

Dioxins and Health Impacts

Dioksinler ve Sağlık Etkileri

Öz

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Dioksinler ilk defa 1976 yılındaki Seveso Kazası'ndan sonra gündeme gelmiştir. Genel bir terim olup, kalıcı organik kirleticilerden biridir. Karbon, klor ve oksijen atomlarının bulunduğu iki benzen halkasından meydana gelir. Toksik ve karsinojeniktir. En bilinen dioksin bileşiği 2,3,7,8-tetraklorodinezo-p-dioksin (TCDD) olup, en toksik olanıdır. Doğada uzun süre kalır ve suda erimez, fakat yağ dokusunda çözündüğü için insanda birikir. Yarı ömrü 7-8 yıl arasında değişir. İlgili kaynaklardan havaya karışan dioksin, yağmurlarla bitki ve toprağa yayılarak besin zinciri ile hayvanlar ve insanlar tarafından alınır. Bu yol en önemli yol olmasına karşın, solunum sistemi ile de alınır. İnsanda biyolojik ve toksik etki gösterir. Bu etkiler tiroid fonksiyonlarında, üreme ve endokrin sistemde gözlenir. Non-Hodgkin lenfoma, akciğer kanseri ve yumuşak doku sarkomu gibi karsinojenik etkiler de göstermektedir.

Korunmada, bu bileşiklerin yan ürünler şeklinde ortaya çıkmasının önlenmesi, ihraç ve ithalinin sınırlandırılması, ilgili sektörlerin düzenli olarak kontrolü ve toplumun farkındalığının artırılması önemlidir. Ülkemizde Stockholm Sözleşmesi'ne göre "Ulusal Uygulama Planı" oluşturulmuş ve Tarım, Gıda ve Hayvancılık Bakanlığı tarafından bir eylem planı geliştirilmiştir.

Anahtar Kelimeler: Dioksin, TCDD, besin zinciri, toksik, karsinojenik, korunma

Abstract

Dioxins have come to the agenda first in 1976 after the "Seveso Accident". It is a general term and they are one of the persistent organic pollutants, and made of two rings of benzene with carbon, chlorine and oxygen atoms. They are toxic and carcinogenic. The mostly known compound is 2,3,7,8-tetraklorodinezo-p-dioksin (TCDD), which is the most toxic compound among dioxins.

They stay in nature and do not dissolve in water, but they dissolve in adipose tissue, so they accumulate in humans. Their half-life changes between 7 and 8 years. The emitted dioxins from the regarding sources, are transmitted to the ground and plants by rain, and they are taken by animals and humans via food chain. Although this route is the most frequent one, they are also taken by respiratory system.

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They show biologic-toxic effects in humans. These effects are seen in thyroid functions, reproductive and endocrinologic systems, and carcinogenic effects such as sarcomas of soft tissue, lung cancer and non-hodgkin lymphoma can also be observed.

In prevention, the reduction of occurrence of these substances as by-products; limitation of exportation and importation; periodic control of related sectors and increasing the awareness of the related population are important. In Turkey, according to the Stockholm Convention; there is a "National Application Plan" and an inventory developed by the Ministry of Food, Agriculture and Livestock.

Keywords: Dioxin, TCDD, food chain, toxic, carcinogenic, prevention

Introduction

Environmental pollutants are examined under four groups; gaseous pollutants, persistent organic pollutants (POPs), heavy metals and particles (1-3). POPs include pesticides, industrial chemical compounds and side products (4-6). Resistant to photolytic, biological and chemical decay, semi-volatile, non-soluble in water and fat, POPs, which are included in the Stockholm Convention in which the persistent organic pollutants are defined (7), can accumulate in adipose tissue, are man-made, and persistent toxic materials that can stay in the atmosphere for a long time (1, 4-6, 8-18).

Definition

A form of POPs, dioxin and similar compounds can be found almost anywhere; posing a threat to human and animal health (18,19). Consisting of carbon, oxygen and hydrogen atoms (11,20,21), "Dioxin" is an aromatic organic compound with chlorine that is formed by two benzene rings combining with two atoms of oxygen (11,12,14,16,18,19,22). Figure 1.

