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EFFECTS OF LINDANE AS AN ENDOCRINE DISRUPTOR CHEMICAL ON HUMAN HEALTH

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ABSTRACT

Over the past decades, a number of substances in the environment have been detected to have detrimental effects on the endocrine system. These substances have been labeled as endocrine disruptor chemicals (EDC) as they mimic or block hormones function and therefore, disrupt the normal body physiological functions. Effects on human beings include decrease in sperm counts and quality, cryptorchidism, hypospadias, testicular and male breast cancer, impairment of ovulatory mechanism and cardiovascular system. One of the examples of these EDC is lindane, a 99% pure gamma isomer of hexachlorocyclo-hexane. Exposures to lindane are either through dermal contact, inhalation or ingestion. Acute toxicity symptoms include headache, gastrointestinal symptoms, convulsion, cyanosis and circulatory collapse. Chronic symptoms include blood disorders, convulsion and disruption of the endocrine system particularly the reproductive system. Lindane has also been anticipated as a carcinogen. The International Agency for Research in Cancer (1991) has classified lindane as Class 2B carcinogen. The United States Environmental Protection Agency (USEPA) has set a maximum contaminant level of 0.2 parts per billion (ppb) in drinking water. Acceptable daily intake (ADI) for lindane by Codex Alimentarius is 0.001 mg / kg body weight per day. Due to its endocrine disruptor characteristic and carcinogen effects, there is a need for a rapid elimination of lindane usage in the pharmaceutical, veterinary and agricultural today. We also need an effective delivery of education programme about the risk of lindane, emphasizing the protection of exposed groups of children, indigenous people and workers.

ABSTRAK

Sejak beberapa dekad yang lalu, terdapat beberapa bahan dalam persekitaran, yang telah dikesan mengakibatkan kesan mudarat ke atas sistem endokrin. Bahan tersebut dilabel sebagai bahan kimia pengganggu endokrin, di mana ia berupaya meniru atau merencat fungsi hormon dan oleh itu, mengganggu fungsi normal fisiologi tubuh. Kesan ke atas manusia termasuk penurunan kuantiti dan kualiti sperma, 'cryptorchidism', hypospadias, barah testis dan payudara lelaki, gangguan ke atas mekanisma ovulasi dan sistem kardiovaskular. Salah satu contoh bahan ini ialah lindane, merupakan 99% isomer gamma dari heksakloroheksane. Pendedahan terhadap lindane berlaku samada melalui kontak kulit, inhalasi atau ingesti. Simptom akut keracunan meliputi sakit kepala, simtom sistem gastrousus, konvulsi, sianosis dan kegagalan sistem peredaran darah. Simtom kronik termasuk gangguan sistem darah, konvulsi dan gangguan sistem endokrin terutamanya sistem reproduksi. Lindane juga dikenalpasti sebagai satu bahan penyebab kanser. Agensi Antarabangsa Untuk Penyelidikan Kanser (1991), mengkelaskan lindane sebagai bahan penyebab kanser kelas 2B. Agensi Perlindungan Persekitaran USA (USEPA) telah menetapkan suatu paras maksima pencemar pada 0.2 bahagian per bilion (bpb) dalam air minuman. Pengambilan harian dibenarkan (ADI) bagi lindane oleh 'Codex Alimentarius' ialah 0.001 mg / kg berat badan sehari. Oleh kerana kesan gangguan endokrin dan bahan penyebab kanser, ada keperluan untuk menghapuskan segera penggunaan lindane dalam bidang farmaseutikal, veterineri dan pertanian hari ini. Kita juga perlukan penyampaian program pendidikan yang berkesan mengenai risiko penggunaan lindane, penekanan terhadap perlindungan bagi kanak-kanak, orang asli dan pekerja yang terdedah.

INTRODUCTION

A big number of substances that exist in the environment have detrimental effects on human endocrine system functions (Richard J.Kavanagh et al 2004). Many research

were carried out to study the endocrine disruption actions of various environmental pollutants. (Edward F. Orlando et al 2004).

The researches focused on the fact that those chemicals have the ability to act as estrogen receptor as well as androgen receptors, either as agonist or as antagonists. These findings proved that these chemicals pose potential threat to

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human and wildlife reproduction and endocrine systems (Hiroyuki Kojima et al 2004).

