Dioxins and their effect on human toxicity

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Abstract

Background: the interaction of human with dioxin and possible outcome from exposure to such compounds was reviewed. Red flag was raised to investigate these compound following media inquiries dealing with assassination of the Ukraine presidential candidate Victor Yushchenko using the most toxic dioxin, tetrachlorodibenzodioxin or TCDD.

Results: Human may be exposed to dioxins following environmental, occupational, or accidental pollutant that when enter the body they are either metabolized then eliminated with different capacity depending on individual's physiology, health, does been administrated, or can be stored in body fat. Detoxification of dioxins occurs by microsomes enzymes that alter their structure by adding oxygen to lipophilic chemicals in the liver.

Conclusions: Dioxins exert carcinogenic action in human, and other morbidities such as atherosclerosis, hypertension, and diabetes, and with extend exposure they can disrupt nervous, immune, reproductive, and endocrine system. From the other hand, exposure to high doses within short time cause liver function impairment and chloracne. Deformed fetuses in many births were attributed to dioxins poisoning. Ramifications on health were documented through scientific reports placing dioxins of high toxicity to human.

Key words: Dioxin, environmental pollution, industrial waste hazard, dioxin danger on human health.

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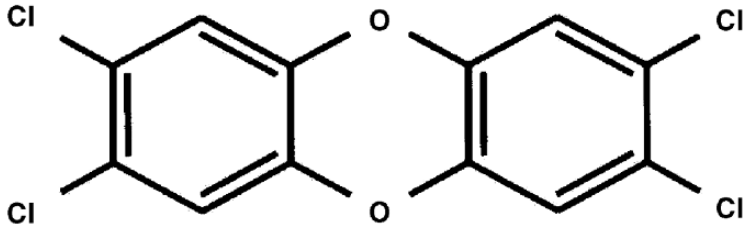
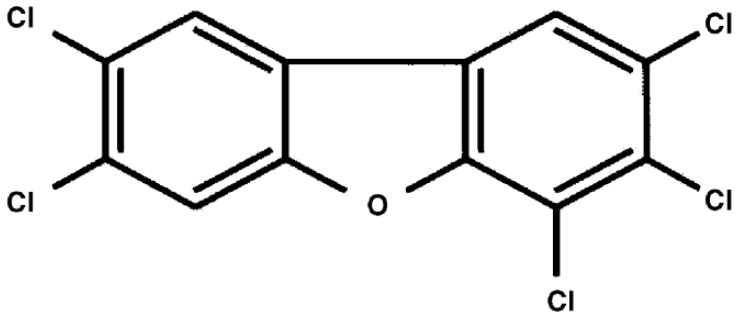
Definition of dioxins

Dioxins are distinctive group of dangerous organic chemicals known to be long lasting pollutants. They are characterized by their stable chemical structure and ability to dissolve in fat when entering human body and remain for more than seven years. While in the environment, dioxins tend to of bioaccumulation criteria extending through the food chain (1).

The scientific name of dioxins is 2,3,7,8. tetrachlorodibenzo-para-dioxin (TCDD) with chemical structure shown in figure (1).



2,3,7,8 – Tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD)



2,3,4,7,8-Pentachlorodibenzofuran (2,3,4,7,8-PCDF)

Figure (1): Chemical structure of a selected dioxin, dibenzofuran

The name dioxin can also be applied to the family of structurally and chemically related polychlorinatec dibenzoparacfioxins (PCDDs), and biphenyls (PBS). With 419 types of dioxin-related compounds have been identified, only about 30 of these are considered to have high toxicity (2).

Contamination by Dioxin

Dioxins are considered as secondary products resulting from industrial processes including smelting, bleaching of paper pulp and the manufacturing of some herbicides and pesticides and biproduct of natural processes, such as volcanic eruptions and forest fires when higher temperature processes produce chlorine containing organic substances coming from incinerators when incomplete combustion takes place (3, 4).

Dioxins are found throughout the environment including soil which contains the highest levels of these compounds, while air and water are with lowest levels. In food they can be detected in dairy products, meat, and fish. In efficient and storage for long time of industrial waste and oils may result in dioxin leakage into the surrounding areas resulting in the contamination of human and animal food supplies. In general, disposing dioxins is not an easy task in presence of the risk of contamination of the environment and human populations (5). However, safe incineration using temperatures over 850^{o} C can results in decomposition of large amounts of dioxin (6).

