



وَقَالَ ابْنُ زَيْنَا



The Effect of Lead Toxicity on Albino Rats' Lingual Papillae and the Possible Protective Role of *Nigella sativa* (Black seed) and Honey

Thesis

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Dedication

I would like to dedicate this work to my precious family; my loving parents, my beautiful sisters, my beloved husband and my adorable sons. Your love and support inspired me to strive for success.

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INTRODUCTION AND REVIEW OF LITERATURE

Lead

Lead is a poisonous heavy metal, which is widely used in many industries. Lead toxicity is a serious occupational hazard which occurs due to accumulative absorption of little amounts of lead into the body until toxic levels are reached. The symptoms of lead toxicity are usually nonspecific thus making its diagnosis difficult (*Gordon et al., 1979*).

Many workers in the lead based industries are ignorant of the dangerous effects of lead and so do not take proper precaution while handling it, leading to higher levels of exposure. Lead industries include; lead production and soldering, manufacturing of batteries, ceramics, plastics and bullets as well as metal radiator repair and recycling lead cables. Some construction work like demolition of old buildings, scraping of lead-based paint, repair of bridges, water tanks, welding of lead painted metal and furniture refinishing may also expose workers to considerable amounts of lead (*Roché et al., 1995*).

Oxidative stress is the main contributor to lead's toxicity as lead directly and/or indirectly can change the antioxidant balance in biological tissues. The following mechanisms were proposed for lead-induced oxidative stress: (1) Lead may change the membrane fatty acid composition (2) Lead may directly bind to cell membranes, thereby increasing the susceptibility of membranes to lipid peroxidation (3) Lead may alter biological antioxidant defense systems (4) formation of reactive oxygen species (*Gurer et al., 1999*)

The damaging effects of its use have been long known. Over the past two decades efforts have been made to reduce its exposure. Toxicity has been relatively controlled in industrialized countries but is still a major health problem in some developing countries. Lead absorption occurs mainly throughout the respiratory and gastrointestinal tracts. Almost 80% of lead fumes and lead dust are absorbed via inhalation while 10-15% is ingested with contaminated food, drinks and tobacco. Once absorbed, lead readily spreads to all the tissues and accumulates primarily in three compartments: blood, soft tissues, and bone. Eventually 80-95% of the body burden is redistributed into the skeletal bone and is slowly released back into the blood with a half -life from years to decades. Generally, lead excretion is low and occurs mainly through the urinary tract although minute amounts are excreted in feces, sweat, hair and nails (*Papanikolaou et al., 2005*).

As a consequence of its capacity to interfere with biochemical events throughout the body, inorganic lead exerts a wide spectrum of multisystem adverse effects. The most harmful effects of lead exposure are on the hemopoietic, nervous, reproductive systems and the urinary tract (*Kosnett et al., 2007*). Moreover, prolonged lead exposure can induce anemia, renal dysfunction and high blood pressure which are major risk factors for heart diseases like myocarditis, tachycardia and strokes (*Navas-Acien et al., 2007*).

The Occupational Lead Poisoning Prevention Program (*OLPPP*) summarized in its 2009 issue the early symptoms of lead toxicity which are usually mild and vague. Affection of the nervous system cause fatigue, drowsiness, insomnia, confusion, memory loss, difficulty concentrating and headaches. The gastrointestinal system may also suffer from abdominal cramps, vomiting, diarrhea or constipation in addition to poor appetite and nausea. Muscle and joint pain may be another complaint. In severe cases

hallucination, seizures and coma may occur as a result of lead encephalopathy, which is a life-threatening condition. Female workers may suffer from sudden abortions, premature births, still birth or reduced birth weight in addition to possible postnatal developmental delay of the newborn. Infertility problems may arise in male workers at high levels of lead exposure **(OLPPP, 2009)**.

The histological effects of lead exposure have been the focus of substantial experimental research throughout the years. A previous study assessed the histopathological changes induced by the oral intake of lead acetate in rat tissues using a short-term exposure to a sub-lethal dose of lead (44 mg/kg body wt/day). The results conveyed that the gastrointestinal tract is the primary target organ and shows pathological changes much before any other organ. The intestinal mucosal epithelium is affected resulting in malabsorption. The proximal tubular cells of the kidney degenerated causing secretion of essential materials such as glucose and amino acids in the urine. Degenerative changes were seen in the liver and affected its enzyme activities **(Karmakar et al., 1986)**.

Another research was conducted to examine the hepatic and reproductive effects of lead toxicity in female rats where tap water containing lead acetate at a dose of 200 mg/L, as drinking water, was given daily for three weeks. The results confirmed hepatotoxic effect of lead. Gross structural disintegration with nuclear displacement, mononuclear cell infiltration and fat accumulation in hepatocytes was evident in histological sections. Reproductive effects were also observed in female rats due to its effect on female hormones **(Abdou and Newairy, 2006)**.