Structural, clinical and transmission aspects of dioxins – Potential environmental pollutants

C. Ganesh Kumar and K. Jayaraj Rao

Dioxins are toxic and potent carcinogenic compounds formed as contaminants in milk and foods. Their occurrence, structure, prevalence in different food products, transmission to man and detection methods are discussed briefly. The dioxins and related compounds are found as trace contaminants in the synthesis of several commercial products, importantly chlorophenols. Dioxins have also been reported to be present in cigarettes, smoke and ash. The air-borne dioxins are transmitted to man either by direct inhalation or via forage, livestock, milk and meat. Mothers who have dioxins in the body could transfer them to the infants through breast milk, which may lead to late haemorrhagic disease in the newborn infants. It is important that there should be a check on the emission of 2,3,7,8-tetrachlorodibenzo-p-dioxins by industries, and pollution laws should take cognizance of these toxic compounds. This aspect is more relevant to India in view of the rapid industrialization taking place today.

IN the recent past, the environmental issues have become a matter of increasing concern in most of the countries. With ever-increasing human activity and industrialization, the number of pollutants to be dealt with are also increasing. Of these pollutants, dioxins – a family of compounds like polychlorinated dibenzo-*p*-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) – are known to be potent carcinogenic compounds and pose health risk to man. Of several dioxins and their congeners, 12 are of utmost importance because of their high toxicity.

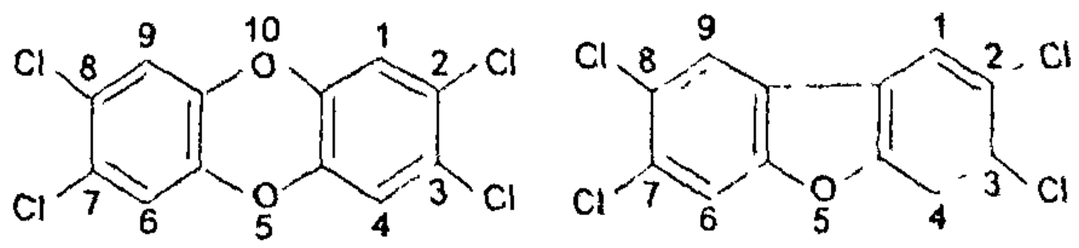
Dioxins are not synthesized commercially, but are formed as trace contaminants during the synthesis of several commercial products, mainly chlorophenols. For example, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) is formed as a contaminant in the synthesis of 2,4,5-trichlorophenol, which is used in the manufacture of 2,4,5-trichlorophenoxy acetic acid (2,4,5-T), a broad spectrum herbicide and defoliant. Several other chlorophenols have wide usage as mold inhibitors, fungicides, insecticides and disinfectants. Of these, the most important one is pentachlorophenol, used as a fungicide for slime control during the manufacture of paper pulp, tanning of leather, etc.

Structure

The typical structure of a dioxin is shown in Figure 1. The dioxins have 75 possible chlorine-substituted bidenzo-*p*-dioxin isomers and 135 possible chlorine-substituted dibenzofuran congeners. The various isomers of dioxins formed due to the number and the position of the chlorine atoms are associated with the degree of toxicity. However, not all isomers are toxic.

Sources of dioxins

The major sources of these compounds are the impurities in chlorinated chemical wastes and the contaminants in ash and gas. Most of the sources are anthropogenic. Some PCDD and PCDF emissions arise from various combustion processes, including the incineration of municipal solid wastes (MSW) or hazardous wastes[1,2], power-producing stations using fossil fuels, and smaller systems such as private heating systems, fireplace and automobiles. Other industrial processes involved include the pulp and paper industry, steel mills, metal refining and the smelting industry. Releases are also reported to occur during hazardous waste accidents, illegal dumping, waste oil releases, and the emission of residues of treated wood, fly ash, and the production and application of pesticides[3]. There are genuine concerns that these emissions could also contaminate animal feeds and human foods such as milk, meat and vegetables[1,4]. The presence of these substances in the chlorine-bleached paper cartons used for milk packaging has also been reported[5,6]. The PCDDs and PCDFs could migrate from



2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) 2,3,7,8-tetrachloro-dibenzofuran (TCDF)

Figure 1. Structure of a dioxin and its congener

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the bleached-paper cartons into the milk during storage. Among several factors which influenced the extent of this migration were the contamination level of the carton and the time of storage[7]. Reports reveal the presence of dioxins even in other food products like chicken and pork[8], fish and shell fish[9].