Incidences inflected dioxin contamination

There are documented incidences caused contamination by dioxin such as a cloud of toxic chemicals, and dioxins covered an area of 15 square kilometers with a population of 37,000 people in Seveso, Italy during 1976. During Vietnam War, Agent Orange used as chemical agent during the chemical warfare. In USA 1997, chickens, and eggs, were contaminated with dioxin when animal feed ingredients were found to be contaminated during manufacture process. Investigations eventually traced the contaminated clay to a bentonite mine were there was no evidence that hazardous waste was buried at the mine, but investigators speculate that the source of dioxins may be prehistoric. However, TCDD was a material for extensive studies regarding health effects linked to it as constitution in some batches of herbicides (7, 8, 9).

Effects, symptoms and vulnerable groups to dioxins

Short time exposure of human to high levels of dioxins may be result in skin lesions, and effect the liver function. Long time exposure is linked to disruption of the immune system, development of nervous system, endocrine system and reproductive functions. TCDD was evaluated by International Agency for Research on Cancer (IARC) in 1997 to be a factor leading to certain types of cancer (10). However, reports yield that the most effected of dioxin fall on fetus, and newly born individuals, while some population may retain high concentrations of dioxin due to their diet that depend on fish, or occupation especially those working in pulp and paper industry, in incineration plants and at hazardous waste sites (11).

Risk assessment of dioxin consumption

Risk assessment mainly depends on amount intake of dioxin by measuring the amount of consumption of contaminated food, levels of exposure, exposure duration, and population affected to assess the actual risk. Consumption of low-fat meat and milk products and cooking food may eventually decrease body tolerance of dioxin compounds. With such information available, policy decisions can be drafted to elaborate the health impact of dioxin. A Tolerable Daily Intake (TDI) can be used as a tool for long term safety assessment since it based on exposure over a lifetime and the accumulated number of dioxins in the body (12). Table (1) shows WHO dioxin equivalency factors that can be used to assess potential health risk of dioxin.

Table 1
World Health Organization (WHO) dioxin toxic equivalency factors (TEFs)

		WHO TEF
Dioxins	2,3,7,8-Tetra-CDD	1
	1,2,3,7,8-Penta-CDD	1
	1,2,3,4,7,8-Hexa-CDD	0.1
	1,2,3,6,7,8-Hexa-CDD	0.1
	1,2,3,7,8,9-Hexa-CDD	0.1
	1,2,3,4,6,7,8-Hepta-CDD	0.01
	OCDD	0.0001
Dibenzofurans	2,3,7,8-Tetra-CDF	0.1
	1,2,3,7,8-Penta-CDF	0.05
	2,3,4,7,8-Penta-CDF	0.5
	1,2,3,4,7,8-Hexa-CDF	0.1
	1,2,3,6,7,8-Hexa-CDF	0.1
	1,2,3,7,8,9-Hexa-CDF	0.1
	2,3,4,6,7,8-Hexa-CDF	0.1
	1,2,3,4,6,7,8-Hepta-CDF	0.01
	1,2,3,4,7,8,9-Hepta-CDF	0.01
	OCDF	0.0001

Protection of public health from dioxins

Recent reports estimated that food supply comprises 90% of human exposure to dioxins. Contamination of food monitoring and assurance of its safety is an important and continuous process from the start of production to its consumption that must be accommodated to ensure that pollution levels are not exceeded. Effective controls and practices during primary production, processing, distribution and sale are all essential to the production of safe food. Identification of dioxin type is a sophisticated procedure limited to certain types of laboratories. There are 100 laboratories are able to analyze dioxins in environmental samples, while only 20 laboratories are able to press reliable reports concerning measurement of dioxins in biological materials. Contingency plans should be accommodated by countries when suspicion of contamination incidents detected including detaining, confiscating and deposition of contaminated material (13, 14, 15, 16).

The total dioxin toxic (TEQ) value expresses the toxicity as if the mixture were pure TCDD have been adopted internationally as the most appropriate way to estimate the potential health risk of mixtures of dioxins (16, 17), especially after multiple reports of contamination in Times Beach, Missouri and in Seveso, Italy following an industrial explosion in 1976 (18,19), Binghamton State Office Building fire of 1981, and assassination attempt of President Viktor Yushchenko of Ukraine in 2004 (20).

Dioxin elevation can be found in blood or other lipid containing tissues such as adipose tissue or milk up to 35 years following exposure as reported in Russian and US (21, 22).

In human dioxins considered as risk factors in cancer (23), immune system deficiency, developmental abnormalities and reproduction problems, inability to have erections or ejaculations, central and peripheral nervous system pathology, headache, insomnia, personality changes, eyelid pathology including meibomian gland and hyperpigmented conjunctivae and may cause endocrine disruption leading to diabetes and thyroid disorders, and disruptive serum testosterone level, interfere with respiration system causing decreased pulmonary functions and bronchitis. Some clinical symptoms like gum pigmentation (24), nausea; vomiting; loss of appetite; skin rashes, including, rarely, chloracne or acne caused by chlorine-containing organic chemicals; hypertrichosis; liver damage; elevated serum cholesterol and triglycerides, pruritis, fatigue, irritability abdominal pain, diarrhea was also attributed to dioxin poisoning and after industrial exposures (25, 26).