Used as a general term for dioxin and similar compounds (18, 20-22), dioxin includes polychlorinated dibenzo-p-dioxin (PCDD), polychlorinated dibenzofuran (PCDF) and polychlorinated biphenyls (PCB) (12,17). They

are in solid-state at room temperature (23); PCDD and PCDF are colorless and crystallized when in liquid-state (12,18,22).

Their toxicity varies due to the location of the bonds of their chlorine groups on the molecule (7,8,12,14,17,18). Being hydrophobic and lipophilic, these compounds are difficult to be metabolized by the vertebrates (10); 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is the well known dioxin compound as well as the most toxic one (15,16). It is the standard one which is used on the related issues (7,11,12, 14-19,25).

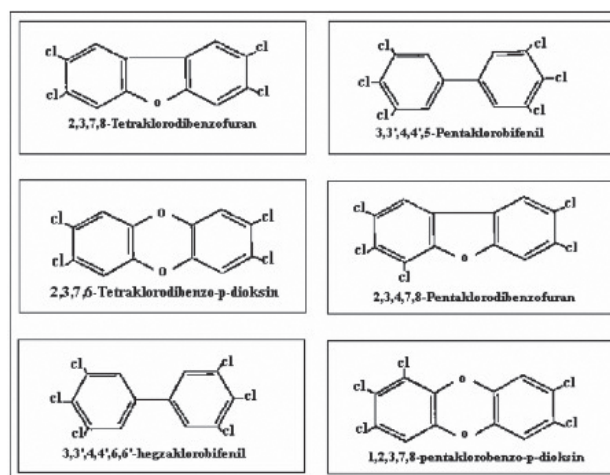


Figure 1.
Chemical structure of some dioxin compounds (22)

Sources of Dioxin

Dioxin is formed as a by-product of industrial activities; either as a chemical pollutant in chlorine or bromine based industrial productions or from the combustion of organic compounds that contain chlorine (16). These activities are; paper-mache bleaching, paper-mache industry, chlorine solutions and plastic matter that contain polyvinylchloride (PVC), paint removers, pesticides and herbicides, metal industry, refineries, cement kilns (16,25) and waste combustion (22). They are produced after the reactions of chlorine containing chemicals and organic compounds in an alkaline environment at 150-250°C (11,12,16,26).

Main dioxin sources are;

- Electricity production and heating
- Exhaust gases of vehicles
- Smoke vapor
- Natural events like forest fires and volcanic eruptions
- Fodder
- Production of chemicals (pesticide, herbicide, tire production, polyvinylchloride, cosmetics industry)
- Leather, textile and paper industries
- Semi-combust organic materials and wild combustion procedures (municipal waste, medical and hazardous waste, combustion of sewage sludge, burning of coal and industrial wood)
- Production of lime, asphalt and cement
- Production of glass and ceramics
- Production of cast iron, sinter and cooking coal
- Production of metals beside iron
- Storage and accumulation (storage of waste oils, sludge treatment)
- Pesticide production
- Timber production
- Vehicles
- Forest fires and volcanic eruptions (11,13,18,19,25).

Plastic cups, plates and bottles, foam materials, toilet paper which have been bleached with chlorine, paper tissue and diapers also contain dioxin which can pass through the food and beverages due to sun exposure (13).

Considering dioxin's entry to the food chain via drinking water, the World Health Organization (WHO) has declared the daily intake of dioxin negligible (9). Suckled children can be exposed to dioxin through breast milk (13). In a conducted study, it is observed that the levels of dioxin and similar compounds in the breast milk are in an inclination to increase and the tolerable intake amount for the babies who are being fed with breast milk are exceeded (27). Even though this limit was exceeded in the past years, WHO mentioned the benefits of breast milk despite the present pollutants in a report concerning the health hazards of dioxin in 1998. The decrease in the levels of dioxin in the breast milk in the past ten years has been documented (28).

