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Environmental Impact of the Y-Isomer of HCH: Unveiling Its Role in Cancer Formation

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ABSTRACT

Currently, over 2,500 chemical compounds are used in food production, primarily to extend shelf life and improve sensory qualities. However, some of these substances— especially toxic ones—can unintentionally contaminate food through packaging materials or technological additives. The presence of residual toxicants and industrial pollutants in food poses a significant health risk and can contribute to the development of cancer. Persistent organic pollutants such as organochlorine pesticides, polychlorinated biphenyls, and by-products of industrial and combustion processes— such as dioxins and furans—are especially concerning. One of the most hazardous among them is the γ-isomer of hexachlorocyclohexane (C6H6Cl6), an organochlorine pesticide. In its pure form, hexachlorocyclohexane is a hydrophobic white crystalline powder with remarkable acid resistance. It is now well established that this compound is a polytropic toxin, primarily targeting the central and autonomic nervous systems of mammals. Though once widely employed in agriculture for pest control, the use of hexachlorocyclohexane has since been globally prohibited. This article reviews the effects of hexachlorocyclohexane on human health.

Keywords: Hexachlorocyclohexane, Toxicity, Human health, Carcinogenesis

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Introduction

Pesticides represent a broad and diverse class of compounds, including organochlorines, organometallics, organophosphates, and natural alkaloids, each differing in their mechanisms of action and toxicity levels toward target cells [1]. A well-established principle regarding these substances is that their long-term application leads to reduced biodiversity. This is largely due to their pronounced reproductive toxicity, which affects virtually all animal species, including humans [2–4].

In 2017, the United Nations refuted the commonly held belief that pesticide use is essential for global food security. Supporting this stance, data were presented showing over 200,000 deaths attributed to pesticide poisoning. Chronic exposure to these toxic substances has been linked to various health issues, including cancer, neurodegenerative diseases like Alzheimer's and Parkinson's, hormonal imbalances, developmental disorders in children, and reduced fertility [5, 6]. Elevated or prolonged exposure to hexachlorocyclohexane (HCH) has been associated with an increased risk of miscarriage in women. Furthermore, lindane—an isomer of HCH—is known to exhibit antiandrogenic effects in men, potentially impairing reproductive development by reducing testicular size, disrupting normal sperm production, and altering hormone levels [7].

There is now unequivocal scientific evidence connecting pesticide exposure to cancer development [8]. For example, a 2019 study reported that young women exposed to dichlorodiphenyltrichloroethane (DDT) are at significantly higher risk of developing breast cancer later in life, due to cellular pathotransformation. DDT's high chemical stability and persistence in bodily tissues contributed to its ban in several countries [9]. Medical literature now includes extensive lists documenting the correlation between specific pesticides and their associated adverse effects [10, 11]. As such, rigorous legislative control over pesticide use in the food industry is critical to prevent widespread human exposure and toxicity. This article reviews the effects of hexachlorocyclohexane on human health.

Results and Discussion

Discovery and physicochemical properties of γ-hexachlorocyclohexane

The γ-isomer of hexachlorocyclohexane ($C_6H_6Cl_6$), an organochlorine pesticide, was once extensively used in agriculture to control insect pests in livestock feed. However, its use is now banned worldwide [12]. The compound was first synthesized in 1825 by Michael Faraday under laboratory conditions. Nearly a century later, G. Bender discovered the insecticidal activity of one of HCH's isomers, leading to the identification and mass production of hexachlorocyclohexane beginning in 1949. At its peak, HCH was the second most widely produced pesticide after DDT.

Pure HCH appears as a white, crystalline, hydrophobic powder with high resistance to acidic degradation. It is commonly synthesized through the chlorination of benzene, as well as through reactions involving cyclohexane and cyclohexene.

Technical-grade lindane (a form of HCH) typically appears yellowish due to impurities like pentachlorocyclohexene and tetrachlorocyclohexadiene, and it emits a characteristic musty odor. While it is hydrophobic, it dissolves readily in non-polar organic solvents such as benzene, acetone, and kerosene [10].

The model of lindane hexachlorocyclohexane is presented in **Figure 1**.

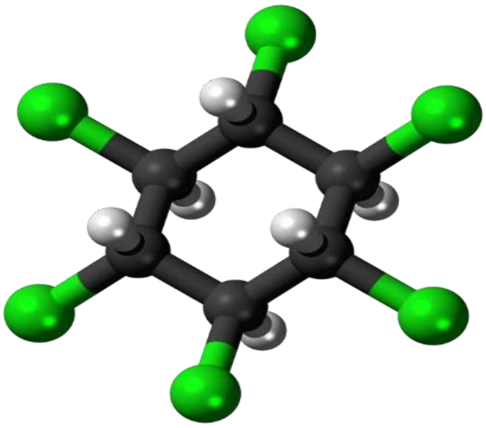

Figure 1. Model of lindane hexachlorocyclohexane.