Method of detection

All other chemicals used were of the analytical grade. Purchased PCDDs, PCDFs and Co-PCBs, as authentic standards, from Wellington Laboratories, Ontario, Canada. (13C12) - PCDDs, (13C12) - PCDFs and (13C12) - PCBs, as internal standards were used. The active carbon column was prepared as follows: the active carbon (Nacalai Tesque, Kyoto, Japan) was refluxed five times with toluene for 5 hr., and vacuum dried from which a weight of 500 mg of the active carbon was mixed with similar weight of anhydrous sodium sulfate (Wako Pure Chemicals Ind, Co. Ltd., Tokyo, Japan). A silver nitrate/silica gel (Wako Pure Chemicals Ind. Co. Ltd., Tokyo, Japan) was purchased. An n-hexane treated distilled water used in this experiment (27).

Preparation and processing of Samples

An exact volume of 5 ml of blood was mixed with 4 g Isolute (International Sorbent Technology Ltd., Hengoed, Mid Glamorgen, UK). After the mixed sample was loaded into the extraction cell (an accelerated solvent extractor ASE-200, Dionex, Sunnyvale, CA), and the (13C12) PCDDs, (13C12) -PCDFs and (13C12) -PCBs, were used as internal standards, were added. Extracted from the blood samples by. The following program was used for extractions procedure: first a pressure of 2000 psi with temperature of 150°C were applied for 10 minutes, followed by a flushing volume of 50 ml, followed by 90 seconds of purging, 60% flushing volume for two cycles, and acetone: n-hexane (1: 4, v/v) was used as the extraction solvent. The extract was treated with anhydrous sodium sulfate (10 g) to near dryness, and gravimetrical method was used to determine the lipid contents. After the lipid was

dissolved in n-hexane it was treated with concentrated sulfuric acid and the separated hexane layer was applied to a silver nitrate/ silica gel column (0.5 g) and eluted with 15 ml of hexane. The eluted solution was loaded to an active carbon column (0.5 g) after being evaporated to 1 ml and separated into two fractions. The first fraction containing mono-ortho-choline substituted biphenyls (mono-ortho-PCBs) was eluted with 10 ml of dichloromethane/n-hexane (1: 9, v/v). PCDDs, PCDFs and non-ortho PCBs were eluted with 25 ml of toluene as the second fraction. The eluate was evaporated to near dryness and transferred to an injection vial, and the syringe standard was added. The column packing (silver nitrate silica gel, active carbon column and anhydrous sodium sulfate) used in this experiment was washed by ASE-200 under the same conditions as the lipid extraction with n-hexane or toluene (28).

Results and Discussion

Low concentrations of PCDDs, PCDFs, and Co-PCBs were found in a 5 ml blood sample, meaning a highly sensitive technique is needed for this purpose. The response of the analytical system can be increased by increasing the volume of the final extract into the GC/MS. A highly efficient technique to analyze PCDDs, PCDFs and Co-PCBs in human blood is the injection system namely Solvent Cut Large-Volume (SCLV). This method comprises two-stages, first a chromatography system including the injection of large volume samples in the GC/MS and second the analytic compound by the precolumn to remove the various interfering substances in the sample (29) and been concentrated at the head of the column by a cold trap. After which, temperature is elevated following certain program and the analytic compounds are separated and determined as extremely narrow peaks (30).

By using HRGC/HRMS with a SCLV injection system, the sensitivity can be increased to 10 times the level of the classical method (Figure 2).

