



Forensic Toxicology Research to Investigate Environmental Hazard

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Abstract

Forensic toxicology focuses on medico-legal aspects of chemical exposure and toxic injury on living organism and an environmental hazard i.e. a substance, state or event which has the potential to threaten the natural environment and / or adversely affect people's health. For instance, aldrin: a cyclodiene-organochlorine pesticide, is classified as persistent organic pollutant (POP). The use of aldrin has been banned long ago but still it is detected in ecosystem in its biotransformed form i.e. dieldrin (metabolite of aldrin) in the quantity higher than acceptable limits. Present editorial provides a baseline data on aldrin toxicity.

Introduction

Poisoning occurs when any substance interferes with normal body functions after it is swallowed, inhaled, injected, or absorbed. The branch of medicine that deals with the detection and treatment of poisons is known as toxicology. Broadly, toxicology is the study of the adverse effects of chemical or physical agents on living organisms. Forensic toxicology is the use of toxicology and other disciplines such as analytical chemistry, pharmacology and clinical chemistry to aid medical or legal investigation of death due to poison and drug. The primary concern for forensic toxicology is not only the legal outcome of the toxicological investigation or the technology utilized, but the obtainment and interpretation of results. For example: Aldrin (hexachlorohexahydrodimethanonaphthalene), a broad spectrum insecticide belonging to cyclodiene class of organochlorine pesticide, is almost immediately metabolized into another substance dieldrin, requires detailed investigation of factors such as source of exposure and chemical purity concentration necessary to confirm diagnosis of aldrin poisoning. The substance may also have been diluted by its dispersal through the body. A blood sample of approximately 05 ml is usually sufficient to screen and confirm most common toxic substances, which provides a profile of the substance to the toxicologist [1].

In today's society, human direct or indirect human exposure to some sort of chemicals is obvious. Firstly, the general concern

of environmental pollution is due to use of chemical substances. Likewise, contaminated food and drink are the main concern throughout the world. Among toxic substance, pesticides characterize potentially grievous vulnerability to human wellbeing [2]. As known, all pesticides are toxic pollutants though; all pollutants are not toxic pesticides. Pesticides are classified as organochlorines, organophosphates, carbamates and pyrethroids. Pesticide in relation to human-health led to two periphery concerns. Firstly the concentration at which it cause toxicity or is poisonous and other being its relative toxicity to other pesticides. The pesticide varies greatly in their toxicity and persistence [3]. The nature of chemical substance suggests the possibility of functional disturbances in a target organ.

Poisoning may be intentional viz. homicidal and suicidal or unintentional viz. accidental (survival or fatal) and occupational (survival with side effects). Curiosity, inability to read warning labels, inadequate supervision mental confusion, poor eyesight, and the use of multiple drugs are the leading reasons for high rate of accidental poisoning. A substantial number of poisonings also occur as suicide attempts or drug overdoses. For instance, in 2016, Arizona department of health sciences evaluated dieldrin in crawl space dirt on the request by residents to be in concentration of 0.88 ppm i.e. higher than acceptable limit. It may be ingested, inhaled and cause potential exposure to residents at place. A news by Japan times in 2015 reported dumping of

whale meat imported from Norway as it consists of aldrin and dieldrin higher than safety limits of 0.1 ppm. Bhadouria et al. discussed in study the current use of aldrin in Kaldeo National park, Bharatpur Rajasthan in India and detected 0.1173 ppm of dieldrin [4].

Aldrin is prepared by Diels-Alder reaction. It has the empirical formula $C_{12}H_8Cl_6O$ and molecular mass 364.90 g/mol. Aldrin was first introduced in 1950's. It is classified by WHO as Class 2B, highly hazardous chemical. It is highly toxic in nature, classified as persistent-organic-pollutant (POP). Aldrin is one of the hazardous occupational and environmental pollutants arising primarily in ecosystem since precedent usage [5]. Aldrin has often been formulated as seed dressing and its principle use has been against soil insects that attack field, forage, vegetables and food crop. The main use of dieldrin was soil treatment including termite eradication but has been used in homes widely against vectors of disease including malaria in the tropic and spot treatment in temperate zone [6]. It is bio-accumulative, persistent (remaining up to 3 decades after use) and toxic in nature.

Although, it is banned long-ago, the past anthropogenic activities (where it was previously used) have led to detection of dieldrin into the environment at concentrations significantly higher than acceptable limits [7]. This owes to its high lipophilic properties, low volatility and resistance to degradation by physical and biological processes [8]. Its accumulation has elicited worldwide concern for many reasons.