Use and toxicity of hexachlorocyclohexane (HCH)

Hexachlorocyclohexane (HCH), particularly its γ-isomer (lindane), was once one of the most widely used pesticides for controlling insect infestations. Due to its potent insecticidal activity, lindane served as an effective contact, systemic, intestinal, and fumigant poison, and was frequently applied in warehouse fumigation [7]. It is now well-established that HCH is a polytropic toxic compound, primarily targeting the central and autonomic nervous systems in mammals. As early as 1985, Soviet scientist Professor Melnikov noted the strong cumulative properties of HCH isomers—especially the α-, β-, and γ-forms—which are associated with chronic poisoning and a potential increase in malignant tumor development [13, 14].

In the past, HCH was produced in several formulations including dust (12% concentration), phosphorous flour-based powders (25%), emulsions, aerosols, and smoke bombs. Although still manufactured in some agriculturally dependent nations, industrialized countries classify lindane and HCH as highly hazardous substances due to their detrimental effects on both environmental and human health [15, 16]. As a result, their use is either strictly controlled or entirely banned.

Impact on human health and oncogenic risk

Acute exposure to high concentrations of HCH can result in significant neurological disturbances, including headaches, vertigo, convulsions, and seizures. Dermatological effects such as burning, itching, dryness, and rashes are also common [17]. While HCH is not considered genotoxic, there is evidence that prenatal exposure to β-HCH and related by-products may alter thyroid hormone levels and potentially affect fetal neurodevelopment. Human exposure pathways include inhalation, dermal contact, ingestion, and mucosal absorption, with levels below 50 mg/m^3 currently not considered critically hazardous [18].

Animal studies have largely informed the toxicological assessment of lindane. In 2001, the U.S. Environmental Protection Agency (EPA) indicated "suggestive evidence of carcinogenicity, but insufficient to assess human carcinogenic potential" [19]. However, by 2015, the World Health Organization (WHO) formally classified HCH as a probable human carcinogen.

Several epidemiological studies have established links between HCH exposure and cancers such as leukemia, brain tumors, lymphoma, and cutaneous melanoma. Additionally, organs like the kidneys, mammary glands (in women), prostate (in men), and gastrointestinal tract have been identified as primary targets for oncogenic processes [20]. Agricultural workers in regions where lindane is still in use face elevated cancer risks. Further research suggests a possible connection between HCH exposure and central nervous system tumors such as gliomas and meningiomas, as well as hematologic malignancies like diffuse large B-cell lymphoma [21].

Moreover, maternal occupational exposure to pesticides during pregnancy has been associated with an increased incidence of pediatric cancers, including leukemia, Wilms tumor, and brain cancer [22].

Molecular mechanisms and prevention

The carcinogenic effects of HCH are believed to stem from its interaction with genetic material at the chromosomal level, resulting in damage to DNA and histone proteins [6]. Cellular studies have also identified structural disruption in critical organelles, including the endoplasmic reticulum, mitochondrial complexes, and nuclear receptors [23].

To mitigate the risks of cancer associated with γ-HCH, the precautionary principle—a central concept in environmental regulation—should guide pesticide policy. The WHO strongly recommends minimizing pesticide use, particularly substances like HCH with proven carcinogenicity. Eliminating such chemicals from agricultural practices is essential [24]. Additionally, enhancing public education in areas of food safety, nutritional hygiene, and disease prevention is a crucial strategy for reducing population-wide exposure risks [25–27].

Conclusion

There is now irrefutable evidence that pesticides contribute to cancer development, with the γ-isomer of hexachlorocyclohexane (γ-HCH) playing a specific role in carcinogenesis through damage at the chromosomal level. Despite widespread bans, residues of this compound—alongside other persistent organic pollutants such as polychlorinated biphenyls, dioxins, and furans—may still find their way into food products via packaging materials or processing additives. These contaminants pose a serious threat to human health by potentially initiating oncogenic processes.

To mitigate these risks, the precautionary principle must be prioritized in pesticide regulation, as emphasized by environmental protection frameworks. The World Health Organization has explicitly recommended limiting pesticide usage, particularly substances like γ-HCH that demonstrate established oncotoxicity. Therefore, it is imperative for the global agricultural sector to fully eliminate such hazardous compounds from all levels of food production.

Additionally, increasing public awareness and education in areas such as food safety, hygiene, and epidemiology is crucial for minimizing exposure to harmful substances.

Ultimately, the presence of toxic chemical residues in food represents a significant public health concern. Strong legislative oversight and effective enforcement of pesticide regulations are essential to prevent widespread human exposure and the associated health consequences, including cancer. A global, coordinated approach to monitoring and managing pesticide use is critical to ensuring food safety and protecting public health.

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