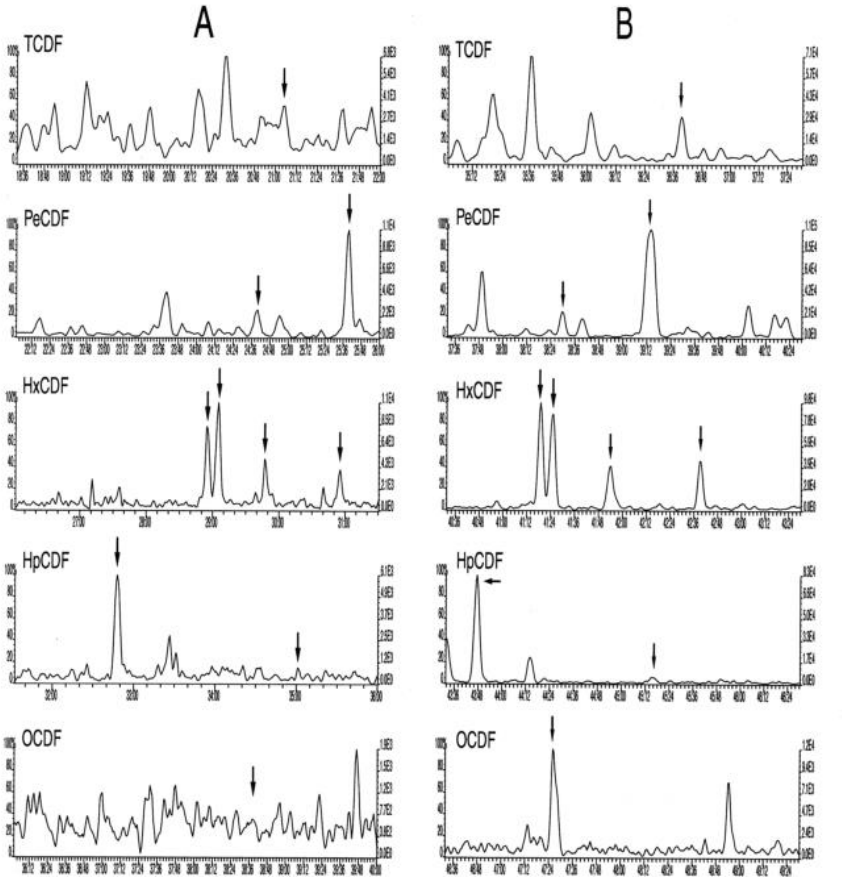


Figure (2): High-resolution GC/ MS chromatograms of PCDFs in the blood

Conclusion

Accidents related to dioxin exposure during the last century showed the potent toxicity of these compounds. Recent reports from WHO showed a reduction in environmental concentrations of dioxin and a decrease of exposure in general population's to PCDDs and PCDFs since incineration processes were upgraded to be safe and complete (27). However, in many countries dioxin monitoring have not been introduced into routine practice because of the high cost of the detection technology. With conclusive evidence that threat assessment of populations exposure to high dioxin levels in through daily life or occupation were relevant for establishing TDI as reference values for dioxins levels. Recently, research been conducted to study dioxin toxicity on genome and their role in altering gene expression, which provides answers about genetic variation and individual differences in response and tolerance to dioxin and other toxins.

A substantial number of health ramifications have been reported through research literature that all agree to classify dioxins to be highly toxic chemicals to man, and helped to understand and develop effective methods to deal with hazardous substances and the need to minimize their release in the environment at all times to protect human health.

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الديوكسينات واثرها السمي على الانسان

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الخلاصة

الهدف من البحث: تتناول مقالة المراجعة تأثر الإنسان مع الديوكسين والنتيجة المحتملة من التعرض لمثل هذه المركبات. للتحقيق في هذا المركب بعد استفسارات وسائل الإعلام حول اغتيال المرشح الرئاسي الأوكراني فيكتور يوشينكو باستخدام الديوكسين الأكثر سمية ، رباعي كلورو ثنائي بنزوديوكسين أو.TCDD

النتائج: قد يتعرض الإنسان للديوكسينات بعد الملوثات البيئية أو المهنية أو العرضية التي عند دخولها الجسم إما يتم استقلابه ثم التخلص منها بطرق مختلفة اعتمادًا على فسيولوجيا الفرد أو صحته أو يتم تناوله أو يمكن تخزينه في دهون الجسم. تحدث إزالة السموم من الديوكسينات عن طريق إنزيمات الميكروسومات التي تغير تركيبها عن طريق إضافة الأكسجين إلى المواد الكيميائية المحبة للدهون في الكبد.

المناقشة: تمارس الديوكسينات نشاطًا مسرطنًا في الإنسان وأمراض أخرى مثل تصلب الشرايين وارتفاع ضغط الدم والسكري ، ومع التعرض الطويل يمكن أن تعطل الجهاز العصبي والمناعة والتناسلية والغدد الصماء. من ناحية أخرى، فإن التعرض لجرعات عالية في غضون وقت قصير يسبب ضعف وظائف الكبد وحب الشباب الكلور. تُعزى الأجنة المشوهة في كثير من الولادات إلى التسمم بالديوكسينات. تم توثيق تداعيات ذلك على الصحة من خلال التقارير العلمية التي تعرض الديوكسينات عالية السمية للإنسان.

الكلمات المفتاحية: الديوكسين، التلوث البيئي، اخطار الفضلات الصناعية، خطر الديوكسينات على الانسان، ماهية الديوكسينات.