent. Alterations in antioxidant parameters indicated that imidacloprid exposure leads to oxidative stress. To prevent adverse effects of imidacloprid, it should be used in limited dose for crop protection and as insecticides in dogs and cats.

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