THE ENDOCRINE SYSTEM

The endocrine system consists of a complex network of hormones and glands that regulates many of the body functions such as growth, development, maturation, as well as the way various organs operate. The endocrine glands for example pituitary, thyroid, adrenal, thymus, pancreas, ovaries and testes, release certain measured amount of respective hormones, into the bloodstream. These hormones act as natural chemical messengers, traveling to different parts of the body, in order to control and regulate many body life functions.

ENDOCRINE DISRUPTORS

The European Commission (EC) defines them as exogenous substances that cause adverse health effects in an intact organism, or its progeny, subsequent to changes in endocrine function. They are synthetic chemicals that, after enter the body, can mimic or block hormones and therefore, disrupts the body's normal functions. This disruption can happen through altering the hormone levels, halting or stimulating the production of hormones, or changing the way hormones travel through the body, thus affecting the function that these hormones control.

These compounds have been reported as being associated with a range of disorders, including cognitive and behavioral disturbances, immune dysfunction, developmental and reproductive abnormalities and cancer.

Communication on a cellular level, defined as chemical signaling, sensing and response, is an essential and universal component in all-living organism. It is the framework that unites all ecosystems. Evolutionary conserved signaling "webs", existing within and between organisms, rely greatly on efficient and accurate interpretation of these chemical signals, by the receptors. Therefore, the endocrine disruptor chemicals (EDCs) have been shown to disrupt hormone signaling in vitro as well as in vivo (Jennifer E. Fox 2004).

One example of endocrine disruptor chemicals is insecticide lindane. It is a 99% pure gamma isomer of hexachlorocyclohexane, first prepared by Faraday in 1825. It is produced as pediculocide and scabicide in 1952 and has been in use for nearly 50 years. It kills insects by

stimulating the nervous system resulting in seizures and death. World Health Organization (WHO) classifies lindane as moderately hazardous. Oral lethal dose 50% (LD₅₀) in rat is 88 mg 1 kg body weight. Human ingesting of 17 mg 1 kg body weight will show severe toxic symptoms and dose above 300 mg 1 kg body weight have proven to be fatal. It is considered as one of the top chemical of concern for the Agency For Toxic Substances and Drug Registry (ATSDR).

Seizure and death in infants have been reported after topical application of 1% lindane lotion in large amounts. The lindane serum concentrations were found to reach a high level of 0.10 µg 1 L after 46 hours of application of lotion. The level was higher compared to mean concentration of 0.005µg/L in most children treated with the 1% lindane lotion. A single application of 1% lindane lotion among 19 geriatrics in managing an outbreak of scabies resulted in 3 of them had seizures (Tenenbeim, 1990). The fatal dose in adults is approximately 10 to 30 gram. Death have been associated with concentration lindane in the serum of 1.3 pgm 1 mL (Kurt, et al. 1986). Serum concentration of 0.6 pgm 1 mL will result in seizures, acidosis, muscle weakness, acute renal failure, myoglobinuria and hypertension.

PHYSICAL AND CHEMICAL PROPERTIES

Lindane is a white, crystalline organic solid. It is one of the 8 isomers of hexachlorocyclohexane that is known. Its formula is C₆H₆Cl₆ and has a molecular weight of 290.8. Its melting point is at 112.5^oC, with density of 1.85. Lindane is stable to heat, light, air, carbon dioxide and strong acids.

ENVIRONMENTAL EXPOSURE

Exposure to lindane may occur via dermal contact, inhalation and ingestion. Lindane also can contaminate drinking water sources. The Los Angeles County Sanitation District estimated that one dose of lindane treatment for head lice can pollute 6 million gallons of water to levels that exceeded the drinking water standards.

OCCUPATIONAL EXPOSURE

Workers who are involved in the production of lindane are subject to exposure at the workplace. Human blood concentration have

been reported ranging from 5 to 188 µg/L. The concentration was found to be highest among people aged 41 to 60 years old. Workers who directly involved in handling of lindane did complain of headache, paraesthesia, giddiness, malaise, tremors, vomiting, decreased libido, vomiting and impaired memory. Serum concentration depends so much on the degree (dose) and duration of exposure.

KINETICS AND METABOLISM

Lindane which taken up from the intestine is transferred to the bloodstream, where the absorption rate is most rapid and more than 50% absorption occurred in the intestine within 30 minutes. Studies have also indicated that a considerable amount of lindane is absorbed after dermal applications.