Dioxin Cycle

Being resistant to natural ways of decomposing (3) and carried airborne (13,16,18), dioxins can be found in water, soil and plants in solid or gaseous state (12,16,17). Dioxin remains in the soil for a very long time since its half-life takes too long (25-100 years) (16). Dioxin cycle is shown in Figure 2. Dioxin mixes into the air, soil and water from the point of origin; and then passes to plants, humans and animals. It can be accumulated heavily especially in animal tissues and soil (11,13,17,18). Humans are exposed to these compounds via food, drinking water, soil, dust, smoke and inhalation (20).

Either in the gaseous form or combined to some particles, majority of the produced dioxin mixes into the air; staying airborne for a long time (16) and can be transferred great distances (13,16,18).

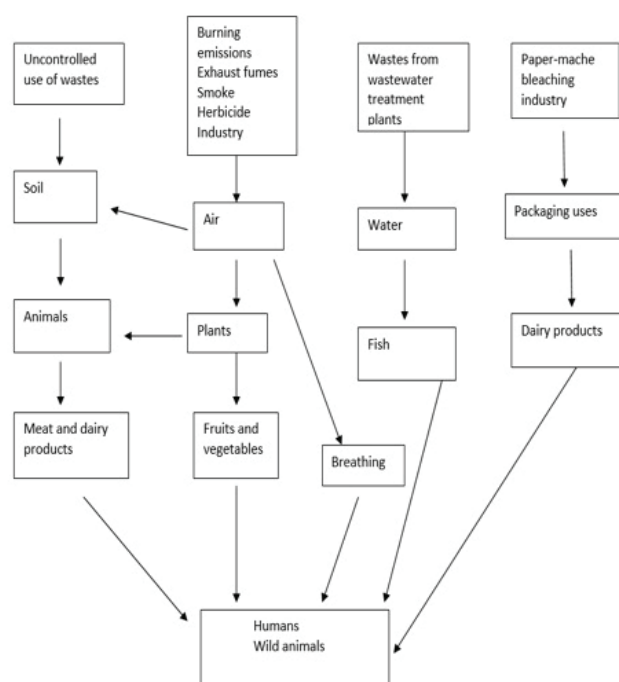


Figure 1.
Dioxin cycle (29,30)

Dioxin passes to water from the soil and other sources via rain, forming 1% of the soil pollution (13,16). It is taken into human metabolism through digestion, which makes up 90% of the dioxin taken through consumption of meat, eggs, whole milk and butter (10,12,16-18), through skin and inhalation (12,16,17) and accumulates in the fatty tissues (12,16-18,31,32). Half-life of dioxin in human metabolism is 7-8 years (12). Being lipophilic, the levels of absorption increase depending on the fat intake of the diet (11,12,17). Because the fish metabolize 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) slower, it accumulates faster in sea foods (8,13), and appears more in the farm fish compared to naturally grown fish (33). Chicken meat contains the most dioxin compared to other meats (18).

Plants are also contaminated by air, soil and water and they can't be cleansed by washing with water (13). As they are mostly taken by the consumption of meat, fish, milk and dairy products (8,13,34), phytonutrients contain relatively lesser amounts of dioxin. Because the adipose tissue of animals is more than plants, the amount of accumulated dioxin is high. Through consumption of contaminated plants, animals can also be affected (13,18).