Permissible and prevalent levels of dioxins

In general, the dioxin content is represented by TCDD toxic equivalents used for assessing and comparing the dioxin and furan contents found in analyses. The proposed tolerable weekly intake of dioxins should not exceed 35 pg TCDD toxic equivalents per kg body weight, as recommended by Environmental Protection Agency (EPA) of the United States[10].

The dioxins have been detected frequently in milk, blood and adipose tissue and the concentrations varied in different tissues corresponding to the fat content. Cow milk is reported to contain 1.5 pg of dioxin/g fat[10]. Dioxins may find their way into the milk through cattle feed, however, some migration was also shown from milk cartons to the extent of 40 pg and 750 pg of TCCD and TCDF per kg fat, respectively. According to the estimates, the daily intake of TCDD toxic equivalents from three glasses of such contaminated milk exceeded the acceptable daily dose[11]. Comparatively, higher dioxin contents are reported in animal products. Over 60% of fat samples of chicken and pork in the study[8] contained more than 10 ng/g of pentachlorophenol (PCP). Of the poultry liver samples, 27% contained more than 50 ng of PCP per gram of liver. Moreover, PCP is known to contain a variety of chlorinated dibenzo-*p*-dioxins and chlorinated dibenzofurans[12].

There are alarming reports on the presence of chlorinated dioxins and dibenzofurans in human milk from several countries. Human milk may contain 10–50 times of these contaminants than cow milk or milk substitutes[13]. Analysis of human milk samples from South Africa, Pakistan, USA, Vietnam and England revealed dioxin toxicity levels as ranging from 8 to 23 ng/kg[14]. But, according to the analytical study conducted by the Federal Health Office (FHO), Berlin, the average daily intake of PCDD/PCDF by a baby was found to be 90 pg/kg body weight toxicity equivalents on a fat basis[15], which exceeds the permissible limits.

Transmission of dioxins to man

The potential source of human exposure to dioxins are phenoxy herbicides and airborne emissions resulting from combustion and waste disposal. The dioxins make an entry into human body through inhalation of contaminated air, but the main sources responsible for entry into human body are the milk and other food products. The dioxins are deposited on the forage/feed and soil.