After the uptake, lindane is distributed to all organs and tissues in the body; with the highest is being in the adipose tissue. Those organs include liver, brain, kidney and muscles. Lindane has also been found in breast milk.

The metabolism of Lindane is through one of these four mechanisms; dehydrogenation which leads to gamma-HCH formation, dehydrochlorination leading to formation of gamma-PCCH, dechlorination leading to gamma-tetrachlorohexene and hydroxylation leading to formation of hexachlorocyclohexanol.

The primary metabolites of lindane are chlorophenols and chlorobenzenes, a part from more than 80 other lindane metabolites, which include chlorinated metabolites found in the urine samples of workers that involved in lindane production. Total of 58% of the lindane

metabolites found in urine is in the form of trichlorophenols. Other metabolites include dichlorophenols, tetrachlorophenols, pentachlorophenols, hexachlorobenzene, tetrachlorocyclohexanols and pentachlorocyclohexane.

In liver, lindane interferes with hepatic oxidative capacity and glutathione metabolism. Another possible mechanism is increased lipid metabolism. Inhibition of Mg ATPase activity has been observed in rat liver tissues suggest ATPase enzymes sensitivity to Lindane (ATSDR 1999). In mammals, including human, after going through the metabolism phase, lindane is eliminated via the urine, feces and breast milk. Only small quantities are eliminated unchanged.

GLOBAL SCENARIO

In June 2002, the environmental ministers from Mexico, USA and Canada resolved to develop a North America Regional Action Plan (NARAP). The task force on lindane gathered in Montreal, Canada in September 2004 to draft the NARAP. In Canada, lindane still is being used in their agricultural activities (Table 1). More than 99% of this use was in three prairie provinces (Manitoba, Saskatchewan and Alberta). However, since December 1999, Lindane is no longer used as a seed treatment for canola, and the levels has declined. The 2002 US EPA Registration Eligibility Decision allows Lindane to be used as a seed treatment for six grain crops like corn, wheat, barley, oat, rye and sorghum. In Canada, all agricultural use of lindane is to stop by 31 December 2004.

Table 1: The estimated annual usage of Lindane in US, Canada and Mexico (tones/year)

Country	1980	1990	1997	1998
US	268	114		
Canada	200	284	455	510
Mexico	23	261		
Global usage	11,900	8,400		

Source: World Wildlife Fund Canada 1999

MALAYSIA

A study that was carried out among 577 school children from 60 schools through out Peninsular had found positive pesticide residual, among them is lindane, in their blood (Mustafa Mohd Ali. 2002) (Table 2). The high risk groups identified include workers in manufacturing of lindane, pesticide applicators who treat buildings

with lindane containing products, farmers and agricultural workers who treat soil and seed with lindane, forestry or timber workers who treat wood using lindane, people who handle lindane-contaminated clothing, pet groomers, veterinary staff who use shampoos that contain lindane and children/adults who receive shampoos that contain Lindane, to treat head lice and scabies.

Table 2: Pesticide residual levels in blood

Pesticide residual	Concentration in blood (ugm per gm)
Aldrin	47.6
Heptachlor	3.8
Lindane	57
P,p' – DDT	3.4
O,p' DDE	1.4
Chlorpyrifos	10.3
Diazinon	103.0

Source: Mustapha A.M. Department of Pharmacology, Faculty of Medicine, UM.

CONCLUSION

Rapid elimination of pharmaceutical, veterinary and agricultural use of lindane, with its use precluded given the availability of safer and affordable alternatives. Commitment to research and education programme that support alternatives to lindane, giving top priority to preventive and least toxic alternatives. Increase resources for research in environmental health are one important component. Need to develop reliable and practical tests for defining hormonal influences of chemicals released by industries in vivo and in vitro. Delivery of education programme about risk of lindane. emphasizing the protection of exposed high-risk groups. Human exposure to environmental synthetic chemicals has changed considerably in the past 70 years. This period has seen major changes in our diets, lifestyle and social practices, some of which, might have profound effects on our health. Reducing exposures by reducing release of chemicals to the environment requires action by industry and government. However, to ensure that Lindane no longer poses a significant threat to our population, there is much to be done. Everybody must participate, the government, the regulatory bodies, the NGOs, state and federal agencies and the community must all be united so that their

mission of limiting the threat, to the most practical, allowable level.

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