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REVIEW

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Contamination of trichlorobenzene isomers in food: toxicity, analytical methods, occurrence in food, and risk assessments

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Abstract
Trichlorobenzenes (TCBs), comprising the isomers 1,2,3-, 1,2,4-, and 1,3,5-TCB, disrupt metabolic processes by inducing liver enzymes involved in xenobiotic metabolism, suggesting a broad toxicological impact. Specifically, exposure to TCBs is associated with significant organ-specific toxicities, such as increased liver and kidney weights in rodents and cytotoxic effects in mammalian cells, which include DNA damage without metabolic activation. Used extensively in industrial and agricultural sectors, TCBs are prevalent pollutants in various ecosystems, including air, food, surface water, groundwater, sediment, soil, and sewage. This is a concern because of their tendency to accumulate in lipid-containing tissues of animals and humans and potentially serious risks to human health and ecosystems. Information showing the presence of TCBs in food, drinking water, and even human breast milk underscores the need for ongoing assessment of the extent of these contaminants in food to measure the potential exposure to these chemicals. TCBs are extracted from various food sample matrices, and then instrumental analysis is performed, typically gas chromatography (GC) coupled with a variety of detectors. This review discusses the occurrence and risk assessment of TCBs in foods, as well as the toxicology and analytical methods related to TCBs.

Keywords Analytical method, Food, Occurrence, Risk assessment, Toxicity, Trichlorobenzene

Introduction

Trichlorobenzenes (TCBs) exist in three isomeric forms: 1,2,3-, 1,2,4-, and 1,3,5-TCB [1]. TCBs belong to a large family of chlorobenzenes (CBs), which are classified according to the number of chlorine atoms bound to the benzene ring into monochlorobenzene (MCB), dichlorobenzene (DCB), TCB, tetrachlorobenzene (TeCB), pentachlorobenzene (PeCB), and hexachlorobenzene (HCB), as summarized in Fig. 1. CBs with less chlorination typically exhibit lower hydrophobicity and are thus more mobile.

CBs undergo priority testing in accordance with the U.S. Toxic Substances Control Act. These chemicals are listed as a priority hazard for regulation by the European Economic Community, especially regarding discharge into the aquatic environment [2, 3]. The U.S. Environmental Protection Agency has classified many of the 12 CBs as hazardous waste and priority toxic pollutants [4]. TCBs are widely used in industrial and agricultural production, including as a solvent, pesticide, dielectric fluid, and deodorant [5–8]. They can also be generated as a byproduct during the microbial reduction process of more highly substituted benzene derivatives [9]. TCBs

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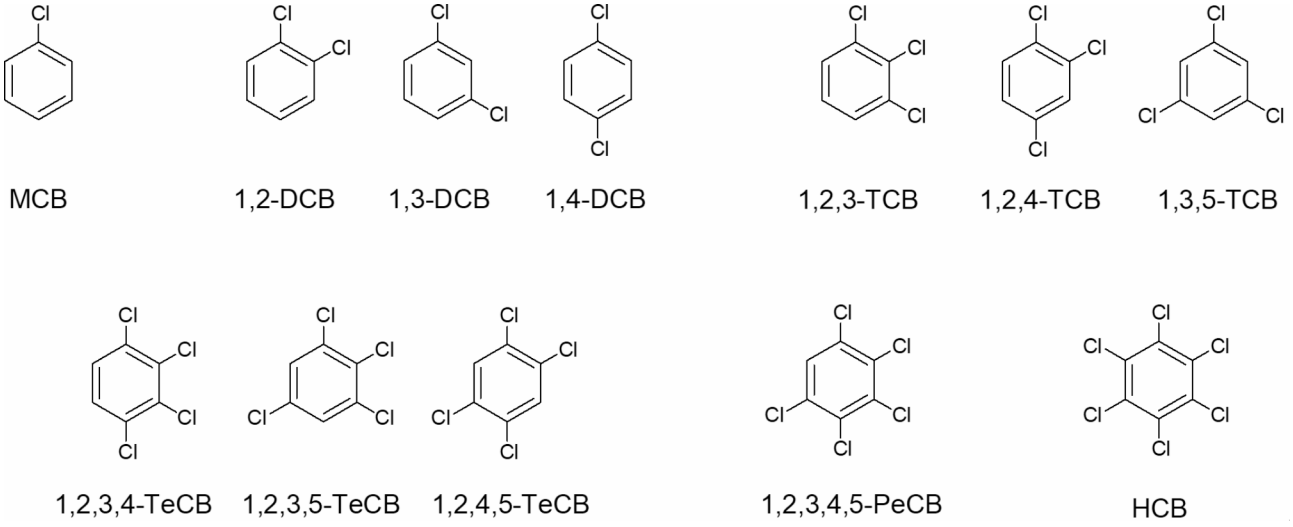

Fig. 1 Types and structures of 12 CBs according to the number of chlorine functional groups

are commonly found not only in atmospheric emissions but also in both solid and liquid industrial waste streams. Over several decades of extensive usage, they have become a widespread contaminant in ecosystems such as surface water, groundwater, sediment, soil, and sewage [7]. Approximately 93% of TCBs are released from industrial emissions into the environment and primarily evaporate into the atmosphere, while approximately 2.6% and 2.4% of TCBs persist in soil and aquatic sediments, respectively, and the remaining small fraction disperses into various water bodies [10]. TCBs exhibit chemical stability in both aerobic and anaerobic environments and tend to accumulate in both soil and groundwater [5, 6]. Classified as a persistent, bioaccumulative, and toxic chemical, TCBs persist in the environment and tend to accumulate in living organisms due to their high toxicity levels, thus being considered a priority substance [6, 11]. These characteristics pose significant risks to both human health and ecosystems [6, 12, 13] and affect food safety [14].