Several monitoring studies globally have been carried out to investigate impact of aldrin and dieldrin residues on water, sediment and biota. It is commonly traceable in nature as reported by many researchers [9-11]. Aldrin released to the environment and gets readily converted to dieldrin. The conversion of aldrin to dieldrin occurs much more rapidly than the subsequent biotransformation and elimination of dieldrin, resulting in the accumulation of dieldrin in lipid rich tissues.

Aldrin is ubiquitous toxic pesticide, a potent inhibitor of gamma amino butyric acid type A receptor, tert-butyl-bicyclopentylphosphorothionate (GABAA-TBPS) binding site [12-14] that disrupts gabarnergic signaling by preventing chloride influx into the GABA(A) receptor ionophore complex [5,14,15]. Thus, facilitates excitatory neurotransmitter release or interferes with inhibitory neurotransmitter action. It has a serious toxicity in humans and animals causing CNS manifestations like: neurotoxic effects with onset of seizures, instability and excitation [5,12].

On acute toxicity, respiratory difficulties [16], sluggishness, anemia, carcinogenicity, atrophy, decrease red blood cell count and reduced hemoglobin concentration have been observed. It is also found to be genotoxic [17]. Renal toxicity has been reported in humans and animals on acute [18], intermediate duration [19,20] and chronic exposure [21,22]. The liver is the most

sensitive target of toxicity in intermediate duration exposure [19,23,24] and chronic-duration studies as in rats [22,25]. The adaptive changes in the liver have been observed in acutely exposed animals [26].

Aldrin has extremely long half-life in the human body and is highly cumulative in fats such as brain [27]. The liver plays primary roles in the metabolism and excretion of xenobiotics with morphological alterations occurring in some toxic conditions [28]. In consideration divalent oxygen play important role in metabolism process which involves oxidative enzymes. In brain, metabolic enzymes for several xenobiotics have been characterized. It has been reported that aldrin starts converting to by-product dieldrin by epoxidation process on metabolism in liver tissue in fish after 8 hours exposure and reached 94% in 32 days [29] and can be distributed in organisms through blood stream. Dieldrin conjugation for its excretion occurs mainly in liver however dieldrin can be created outside the liver which would have a greater chance of causing toxic effects. Aldrin metabolism involves the major role of mixed function oxidase (MFO) activity in fish [30].

Being toxic to many species of animals, aldrin toxicity relies on many factors such as animal weight [31], time / duration of exposure [32] and temperature [3]. Literature reported shows that (lethal dose) LD50 for *Rana hexadactyla* under aldrin was found to be 2.4 ppm [33]. In fish, *Saccobranchus fossilus* was found to be 0.44 ppm. Aldrin on comparison to other organochlorine is found to be less toxic than drins (isodrin, endrin and dieldrin) while more toxic than D.D.T, endosulphan, heptachlor, lindane and chlordane [21,34].

It has been reported median tolerance limit for fish exposure to aldrin concentration ranging from 0.089 ppb to 0.018 ppm at 24 hours. Singh et al. found that increased levels of magnesium and phosphate in blood plasma were related to diminish entrance of calcium through damage gills of fish exposed to aldrin[35]. Aldrin affects the growth and vital functions of zebra fish at very low (0.01 $\mu\text{g/l}$) concentrations [21]. During zebra fish development dieldrin causes apoptosis, disorganized motor neuron axon formation and significant damage of dopamine nerve cells in the brain [36]. Aldrin exposure causes oxidative stress in zebra fish indicated by increase in MDA level, decrease in superoxide dismutase activity and gene expression at sub-lethal concentrations. [37-39]. Lipodosis occur in liver on exposure to OCP's in the eel *Anguilla Anguilla* [40]. Exposure to dieldrin disrupts reproductive processes in teleost fish and a high level of GABA is found in hypothalamus and cerebellum [5].

In rats, acute oral toxicity dose of aldrin is 20-70 mg/kg while increase in body weight and mortality was observed with repeated dose at 300 ppm of aldrin. The estimated lethal dose for man is approximately 5 g in human, blood concentrations exceeded 20 $\mu\text{g}/100\text{ ml}$ in exposed patients showing signs of aldrin intoxication [41].

Conclusion

Aldrin and dieldrin clearly affects food chain. Mechanisms of effect would be better understood if there was more central data collection reporting systems. There is a biologic gap in the research on aldrin and dieldrin toxicity. The relationship of environmental exposure and public health is now becoming a very active field of research. It is apparent from the data sources reported that dieldrin remains in the environment at high levels on aldrin exposure; therefore, it raises significant issues for public health. Tools to find and use information are rapidly improving. Aldrin and dieldrin has been used in this review as a pathway in forensic toxicology research to investigate environmental hazard.

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