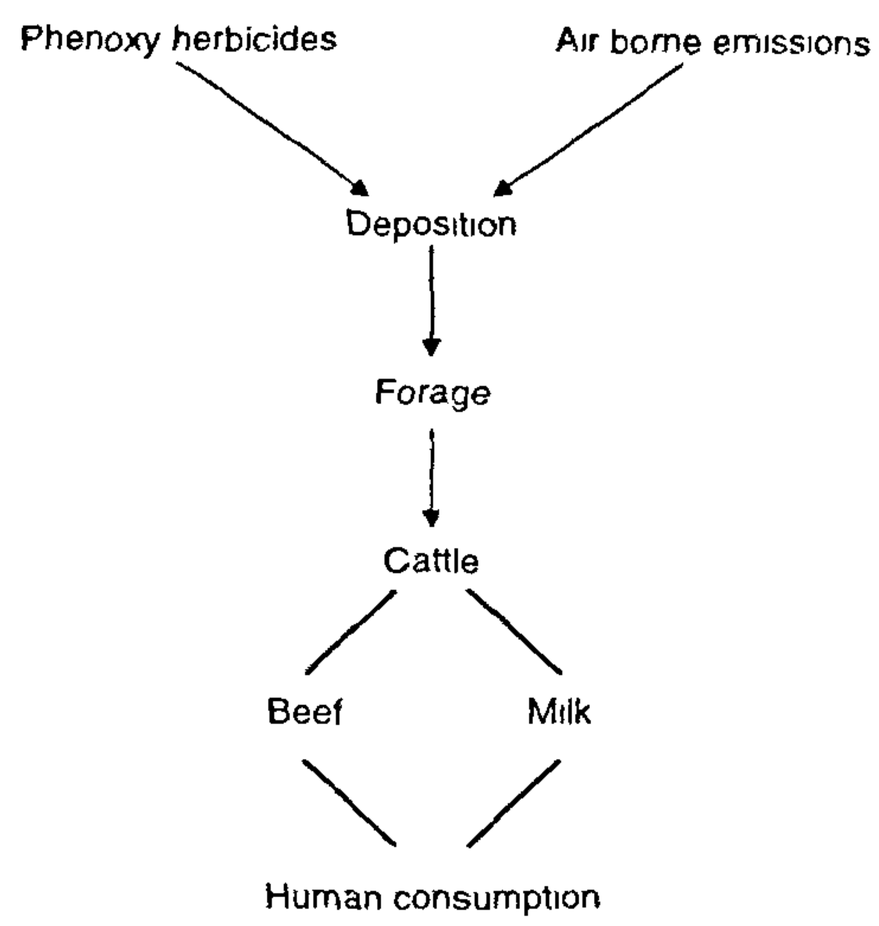

Figure 2. Flowchart for the transmission of dioxins to man

They enter the body system of cattle when the latter ingest the contaminated feed[4, 17] or soil during grazing[16] (Figure 2). Of the total dioxins taken in by a cow, approximately 20% of the TCDD toxic equivalents are reported to be excreted in the milk[17].

Human population might be prone to dioxins where eating of smoked foods like sausages, fish and cheese is prevalent. It is important in this context to mention some of the smoked Indian dairy products like *Bandal* cheese and *Chhurpi*. *Chhurpi* is severely smoked and dried before selling in the market. This product is regularly consumed by tribal people and no studies as yet have been conducted to check possible dioxin transmission to these people. Another important source of dioxins may be the *khoa*, which is inadvertently smoked while being made over firewood in villages. This practice, however, is now discouraged and instead steam pans are used by the organized sector. Bluthgen and Heeschen[18] showed that 50% of average daily dioxin intake could be via milk products.

Studies relating to transmission of dioxins and their congeners have drawn much attention, especially with regard to transfer of these compounds from mother to child. The main factors influencing the transfer are the mother's dietary habits and personal habits such as cigarette smoking. The presence of dioxins in cigarette smoke has already been proved[19]. It could be said that in this modern society, more so in the western society, smoking even by pregnant women has become a fashion, which may lead to the passage of dioxins from the mother to child. Effects of passive smoking have also to be considered. Mothers who have dioxin content could transfer them to the infants through breast milk which may lead to late haemorrhagic disease in the newborn child[20]. In spite of these, encouragement of breast feed-

ing is recommended as its positive effects are considered more important than the risk of dioxins[21].

Clinical manifestations of dioxins

The dioxin 2,3,7,8-TCCD on long-term effect in small doses is carcinogenic, produces adverse reproductive effects and alters the body's immune response. Human beings exposed to large amounts of dioxins show many different symptoms like psychological disturbances, various sorts of physical disturbances, and neurological effects. The toxic syndromes produced by TCDD and related compounds[22] are:

1. Wasting syndrome.
2. Lymphoid ovulation – TCCD & congeners produce a loss of lymphoid tissue, especially in the thymus, but also in the spleen and lymph nodes.
3. Hepatotoxicity – TCCD and related compounds produce hepatotoxicity in all species even at low doses well below the lethal dose.
4. Gastric lesions.
5. Urinary tract hyperplasia. In the guinea pig, monkey and cow the transitional epithelial lining of the urinary tract (renal pelvis, ureter and urinary bladder) proliferates to 2–3 times its normal thickness.
6. Chloracne, a rare and potential debilitating disease, but important acneiform eruption is often associated with the ingestion of chlorinated phenolic agents such as dioxins.