Gas chromatography (GC) is the most widely used method for TCBs analysis in a variety of matrices and is typically coupled with mass spectrometry (MS) [15–17] and various sensors, such as a flame ionization detector (FID) [2] and an electron capture detector (ECD) [2, 3, 13, 15, 18–22]. All methods involve extraction from the matrix prior to analysis, and common extraction methods include liquid extraction [2, 3, 15, 16, 18, 19, 21, 22], liquid–liquid extraction (LLE) [21, 23], solid-phase extraction (SPE), and solid-phase microextraction (SPME) [13].

Studies highlight TCB's ability to disrupt metabolic processes by inducing liver enzymes involved in xenobiotic metabolism, suggesting a broader toxicological impact. Exposure to TCBs is associated with significant organ-specific toxicities, including liver and kidney weight increases in rodents, and cytotoxic effects in mammalian cells, which demonstrate DNA damage without metabolic activation [24–29]. Exposure to these harmful substances can pose specific health hazards as well. Therefore, the purpose of this review is to provide comprehensive information on TCB isomers, with a particular focus on toxicity, analytical methods, occurrence in foods, and risk assessment. This review integrates the findings of existing literature from various disciplines on TCBs.

Toxicity

Table 1 offers a detailed summary of the negative effects linked to TCB. This table categorizes and lists the specific adverse health outcomes observed in studies involving these chemicals, providing a comprehensive resource for understanding the potential risks associated with exposure to different TCB derivatives.

Mutagenicity

In an investigation using the *Salmonella*/microsome assay, the mutagenic and liver enzyme-inducing abilities of a PCB mixture (Aroclor 1254), two industrial insecticides (mirex and Kepone), and a pesticide degradation product (1,2,4-TCB) were tested. None of these substances caused genetic mutations in *Salmonella* strains TA1535, TA1537, TA98, or TA100 under both activated and non-activated conditions. However, liver microsomal extracts from rats treated with 1,2,4-TCB exhibited a different capacity to promote mutagenesis of 2-aminoanthracene compared to extracts from control or Aroclor 1254-treated rats. 1,2,4-TCB was administered via intraperitoneal injection at dosages of either 50 mg/kg/day or 200 mg/kg/day for 2 or 4 days. At these dosages,

Table 1 Toxic effects categories

Sample used	Dose/Concentration and Method	Toxic effects categories	References
Liver Enzyme	Liver enzyme stimulation	Hepatotoxicity	[24]
	Liver enzyme stimulation		[25]
Rats	1-1000 ppm (diet, 13 weeks), NOAEL at 100 ppm	Hepatotoxicity, Endocrine toxicity	[26]
Liver Enzyme	Liver enzyme stimulation	Hepatotoxicity	[27]
	Liver enzyme stimulation		[28]
Mammalian Cells (V79 Cells)	DNA damage, no metabolic activation	Cytotoxicity, Genotoxicity	[29]
Rats	Salmonella strains with/without activation	Genotoxicity	[30]
	Negative results with/without activation		[31]
Rabbits	97 mg/kg, topical for 13 weeks	Dermatotoxicity, Hepatotoxicity	[32]
	Up to 450 mg/kg, topical for 4 weeks		[33]
Diatom Species	0.3 ppm, 10-day exposure during specific light cycle phases	Ecotoxicity	[34]
Daphnia Magna	2.1 mg/L (LC50), 0.69 mg/L (LOEC)	Aquatic toxicity	[35]
Rats	25–100 ppm (inhalation, 26 weeks)	Metabolic toxicity	[36]
Male Rats, Rabbits, and Dogs		Hepatotoxicity	
Rats	500 mg/kg (oral)	Metabolic toxicity	[37]
Chinchilla rabbits		Metabolic toxicity	
Rats (Vapor Exposure)	70–200 ppm (vapor, 15 sessions)	Neurotoxicity, Weight impact	[38]
Tetrahymena	IC50 via microcalorimetry	Cellular toxicity	[40]
Rats, mice	LD50 = 756 mg/kg (oral), 6139 mg/kg (dermal)	Acute toxicity	[41]
Rats	LD50 = 166 mg/kg (oral)	Metabolic toxicity, Enzyme induction	[42]
Rats	500–730 mg/kg/day	Hepatotoxicity	[43]
Rats, Rabbits, Monkeys	25–100 ppm (26 weeks, inhalation)	Hepatotoxicity, Nephrotoxicity, Systemic toxicity	[44]
Female rats	250–500 mg/kg (injection, 3 days)	Hepatotoxicity, Adrenal hypertrophy	[45]
Pregnant rats	360 mg/kg/day, NOAEL at 120 mg/kg/day	Developmental toxicity	[46]
Rats	10–40 mg/kg/day (14-day study), sustained effects	Liver weight increase	[47]
Sprague-Dawley rats	150–600 mg/kg/day (gestational exposure)	Hematotoxicity	[48]
Liver Enzyme	Liver enzyme stimulation	Hepatotoxicity	[49]

TCB exhibited toxic effects in the Salmonella assay, particularly at the higher dose of 200 mg/kg/day, which caused a significant reduction in colony numbers and other indicators of toxicity, although it did not induce mutagenesis in the tested strains [30]. Kubo et al. [31] have shown that TCBs are not mutagenic. The tests were conducted on different strains of *Salmonella enterica* ser. Typhimurium, both with and without metabolic activation in the incubation medium, consistently yielded negative results for gene mutation. The experiments utilized the Ames test, employing Salmonella strains TA98 and TA100. Both with and without metabolic activation (using S9 mix from rat liver), the tests consistently showed no mutagenic effects of TCBs, as no increase in revertant colonies was observed.

Ecotoxicity

Toxicity of technical grade 1,2,4-TCB was observed when applied to rabbits. Over a 13-week period, rabbits were administered 0.2 mL of a 100% solution of 1,2,4-TCB (97 mg/kg) to the ear three times per week. The results indicated no histological alterations in vital organs such as the heart, liver, kidneys, and spleen. However, topical application resulted in minor redness accompanied by slight scaling and peeling on the ear's ventral surface, although these symptoms did not worsen even after 39 exposures. The treatments also had no impact on body weight. These findings suggest that while the compound can cause minor local skin irritation, it does not appear to induce significant internal organ toxicity under the conditions tested [32].