Effects of Dioxin

1. Seveso Disaster

Dioxin attracted global attention because of "Seveso Disaster" (35). Safety valve of the

Industrie Chimiche Meda Societa Azionaria (ICMESA) factory, which belonged to Gevaudan Hoffman-La Roche group, got loose because of an unknown reason; causing a reaction which exceeded the safety limits and produced 320 hectares of white colored clouds (19,34) on the July 10th of 1976 at Seveso, a sub-urban city of northern Milano, Italy. It has been detected that the clouds contained trichlorophenol and 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) (19,35), affecting the vegetation, birds and animals severely. The ones who got exposed to the clouds exhibited nausea, headache and irritation on the eyes, and some children admitted to hospitals because of skin lesions. A program was started to

determine the levels of exposure and pollution; so, soil and land analysis which exposed to TCDD were conducted and mapping of the related regions were achieved between 1976 and 1986. Three regions; A, B and R were determined according to the findings. Region A was the most polluted of all, containing 15.5-580 microgram/m² of TCDD in the soil whereas the region B contained up to 5 microgram/m² at most and the region R contained less than 1.5 microgram/m². TCDD consisted of the 90% of the total amount of released dioxin (35).

a) Short and Mid-Term Effects

One of the short-term effects was chloracne. Mid-term effects consisted of peripheral neuropathy and an increase in liver enzymes in some cases. Children also exhibited immunological effects, causing an increase in the lymphocyte and complement levels. Women exhibited spontaneous abortions and congenital fetal anomalies (35).

b) Long-Term Effects

Mortality and cancer levels increased. Men exhibited cardiovascular disease and chronic obstructive lung disease; women exhibited chronic rheumatic heart disease and hypertension related deaths in the Region A. Diabetes related deaths, lymphohaemopoietic cancers such as cancer of gastrointestinal tract, and leukemia related deaths increased in Region B. Risk of soft tissue sarcoma and esophagus cancer in men increased (35).

2. Health Effects

Health related effects of dioxin came to the fore after Seveso Disaster (19,25). It caused a) toxic and biological; b) carcinogenic effects in humans (31,32). Toxic and biological effects are mainly seen in industrial environments or after intoxication accidents (32). Dioxins present their effects by attaching onto aryl hydrocarbon receptors (AhR) (10,12,20,32,36).

The first symptoms exhibited are conjunctivitis, nausea and headache (19) upon acute exposures. Chloracne is another symptom that is seen after

2-4 weeks of the exposure and can regress up to 6 months to 3 years. Chloracne can be recognized via its location, lack of inflammation, spread of the closed comedones and histological absence of sebaceous gland from common acne (37).

a) Toxic and biological effects are seen one; a) thyroid functions; b) reproductive system; c) endocrine system. (25);

a) Thyroid functions: While some studies could not find any links to thyroxin binding globulin (TBG) (38), others found a positive relation between TBG and TCDD concentration; the more the TCDD levels, the more the meaningful Thyroid Stimulating Hormone (TSH) levels increased (25). In a study conducted by Chevrier et al. on the 260 women who were affected by the Seveso Disaster revealed a negative correlation between the TCDD levels during the exposure and the T4 serum concentration levels after 20 years of the accident (39,40).

b) Reproductive system: While some studies showed decreased testosterone levels and increased gonadotropin levels, others revealed no significant correlation between the two. An increase in the rate of girl babies being borned is documented after the Seveso Disaster. An increase in the frequency of endometriosis is another one of the effects (25). Another study revealed that the exposure to PCB reduces the motility of sperm cells (41).

c) Endocrine system: Several studies showed that the TCDD exposure decreased the mean glucose concentration, diabetes frequency, oral usage of anti-diabetic agents and latent period of diabetes but others did not find any significant correlations. Death rate related to diabetes in women increased in Regions A and B in Seveso (25).

b) Carcinogenic effects: TCDD was recognized as Group 1 carcinogenic for humans by International Agency for Research on Cancer (IARC) in 1997 (9,21,25,32). In the atlas of chemical agents and related occupations published by the IARC in 2012, TCDD was clarified as carcinogenic that was related to soft tissue sarcoma, lung cancer and non Hodgkin's

lymphoma (42). The cohort studies conducted after the Seveso Disaster, an increase in the number of the cancer cases and cancer related deaths were observed (25,32,43). The dose-response relationship was evaluated in a meta-analysis study conducted in a three occupational cohort by Kenny S. Crump et al., and a statistically significant association was discovered between dioxin exposure and cancer mortality (44). The most commonly seen cancers are; lymphoma, multiple myeloma, soft tissue sarcoma, lung cancer, breast cancer, endometrial and testicular cancer (25).