Italian researchers have shown TCDD to produce chick oedema disease in fowls. Postmortem examination of the intoxicated fowls showed subcutaneous oedema, hyperpericardium, ascites, enlarged liver, oedema of myocardium, lungs and skeletal muscle, atropy of lymphoid tissue of the spleen and atropy of ovaries/testes[23,24].

Detection and quantification

Detection procedures vary from laboratory to laboratory and also with the type of sample to be analysed. The most commonly employed are chromatographic, spectrometric or immunological methods.

The dioxins and related compounds are soluble in organic solvents and hence are extracted from a product using acetone–hexane mixtures or hexane alone. These are then purified and chromatographed before determination by a combination of gas chromatography and mass spectrometry (GC–MS)[25]. Other techniques like capillary column high-resolution gas chromatography/high-resolution mass spectrometry (HRGC/HRMS), packed column gas low-resolution gas chromatography/high-resolution mass spectrometry (LRGC/HRMS) and radioimmunoassay have also been employed[26,27]. The detection limits varied from 0.005 to 6 pg/g of the sample analysed.

Conclusions

Reports till date on dioxins and related compounds establish that these compounds could be a potential health risk in the long run if adequate precautionary measures are not taken. This is significant at a time when all the countries in the world are planning for a concerted action to check environmental pollution. Incidence of dioxins is high in industrialized countries and extensive work is being carried out in countries like USA, Germany, Sweden, Japan, etc. In the Asian context, India is the highest producer of livestock, and thus the dependence of humans on livestock and its products is high. These livestock are dependent on the soil and plant systems, which are being highly influenced by the 'modern agricultural systems'.

India is entering a fast growth phase of industrialization. The emissions from the chemical industries will result in the emission of PCBs, PCDDs and PCDFs in the surrounding environment, which will have an impact on the soil–plant systems of that area. It is desirable to assess the TCDD values in soil and crops around the sources of emission. Several studies have been attempted to determine the formation mechanism of PCDD/PCDF, but there still exist many areas where the information is incomplete.

Sufficient data are lacking in India to compare the levels of dioxin emission and consumption with the standards already established in developed countries. The standards and check levels of the industries around the farms should be introduced and implemented to the maximum level.

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The birth of the semiconductor superlattice*

L. Esaki

IN 1969, research on artificially structured materials was initiated with a proposal for an engineered semiconductor superlattice with a one-dimensional periodic potential by Esaki and Tsu[1,2]. In anticipation of advancement in controlled epitaxy of ultrathin layers, two types of superlattices were envisioned: doping and compositional, as shown at the top and bottom of Figure 1, respectively.

Before arriving at the superlattice concept, we were examining the feasibility of structural formation of potential barriers and wells that were thin enough to exhibit resonant tunneling[3]. A resonant tunnel diode[4,5] appeared to have more spectacular characteristics than the Esaki tunnel diode[6], the first quantum electron device consisting of only a single tunnel barrier. It was thought that advanced technologies with semiconductors might be ready for demonstration of de Broglie electron waves. Resonant tunnelling can be compared to the transmission of an electromagnetic wave through a Fabry–Perot resonator. The equivalent of a Fabry–Perot resonant cavity is formed by the semiconductor potential well sandwiched between the two potential barriers.

The idea of the superlattice occurred to us as a natural extension of double-, triple- and multiple-barrier structures: the superlattice consists of a series of potential wells coupled by resonant tunnelling. An important parameter for the observation of quantum effects in the structure is the phase-coherent, length which approximates to the electron mean free path. This depends on bulk as well as the interface quality of crystals, and also on the temperatures and values of the effective mass. As schematically illustrated in Figure 2, if characteristic dimensions such as superlattice periods or well widths are reduced to less than the phase-coherent length, the entire electron system will enter a mesoscopic quantum regime of low dimensionality, being in a scale between the macroscopic and the microscopic. Our proposal was indeed to explore quantum effects in the mesoscopic regime.