Rabbits received technical-grade 1,2,4-TCB applied to a cleared section of their back skin in quantities up to 450 mg/kg, administered 5 days a week for 4 weeks. A thorough examination revealed no notable histological modifications in a variety of key organs and systems, including the respiratory and gastrointestinal systems, heart, liver, kidneys, spleen, thymus, lymph nodes, skeletal and bone tissues, pituitary gland, pancreas, adrenal gland, and the thyroid and parathyroid glands. Furthermore, no changes related to the treatment were observed in the brain, spinal cord, peripheral nerves, or eyes. While a mild pallor was noticed in the livers of rabbits that received the highest dosage, it was not associated with any histological harm. Additionally, the study

documented that body weight and hematological parameters were not impacted by the treatment [33].

Experiments were conducted with four diatom species, exposing them to 0.3 ppm of 1,2,3-TCB. These experiments started during the 8th and 11th hours of their 16-h light phase of a 16:8 h light/dark cycle at 20 °C. Over a period of 10 days, the cell population, lipid amounts, and types of lipid classes were tracked. *Melosira italica* showed the most significant long-term changes. On the 10th day, substantial reductions in cell numbers and chlorophyll levels were observed in *Synedra filiformis* when exposure began at the 11th hour and in *M. varians* when it started at the 8th hour of the light phase. The study indicated that immediate impacts were more pronounced when the exposure coincided with phases of elevated polar lipid levels or during their synthesis. Conversely, long-term impacts were more marked when exposure started during phases with high neutral lipid levels and total extractable lipids. This suggests that diatoms' response to low concentrations of chlorinated benzenes may hinge on the natural daily fluctuations in their lipid compositions. These effects were consistent and varied between species, and the timing of exposure initiation throughout the day led to notably different outcomes [34].

Chronic and acute (28 days and 48 h, respectively) toxicity of various chlorinated benzenes were assessed in the water flea *Daphnia magna*. Specific toxicity tests for 1,2,4-TCB on *D. magna* revealed that the 48-h lethal concentration 50 value was 2.1 mg/L. Additionally, the lowest observable effect concentration, which evaluates effects on growth or reproduction, was identified at 0.69 mg/L. These results underscore the considerable toxicity of TCB at relatively low levels in comparison to other chemicals tested [35].

Male rats, rabbits, and dogs were exposed to concentrations of 0, 30, or 100 ppm of 1,2,4-TCB over 44 days, with exposure sessions lasting 7 h per day across 5 days each week. This prolonged exposure resulted in no notable alterations in body weight gain, blood test outcomes, or overall and microscopic tissue structures across all tested species. However, the study did observe an increase in liver weight in both rats and dogs at the 100 ppm concentration, suggesting that TCB has the potential to induce specific organ toxicity under sustained exposure conditions. This result is particularly significant for assessing the environmental impact of TCB, as it points to potential risks for wildlife exposed to similar concentrations [36].

Research conducted by Jondorf et al. [37] demonstrated the metabolism and elimination patterns of TCB isomers in Chinchilla rabbits. Following a single oral administration of 500 mg/kg, 1,2,4-TCB was primarily converted into trichlorophenols (TCPs), with 42% of the dose excreted as such within 5 days. In contrast, 1,3,5-TCB showed a lower excretion rate of TCPs at 9%, but 23% of the administered dose was eliminated in the form of oxygen conjugates. The rapid elimination of these metabolites, including significant proportions of glucuronic and sulfuric acid conjugates, indicates efficient processing and excretion following exposure, although the details on direct toxic effects are limited.

Rats exposed to 1,2,4-TCB vapors displayed several physiological responses. Notably, exposure to 70 ppm of the vapor for 6 h a day across 15 sessions resulted in symptoms such as lacrimation (tearing) and lethargy. Moreover, these rats showed diminished weight gain, although detailed data on this aspect was not provided. Crucially, even with exposure levels reaching up to 200 ppm, no noticeable changes were observed in the adrenal glands or spleen of the rats, either through macroscopic or microscopic examination [38].

Genotoxicity

Rats were given an oral dose of ^{14}C-labeled 1,2,4-TCB at 50 mg/kg to examine its distribution and excretion patterns. Over the course of 7 days, approximately 66% and 17% of the dose were eliminated through urine and feces, respectively. Only 2.1% of the dose appeared in exhaled air, with trivial amounts of labeled CO_2 detected. TCB was fairly evenly distributed throughout various body organs and tissues, with a somewhat greater concentration found in fat tissue. Regarding excretion, the primary substances detected in urine were free 2,4,5- and 2,3,5-TCP along with their conjugates. Minor metabolites identified included derivatives of TCB, such as 5- or 6-sulfhydryl, methylthio, methyl sulfoxide, and methyl sulfone. In exhaled air, minor quantities of DCB and unchanged TCB were present, indicating that reductive dechlorination might occur with the aid of enzymes from the gut microflora [39].

The impact of CBs on the growth metabolism of *Tetrahymena*, a protozoan, was investigated using microcalorimetry to assess their toxicity. Among the CBs tested, 1,2,4-TCB exhibited the highest toxicity. The inhibitory concentration 50 values, which reflect the concentration required to inhibit the growth metabolism by 50%, were calculated based on kinetic parameters such as the growth constant, peak time, and generation times. The study also highlighted that the presence of multiple chlorine substitutions increases the compound's toxicity. The relatively high toxicity of 1,2,4-TCB is linked to its capability to disturb cellular membranes; 1,2,4-TCB disrupts the cell membrane structure by interacting with components such as amide groups and the phosphodiester bonds in phospholipids, especially at the hydrophobic ends that face the outer layer [40].