Toxic Equivalent Factor (TEF) and Toxic Equivalency (TEQ)

WHO and other international institutions came up with the definition of "Toxic Equivalent Factor" because of these materials' fluctuant levels that present toxic effects to nature and living organisms. This value is based on; exposure duration, in vivo and in vitro biochemical reactions. TCDD's TEF value is taken as 1 and other compounds toxic effects are evaluated according to this number (as a standard). Toxic Equivalency value of every compound is determined by the multiplication of the TEF values of each compound (12).

Tolerable Daily Intake (TDI)

WHO set the tolerable daily intake of dioxin containing compounds to 1-4 pg/kg TEQ at a conference in Genova in 1998. This amount can increase up to 2-6 pg/kg TEQ in more developed countries but considering future negative effects it is decided on 1 pg/kg TEQ (9).

Stockholm Convention

On 22-23 May 2001 an international agreement; Stockholm Convention was signed within the context of United Nations Environmental Program by 125 countries one of whom was being Turkey in order to limit or eliminate POP absorption. This convention came into force on May 17 2004 (45) and promulgated on July 30 2009 (46).

The Convention (46,47) includes;

- Obligations on POPs production and usage, import and export of POPs, release and disposal of POPs
- Encouraging and sometimes forcing countries to use the best technical and environmental applications in order to reduce and/or reduce POPs that is generated through certain burning and chemical activities;
- Prevention of producing new POPs; having provisions regarding newly produced POPs (45).

Twelve defined POPs in the convention are separated into three groups (45). Table 1. In this context, the polychlorinated biphenyls (PCBs) included in the App-A are not to be used after 2025; not importing and exporting the equipment that contain PCB aside the way they are to be used in environmentally safe waste management purposes; not allowing liquids that contain biphenyls to be reused in the other equipment in order to reutilize them; serious effort should be made in an environmentally safe way of waste management. Reducing and elimination of the emissions of the involuntarily produced POPs included in the App-C is aimed (45).

According to the article 7 of the Stockholm Convention in order to fulfill their mandatory

requirements, every member country has to prepare and apply “National Application Plan”; cooperating with women’s organizations and children health related organizations in a global, regional or a sub-regional scale in order to ease its application plan, management and updating when required (46). The aim of the plan is holding every country who signed the convention responsible towards all the other countries that signed the convention in regards of making sure their applications of terms of the convention is up to date and also informing them on future endeavors. The plan includes related laws, determined standards and proper applications (47). In order to fulfill its obligations stated by the Stockholm Convention, Turkey started working on the improvements and formed Research and Study Group, Pollution Study Group, Emission Study Group, Investigative Study Group, Health Study Group and National Chemical Profile Studies Group in 2004 under the coordination of the special unit that is formed by the Ministry of Environment and Urban Planning (45).

National Legislation

Turkey’s dioxin inventory was published in 2006. Inventory was reevaluated by taking the new data and emission factors into account and was renewed in 2010 (45). According to the inventory that is

Table 1 Classification and Control Regards of POPs According to Stockholm Convention

App-A Items that should be removed	Aldrin, chlordane, dieldrin, endrin, hexachlorobenzene, mirex and toxaphene, Polichlorinated biphenyls (PCB)
App-B Items that should be restricted to use	DDT
App-C Items that are produced inadvertently	Dioxin and furans Hexachlorobenzene, Polycarbonated biphenyls

published in 2012, the biggest sources are production and disposal of iron and other metals. While the production of iron, steel and copper is the biggest source of production, the storage of the domestic and mixed waste is the biggest source of disposal; considering the changes through 2006 inventory to 2012 inventory, reducing the emission during the production of iron and other metals has the biggest impact on reducing the total emission. The 2014 report of the National Application Plan emphasized that the reduction of the emission in this sector happened due to the investments and improvements done in the air pollution control, especially the pollution control studies done in the POPs and sintering facilities (48). Dated 17.05.2008 and numbered 2008/26, "Rescript on the Pollutants' Maximum Limits on Foods" was published by the Ministry of Food, Agriculture and Livestock; providing the maximum limits of the certain pollutants on foods (49).