The introduction of the one-dimensional superlattice potential perturbs the band structure of the host materials, yielding a series of narrow subbands and forbidden gaps which arise from the subdivision of the Brillouin

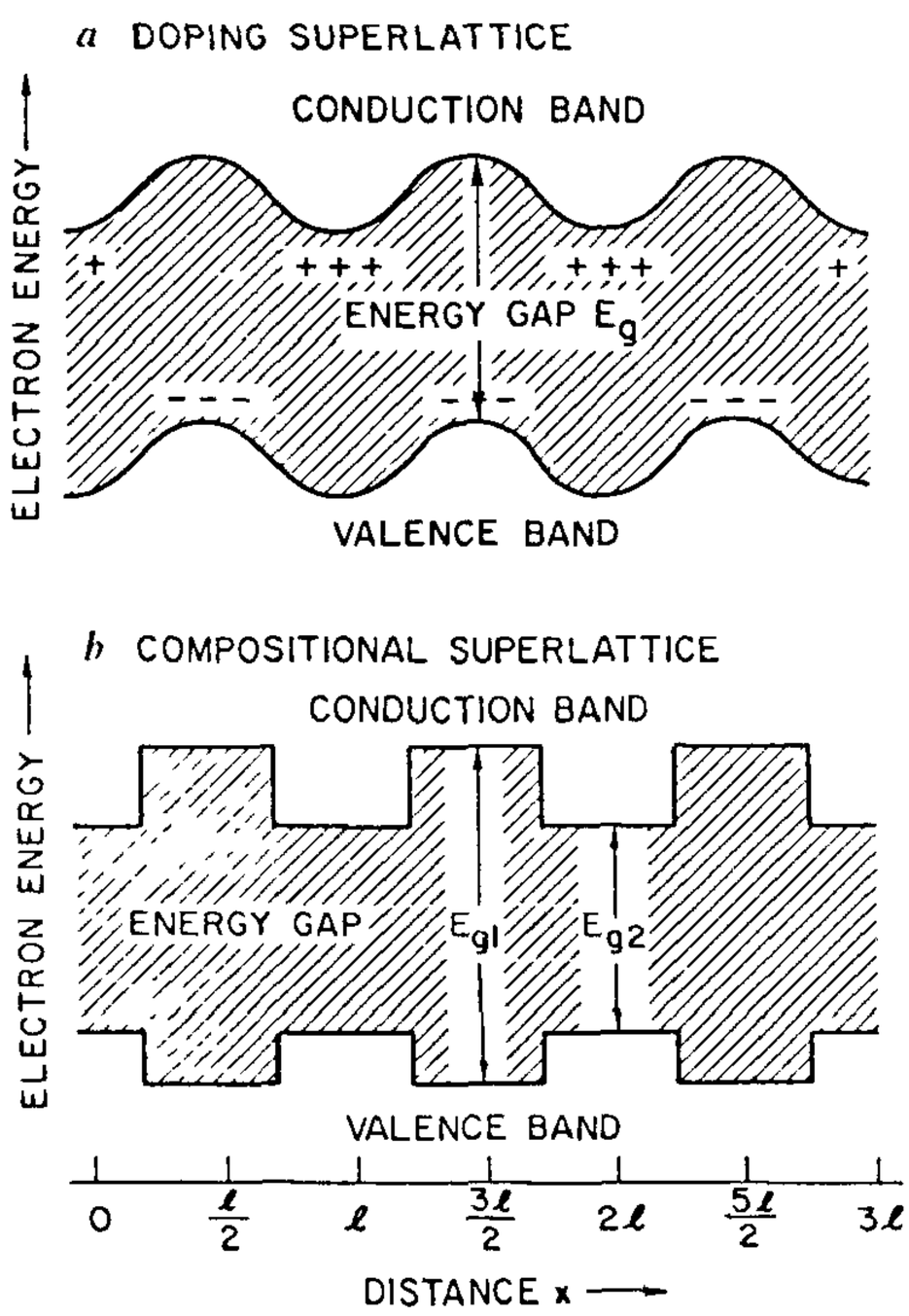

Figure 1. Spatial variation of the conduction and valence band edges in two types of superlattices: *a* doping, *b* compositional

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