Research by Fratello et al. [29] identified the cytotoxic properties of TCB isomers on mammalian cells. DNA damage was observed with both 1,2,3- and 1,2,4-TCB, as evidenced by DNA fragment release in cytofluorimetric analyses. Additionally, these chemicals demonstrated cytotoxic effects in studies involving Chinese hamster V79 cells, a model that operates without metabolic activation, suggesting that the compounds' toxicity is intrinsic. 1,3,5-TCB exhibited considerably lower cytotoxicity compared to 1,2,3- and 1,2,4-TCB. Again, the harmful effects of these chemicals seem to be associated with their capacity to interfere with cellular membranes.

1,2,4-TCB has an acute oral lethal dose 50 (LD50) value of 756 mg/kg in rats and 166 mg/kg in mice when administered in a single dose. The acute dermal LD50 for rats is 6139 mg/kg. Continuous administration of sub-lethal doses to guinea pigs has led to liver injury. This substance mainly causes skin irritation owing to its degreasing effects and is unlikely to cause acute contact dermatitis [41].

Developmental toxicity

Rats were given 1,2,4-TCB at a daily dosage of 7 mmol/kg for a week, with observations continuing afterward to evaluate the decrease in enzyme induction. ^{14}C-labeled TCB facilitated the monitoring of radioactivity dispersion throughout the body. Additionally, research explored the impact of starvation and phenobarbital on the enzyme-inducing effects of TCB. Although the activity of *p*-nitroanisole demethylation and EPN detoxification decreased over time, they remained elevated 16 days after cessation of TCB dosage. Cytochrome P-450 and NADPH-cytochrome *c* reductase levels were induced by TCB, with the greatest enzyme levels observed 4 days into starvation following a week of treatment and recovery. Starvation increased plasma, fat, and liver concentrations and heightened urinary excretion of ^{14}C-TCB post-treatment. Conversely, phenobarbital treatment reduced the induction levels of TCB [42].

The toxic effects of 1,2,4-TCB on rats, particularly impacting liver health and porphyrin metabolism, were examined. Key findings included intense necrosis and fatty changes in the liver when it was administered once daily at 500 mg/kg for 10 days, or increased urinary excretion of porphyrins, elevated liver porphyrin levels, and the induction of δ-aminolevulinate synthase—an enzyme critical for heme biosynthesis—when a higher dose of 1,2,4-TCB was administered (730 mg/kg per day). This enzyme induction is associated with the development of porphyria. Additionally, these doses led to notable weight loss and appetite reduction in the rats, highlighting the compound's significant metabolic disruptions [43].

Three animal groups (monkeys, rabbits, and rats) were exposed to 1,2,4-TCB for 26 weeks, with each group also having a corresponding control group. The levels of 1,2,4-TCB exposure were set at 25, 50, and 100 ppm. Pulmonary function and behavioral tasks were tested in monkeys, along with eye health evaluations in both rabbits and monkeys. Additionally, measurements of body weight, blood, and serum biochemical profiles were conducted for all species both before and during the exposure period. Detailed microscopic examinations of select rat tissues were performed after 1, 3, and 6 months. Although there were observations of cellular changes in the livers and kidneys of rats at 4 and 13 weeks, no structural deformities or harmful effects related to exposure were detected in any of the species by the end of the 26 weeks [44].

Young female rats were administered intraperitoneal injections of 0, 250, or 500 mg/kg of 1,2,4-TCB over three consecutive days. The results showed no estrogenic activity, but there was an increase in the size of the liver and adrenal glands and a reduction in uterine weight. These outcomes suggest that 1,2,4-TCB may lead to adrenal gland enlargement in rats without exhibiting estrogen-like effects [45].

Kitchin and Ebron [46] identified significant toxicological effects of 1,2,4-TCB in pregnant rats. High doses of 360 mg/kg/day administered between gestational days 9–13 led to severe outcomes, including high mortality, with all six pregnant rats dying within 3 days of beginning the dosage. At this same dose level, noticeable weight loss in pregnant rats and developmental delays in their fetuses were observed, suggesting a direct link between maternal stress from exposure and impaired fetal development. Additionally, moderate hepatocellular hypertrophy was evident in rats at a dose of 360 mg/kg per day, while 120 mg/kg per day was established as the no observed adverse effect level (NOAEL) for this specific liver effect.

In a study by Kociba et al. [36], rats exposed to 30 or 100 ppm of TCB displayed an increased excretion of urinary porphyrins, indicative of liver enzyme stimulation. This response suggests that TCB exposure can affect metabolic processes related to liver function, which are crucial during developmental stages in mammals. Such changes in liver and kidney weights, alongside modifications in metabolic excretion, could potentially influence developmental processes, hinting at developmental toxicity due to alterations in organ development and metabolic regulation in young or developing animals.

Investigating the impacts of 1,2,4-TCB on rats, noteworthy findings include a dose-dependent increase in liver weight, observed both in acute and chronic exposure scenarios. Specifically, in a 14-day gavage study, liver weights increased by 15.3% at 10 mg/kg per day and 28.9% at 40 mg/kg per day. A 90-day study further

confirmed these effects, with liver weights increasing by 14% even after a 30-day recovery period [47].

In a series of studies, Sprague-Dawley rats were administered TCB isomers and observed for toxic effects. Significant toxic effects included reduced hemoglobin and hematocrit levels observed in rats treated with 1,2,4-TCB at 150 and 300 mg/kg per day and with 1,2,3- and 1,3,5-TCB at 600 mg/kg per day during gestational days 6–15. Furthermore, fetuses from dams treated with 1,2,4- and 1,3,5-TCB exhibited structural changes in the eye lenses, such as cellular disorientation and disaggregation. However, no significant embryotoxic or teratogenic effects were noted, indicating that while TCBs can cause specific toxic changes, they do not broadly affect developmental outcomes [48].