The regulations published by the Ministry of Environment and Forestry on polychlorinated biphenyls and terphenyls on December 27 2007 includes preparing the inventory of the materials and equipment containing used polychlorinated biphenyl and polychlorinated biphenyl; temporary storage, transporting, purification and disposal; restrictions and responsibilities on import and export; measures to take; inspections and legal and penal responsibilities (50). Another rescript published by the Ministry of Food, Agriculture and Livestock on July 29 2015 includes the criteria for sampling the food, preparing and analyzing the official control of the levels of dioxin and furans, dioxin-like compounds and non-dioxin based biphenyl on certain foods (51). "Seveso Directives" was created by the European Union after the disaster happened at the city of Seveso in order to prevent and take necessary precautions for the industrial accidents such as uncontrolled emissions, fires and explosions that can harm the health of the environment and humans. In this context, legislation about "Prevention of the Major Industrial Accidents and Reducing Their Impact" was published in 2013 according to the latest Seveso II Directives by our country's Ministry of Labor and Social Security and Ministry of Environment and Urban Planning and came into effect in the same year (52).

Prevention

Dioxin is mainly produced by combustion and incineration. Soil is contaminated by combustion and incineration processes and by industrial and reservoir sources (53). Eliminating or limiting the production of these hazardous compounds that pose a threat against human health and environment if eliminating is not possible; treating / decomposing before releasing them into the environment and preventing them to enter into the food chain should be aimed. Primarily, the correlation between chlorine and pre-agents should be understood well; the limiting factors of the chlorine, carbon and oxygen reactions in combustion and incineration procedures should be determined (53). Various facilities that decompose dioxin and furan compounds and pre-agents that enable the formation these compounds have been established in our country: some of them which are Hazardous Waste Combustion Facility of İzmit (İzmit Waste and Waste Treatment, Incineration and Evaluation Joint Stock Company: İzmit Atık ve Artıkları Arıtma, Yakma ve Değerlendirme A.Ş.-İZAYDAŞ) and Medical Waste Combustion Facility of İstanbul (İstanbul Environmental Protection and Waste Material Evaluation Industry and Trade Joint Stock Company: İstanbul Çevre Koruma ve Atık Maddeleri Değerlendirme Sanayi ve Ticaret A.Ş.-İSTAÇ) (11).

Conclusion

Being lipophilic and not eliminable in mammal tissues, dioxin and similar compounds cause toxic, biological and carcinogenic effects through accumulation. Thus, it has a major threat to public health (9,12,17,23). The main emission source for our country is heavy metal industry (45,48). By the measures taken and investments through the years, the emission sources are shifting (26). The main dioxin source of the combustion of medical waste is polyvinyl chloride (PVC). This is why there is a huge responsibility on the healthcare professionals over reducing the dioxin production; policies that reduce the use of PVC should be made and followed (53).

Reducing the amount of fat in diets and increasing the

intake of the fibrous foods can reduce the exposure of dioxin to humans through the food chain. Routine controls of the food and fodder can help reduce the contamination (53). National standards should be made for a less risky and more reliable food production and the most accurate analysis techniques should be applied (13).

Ultimately, in order to limit the hazardous effects on human health and environment, these compounds need to be produced less or their production should be eliminated and eliminated properly using the most advanced methods, thus preventing them to enter the food chain. Raising the awareness of the public on this topic, creating and applying legislations that support the reduction of the emission of these compounds, using the best and the most advanced technical methods in order to reduce or eliminate the involuntarily produced POPs such as mentioned in the Stockholm Convention (13,46), and encouraging the regulation of their source and formation must be mandatory. These results reflect the significance of regularly conducted inventory studies, maintenance by every country such as suggested in the Stockholm Convention (46).

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