Another study explored the toxic effects associated with the consumption of TCB-contaminated fish found in the Great Lakes. Weanling rats from both genders were given diets laced with different concentrations of TCB isomers—1, 10, 100, or 1000 ppm—over 13 weeks. The male rats that ingested 1000 ppm of 1,2,3-TCB experienced a decrease in weight gain, although no additional toxic effects were noted. Significant increases in liver and kidney weights were observed in male rats at the highest concentration for all TCB isomers. In particular, 1,2,4-TCB at 1000 ppm resulted in increased activities of hepatic aminopyrine demethylase and aniline hydroxylase in male rats and aminopyrine demethylase in female rats. There were no alterations in serum biochemical or hematological measures. Moderate histological alterations were observed in the liver and thyroid of male rats exposed to 1000 ppm of all TCBs, while only 1,3,5-TCB caused similar changes in kidney tissues at this concentration. Female rats exhibited less severe histological changes compared to males. The research established that the NOAEL for all three isomers was 100 ppm in the diet, equivalent to 7.6–7.8 mg/kg body weight per day depending on the dietary intake [26].

Animal research indicates that TCB isomers promote the breakdown of xenobiotics by stimulating the production of various liver enzymes responsible for drug metabolism, including cytochromes *c* and P-450, glucuronyltransferase, glutathione *S*-transferase, and microsomal proteins [24, 25, 27, 28, 49].

Analytical methods

Analysis of TCBs is often performed individually or in combination with other CBs or chlorinated organic pollutants. For analysis, the TCBs present in the sample are extracted, and then instrumental analysis is performed. As mentioned in Lee SY et al. [50], non-volatile high molecular weight compounds such as vitamins are suitable for liquid chromatography (LC), but TCBs are volatile low molecular weight compounds, so GC is more suitable. Therefore, for the analysis of TCBs, GC is preferred over LC [23]. GC-ECD, -FID, -MS, or tandem mass spectrometry (MS/MS) with/without a headspace (HS) sampler are the most common analytical methods. ECD is suitable for the analysis of compounds containing halogen atoms such as chlorine, while FID is used for the analysis of almost all organic compounds [51]. MS and MS/MS are commonly used detectors for the analysis of residual contaminants in food, and MS/MS offers high sensitivity and selectivity, enabling accurate analysis even at very low concentrations compared to other detectors [52]. Table 2 from the literature summarizes some common analytical methods for TCBs.

Extraction and pretreatment

In general, ultrasonic extraction, which elutes substances by increasing the mass transfer rate with ultrasound, is used for food analysis [53]. However, TCBs used liquid extraction, LLE, SPE, SPME, and Soxhlet extraction as common extraction methods. Among them, the liquid extraction method is widely used. In most cases, hexane was used during the extraction process. Surma-Zadora and Grochowalski [22] subjected samples to a semipermeable membrane (SPM) to facilitate the analysis of high-fat samples. SPMs allow for the diffusion of smaller analytes out of the extract through the membrane to a solvent outside the membrane, while lipid molecules and other larger matrix components remain enclosed by the membrane. This method has the advantage of allowing samples to be prepared non-destructively.

Robles-Molina et al. [23] evaluated the performance of three extraction methods. Wastewater samples were analyzed for a range of organic pollutants, including priority compounds described in the European Water Framework Directive. The first method was LLE using *n*-hexane. LLE has the advantage of allowing thorough extraction of the entire water sample. The second method (SPE) used C18 cartridges and elution with ethyl acetate: dichloromethane (1:1, v/v). The disadvantage of SPE is that the sample typically needs to be filtered to prevent clogging of the cartridge. A HS-SPME method using two different SPME fibers was also evaluated. SPME is a well-established technique for volatile compounds. It is known for its fast and easy automation and solvent-free nature, with minimal influence on the native state of the sample, making it a popular method for environmental analysis. In addition, HS-SPME has the advantage of being environmentally friendly in terms of solvent consumption and waste generation compared to SPE and LLE.

Instrumental analysis

Robles-Molina et al. [23] evaluated three different pretreatment methods, including the previously mentioned LLE, SPE, and HS-SPME, to extract TCBs from

Table 2 Method of analysis of TCBs

Analyte	Sample	Sample preparation	LOD	LOQ	Instrumental analysis	References
1,2,3-TCB	Water	Liquid extraction	0.002 mg/l		GC-FID, GC-ECD	[2]
					GC-ECD	[3]
			0.005 ng/l		GC-MS	[16]
					GC-ECD	[18]
					GC-ECD	[19]
					GC-ECD	[21]
		LLE			GC-ECD	[20]
			0.1 ng/L		GC-ECD	[53]
				1.7 ng/l	GC-TQMS	[23]
		SPM		1.9 ng/l	GC-TQMS	
		HS-SPME		5.0 ng/l	HS-GC-TQMS	
	Fruit, Vegetables	Soxhlet extraction	0.007-0.01ug/kg		GC-ECD	[13]
	Blood	Liquid extraction			GC-ECD, GC-MS	[15]
	High-fat food	SPM, Liquid extraction	0.25 ng/ml	0.74 ng/ml	GC-ECD, GC-MSMS	[22]
	Fat	Liquid extraction			GC-FID	[55]
1,2,4-TCB	Water	Liquid extraction	0.002 mg/l		GC-FID, GC-ECD	[2]
					GC-ECD	[3]
			0.006 ng/l		GC-MS	[16]
					GC-ECD	[18]
					GC-ECD	[19]
			0.1 ng/L		GC-ECD	[53]
		LLE			GC-ECD	[20]
			2.2 ng/l		GC-TQMS	[23]
		SPM			GC-TQMS	
		HS-SPME		5.0 ng/l	HS-GC-TQMS	
		SPME	0.0001 mg/l		GC-MS	[17]
	Fruit, Vegetables	Soxhlet extraction	0.007–0.01 ug/kg		GC-ECD	[13]
	Blood	Liquid extraction			GC-ECD, GC-MS	[15]
	High-fat foods	SPM, Liquid extraction	0.70 ng/ml	2.13 ng/ml	GC-ECD, GC-MSMS	[22]
	Fish	Ultrasonic extraction			GC-MSMS	[52]
	Vegetables	LLE	0.1 ug/kg		GC-ECD	[54]
	Fat	Liquid extraction			GC-FID	[55]
1,3,5-TCB	Water	Liquid extraction	0.005 ng/l		GC-MS	[16]
					GC-ECD	[18]
		LLE			GC-ECD	[20]
			0.1 ng/L		GC-ECD	[53]
				1.8 ng/l	GC-TQMS	[23]
		SPM		2.7 ng/l	GC-TQMS	
		HS-SPME		0.7 ng/l	HS-GC-TQMS	
	Fruit, Vegetables	Soxhlet extraction	0.007–0.01 ug/kg		GC-ECD	[13]
	Blood	Liquid extraction			GC-ECD, GC-MS	[15]
	Fat	Liquid extraction			GC-FID	[55]

wastewater samples. All extracts were analyzed using a CP-3800 GC apparatus (Varian Inc., Walnut Creek, CA, USA) with a 1079 universal capillary injector, allowing programmed temperature injection (PTV injection port) and electronic flow control, coupled with a model 300-MS triple quadrupole mass spectrometer (TQMS; Varian Inc.). An automatic sampler capable of accommodating HS vials was connected to the system for HS-SPME analysis.

To measure the concentration of 1,2,3-TCB in an aquarium water sample, extraction was carried out using hexane. Following extraction, the sample underwent GC-ECD analysis using a Hewlett Packard 5890 GC instrument fitted with a 50 m HP Ultra 2 column and operating in splitless mode [21]. Six types of CBs, including 1,2,3- and 1,2,4-TCB, were analyzed in a water sample to explore the hazards posed by the chemicals to aquatic organisms, such as water fleas. Extraction was performed with *n*-hexane (1:25). Analysis was conducted using GC

equipment, including a Hewlett-Packard 5750 chromatograph equipped with an FID, a Fractovap C. Erba 4200 chromatograph equipped with a Ni-63 ECD, and glass columns (2 m × 6 mm outer diameter) filled with 3% SE 30. The limit of detection (LOD) was 0.002 mg/L [2]. In a related study, water samples were collected for toxicokinetic analyses of 1,2,3- and 1,2,4-TCB in rainbow trout (*Salmo gairdneri*). Hexane was used for extraction. Quantitative analysis was conducted using GC-ECD (Fractovap 4200, C. Erba) [3]. Lu et al. [54] collected 73 fish samples from three locations in Qingyuan, China, and analyzed six regulated pollutants, including 1,2,4-TCB. Dichloromethane (20 mL) was added to the sample, centrifuged, and subjected to ultrasonic extraction. The analysis was performed on a Thermo Scientific TRACE™ 1300 GC equipped with a Thermo Scientific TG-5MS capillary column (30 m × 0.25 mm × 0.25 µm) and TSQ 8000 Evo MS/MS system (Thermo Scientific, USA).

Water samples from the water sources used by 50 food processing or beverage manufacturing companies in Nanning, China, were gathered and tested for the presence of six different chlorinated organic pollutants. As a pretreatment, 6 mol/L HCl was added to adjust the pH to 2, and SPME was performed. Analysis was carried out using an Agilent DB-1701 capillary separation column (30 m × 0.25 mm × 0.25 µm) mounted on a GC-7890 (USA Agilent Company) coupled to an 5975 C MS (USA Agilent Company). The LOD for 1,2,4-TCB was 0.0001 mg/L [17]. Oliver and Nicol [20] subjected water samples collected from the Niagara River to LLE with hexane. TCBs were quantified in the extracted samples using a Varian 4600 GC with an ECD and interfaced with a data processor (Varian Vista 402). Two capillary columns with different polarities, SE54 and OV-1, were used for chromatographic separation.

Several other studies have performed GC analysis of TCBs in water samples. Water samples collected from the Aire, Calder, Don, and Trent rivers in England were extracted with hexane before TCB analysis by GC-MS (Hewlett Packard 5890 GC coupled to a 5972 A MS and a 7673 autosampler). The column used was connected to a 25 m × 0.22 mm non-polar deactivating column (SGE (UK) Ltd.) using a 50 m × 0.22 mm i.d. glass press-fit connector. The LOD was 0.005 ng/L for 1,2,3-TCB, 0.006 ng/L for 1,2,4-TCB, and 0.005 ng/L for 1,3,5-TCB [16]. To analyze isomers of TCB, HCB, and chloroform in water samples from the Forth estuary, Scotland, they were extracted with hexane and analyzed using a Hewlett Packard 5890 GC equipped with a Ni-63 ECD and a DB5 capillary column (30 m × 0.25 mm i.d.; J&W) [19]. Rhine River water samples underwent three extractions with petroleum ether. The extracted samples were subsequently analyzed on an HP 5890 A GC equipped with dual Ni-63 ECD, a splitless injector, and an automatic sampler (HP 7673 A). Dual capillary columns (CPsi18 and CPsill9, 50 m × 0.22 mm × 0.12 pm) were used [18]. Water collected from an estuary in Scotland was subjected to LLE with *n*-pentane. Analysis was performed using a Perkin-Elmer 8500 capillary GC equipped with a 60 m Durabond 1 (DB-1) column (Jones Chromatography Ltd.) and an ECD [55].

Bristol et al. [15] analyzed blood samples collected from 36 residents and 12 volunteers from Ring III in the Love Canal area of Niagara Falls. After adding hexane to the blood sample, centrifugation was performed to separate the supernatant, which was then concentrated and analyzed. The analysis used two Tracor MT-222 GC equipped with a pulsed linear Ni-63 ECD. Analysis was performed using an HP 5700 GC coupled to a Hewlett-Packard model 5930 A mass spectrometer. One of the blood samples from 36 residents measured a concentration of 0.7 ppb of 1,3,5-TCB.

Wang and Jones [13] and Zhang et al. [56] analyzed vegetables. Wang and Jones [13] subjected nine vegetables collected from retail supermarkets in the United Kingdom to Soxhlet extraction using hexane–acetone (2:1, v/v), followed by GC-ECD analysis using a DB-Wax column. The LOD was 0.007–0.01 µg/kg. Zhang et al. [56] collected spinach, cabbage, celery, radish, and carrot samples from three locations near the Qiantang River, China, to analyze 1,2,4-TCB among several CBs. LLE was performed with an acetone–hexane solution. Analysis was performed using a SP2000 GC equipped with a PEG20M (30 m × 0.53 mm × 0.10; Supelco, USA) column and Ni-63 ECD. The LOD of vegetables was 0.1 µg/kg. Surma-Zadora and Grochowalski [22] and Nichol et al. [57] analyzed fat. Surma-Zadora and Grochowalski [22] used SPM to process high-fat food samples such as pork fat, beef fat, butter, egg yolk, and chocolate and then extracted them with hexane to remove chlorinated persistent organic pollutants. Gas chromatographic separation was performed using a Varian CP-3800 GC equipped with an ECD system and a CP-Sil 5 CB column (30 m × 0.32 mm × 0.25 µm; Supelco). In addition, fat in food samples was separated and analyzed using a CE Trace 2000 GC coupled to a Finnigan GCQ Plus GC-MS/MS system and installed with a ZB 5-MS column (60 m × 0.25 mm × 0.25 µm; Zebron). The LOD for 1,2,3- and 1,2,4-TCB were 0.25 and 0.70 ng/mL, respectively, while the corresponding limit of quantification (LOQ) were 0.74 and 2.13 ng/mL, respectively. Nichol et al. [57] used cyclohexane to extract 1,2,4-TCB from adipose tissue attached to sheep bones before analysis using a Pye-Unican 104 GC equipped with an FID.

Occurrence

Table 3 provides a comprehensive overview of the occurrence of TCBs in various food samples. It compiles data

Table 3 Occurrence of TCB in food samples

Analyte	Sample	Concentration	References
1,2,3-TCB	Tomatoes	0.0440 ug/kg	[13]
	Potato	0.0484 ug/kg	
	Onion	0.0490 ug/kg	
	Carrots	ND[1]	
	Cabbage	ND[1]	
	Cauliflower	ND[1]	
	Lettuce	ND[1]	
	Beans	ND[1]	
	Peas	ND[1]	
	Trout (Lake Superior)	0.1 ppb	[56]
	Trout (Lake Erie)	0.1 ppb	
	Trout (Lake Huron)	0.2 ppb	
	Trout (Niagara River)	0.2 ppb	
	Trout (Lake Ontario)	1 ppb	
	Lake trout	0.3 ng/g	[57]
	Soybean (U.S.A.)	0.02 mg/kg	[58]
	Poppy (Yugoslavia)	0.03 mg/kg	
	Rape (Yugoslavia)	0.08 mg/kg	
	Hazelnut (Turkey)	0.12 mg/kg	
	Sunflower (Yugoslavia)	0.15 mg/kg	
	Sesame (China)	0.15 mg/kg	
	Peanut (China)	0.20 mg/kg	
	Walnut (Yugoslavia)	0.20 mg/kg	
	Corn (Yugoslavia)	0.85 mg/kg	
	Leafy vegetable	0.00011 ug/g	[59]
	Fruit	ND[1]	
	Root vegetables including potatoes	ND[1]	
	Milk	ND[1]	
	Eggs/Meat	ND[1]	
	Catfish (Junction of Calcasieu River and Bayou d'Inde)	0.37	[60]
	Catfish (Bayou d'Inde)	0.77	
	Catfish (Lake Charles)	ND[1]	
	Vegetables (Mean)	0.010 mg/kg	[62]

Table 3 (continued)

Analyte	Sample	Concentration	References
1,2,4-TCB	Potato	ND[1]	[13]
	Cabbage	0.0038 ug/kg	
	Cauliflower	0.0068 ug/kg	
	Lettuce	0.0309 ug/kg	
	Onion	ND[1]	
	Beans	ND[1]	
	Peas	0.0342 ug/kg	
	Tomatoes	ND[1]	
	Trout (Lake Superior)	0.6 ppb	[56]
	Trout (Lake Huron)	1 ppb	
	Trout (Lake Erie)	0.5 ppb	
	Trout (Lake Ontario)	5 ppb	
	Trout (Niagara River)	2 ppb	
	Lake trout	3.7 ng/g	[57]
	Corn (Yugoslavia)	0.010 mg/kg	[58]
	Soybean (U.S.A.)	tr[2]	
	Rape (Yugoslavia)	tr[2]	
	Sunflower (Yugoslavia)	0.003 mg/kg	
	Peanut (China)	0.005 mg/kg	
	Sesame (China)	tr[2]	
	Walnut (Yugoslavia)	tr[2]	
	Hazelnut (Turkey)	tr[2]	
	Poppy (Yugoslavia)	tr[2]	
	Leafy vegetable	0.0004 ug/g	[59]
	Fruit	0.00014 ug/g	
	Root vegetables including potatoes	ND[1]	
	Milk	0.00014 ug/g	
	Eggs/Meat	0.00074 ug/g	
	Catfish (Bayou d'Inde)	3.9 ug/g	[60]
	Catfish (Junction of Calcasieu River and Bayou d'Inde)	1.9 ug/g	
	Catfish (Lake Charles)	ND[1]	
	Vegetables (Mean)	0.002 mg/kg	[62]

Table 3 (continued)

Analyte	Sample	Concentration	References
1,3,5-TCB	Carrots	ND[1]	[13]
	Potato	0.010 ug/kg	
	Cabbage	0.0225 ug/kg	
	Cauliflower	ND[1]	
	Lettuce	0.0030 ug/kg	
	Onion	0.363 ug/kg	
	Beans	ND[1]	
	Peas	0.117 ug/kg	
	Tomatoes	ND[1]	
	Trout (Lake Superior)	0.6 ppb	[56]
	Trout (Lake Huron)	0.3 ppb	
	Trout (Lake Erie)	0.1 ppb	
	Trout (Lake Ontario)	4 ppb	
	Trout (Niagara River)	4 ppb	
	Lake trout	1.0 ng/g	[57]
	Corn (Yugoslavia)	0.07 mg/kg	[58]
	Soybean (U.S.A.)	tr[2]	
	Rape (Yugoslavia)	tr[2]	
	Sunflower (Yugoslavia)	0.02 mg/kg	
	Peanut (China)	0.01 mg/kg	
	Sesame (China)	0.005 mg/kg	
	Walnut (Yugoslavia)	0.01 mg/kg	
	Hazelnut (Turkey)	0.01 mg/kg	
	Poppy (Yugoslavia)	tr[2]	
	Leafy vegetable	0.00028 ug/g	[59]
	Fruit	0.00012 ug/g	
	Root vegetables including potatoes	ND[1]	
	Milk	0.0012 ug/g	
	Eggs/Meat	0.0007 ug/g	
	Catfish (Bayou d'Inde)	0.48 ug/g	[60]
	Catfish (Junction of Calcasieu River and Bayou d'Inde)	0.25 ug/g	
	Catfish (Lake Charles)	ND[1]	
	Vegetables (Mean)	0.026 mg/kg	[62]

ND[1] = Not Detected, tr[2] = trace

from multiple studies to illustrate the presence and concentration of TCBs in different food types, including vegetables, fruits, dairy products, meats, and fish, across diverse geographical locations.

The concentrations of CBs were assessed in the sediment, water, and fish within the Great Lakes regions. Notably, 1,3,5-TCB was not found in any drinking water samples. However, 1,2,4- and 1,2,3-TCB were present, recorded at approximately 2 and 0.1 ppb, respectively. Among the small selection of fish examined, trout from Lake Ontario contained 1,2,4- and 1,3,5-TCB at 4 ppb each and 1,2,3-TCB at 1 ppb; these values were higher compared to other regions where the concentrations were below 1 ppb [58].

In the water and suspended particulates of the Niagara River, as well as in the sediments and bottom-dwelling organisms of western Lake Ontario, the concentrations of 10 types of CBs, hexachlorobutadiene, and PCBs were analyzed. TCBs were detected at levels ranging from 0.1 to 1 ng/g (1,2,3-TCB), from 0.5 to 5 ng/g (1,2,4-TCB), and from 0.1 to 4 ng/g (1,3,5-TCB). The highest concentrations were observed in trout from either Lake Ontario or the Niagara River, with trout near the Niagara River's mouth in Lake Ontario showing 1,3,5- and 1,2,4-TCB levels of 1.0 and 3.7 ng/g, respectively [59].

Peattie et al. [60] reported the detection of TCB isomers in various seed oils derived from crops at concentrations ranging from 0.005 to 0.85 mg/kg. In Ontario, Canada, isomers of TCBs were found in a range of food items, such as vegetables, fruits, milk, eggs, and meat bought from supermarkets [61]. Catfish sourced from Bayou d'Inde in Louisiana, close to a facility manufacturing trichloroethylene and perchloroethylene, showed 1,3,5-, 1,2,4-, and 1,2,3-TCB concentrations of 480, 3,900, and 770 ng/g, respectively [62].

TCBs were detected in a variety of environmental samples, including plants, fish, wildlife, and food products. For example, 1,2,4-TCB was identified but not quantified in various plant materials grown at a coal refuse reclamation site in Illinois [63]. Additionally, this compound was found in vegetation, averaging 0.002 mg/kg, in regions impacted by agricultural chemicals and municipal waste [64].

Nine different vegetables from supermarkets in the United Kingdom were sampled and subjected to analysis. CBs were found in several of the tested vegetables. The peel of root vegetables showed higher concentrations of CBs than their inner parts. In leafy vegetables, the concentration of CBs was greater in the outer leaves compared to the inner leaves. The three TCB isomers were identified in the vegetables, with the highest recorded levels being 0.1599 ppb for 1,3,5-TCB, 0.0676 ppb for 1,2,4-TCB, and 0.0498 ppb for 1,2,3-TCB [13].

A study was conducted on five types of seasonal vegetables from three different cultivation areas in Hangzhou, China, to measure the concentration of 1,2,4-TCB together with three other CBs. Each vegetable sample from each location was further divided into leaf, stem, and root sections for detailed chemical analysis to determine the accumulation of CBs. The findings revealed that all vegetables contained detectable levels of all four CBs. In spinach, Chinese cabbage, and celery, the highest level of CBs was detected in the roots, followed by the leaves. Conversely, in radishes and carrots, the leaves exhibited the highest CB concentrations, followed by stems. The distribution patterns of CBs across these vegetables were strongly associated with the lipid content in the vegetable tissues, the Henry's law constant (H), the octanol–water partition coefficient (K_{ow}), and the specific physiological characteristics of each vegetable type [56].

Risk assessments

A risk assessment specific to marine ecosystems was performed for 1,2,4-TCB, adhering to the methods prescribed in European Union (EU) Risk Assessment Regulation 1488/94 and the guidance outlined in EU Existing Substances Regulation 793/93. This analysis involved collecting and reviewing data on environmental levels and impacts from systematic monitoring in key rivers and estuaries that flow into the North Sea. The evaluation involved comparing the predicted environmental concentrations (PECs) of the substance with the predicted no-effect concentrations (PNECs) for marine environments. Toxicological evaluations spanning three trophic levels—aquatic plants, invertebrates, and fish—resulted in establishing PNEC values at 0.3 μg/L for water and 38 μg/kg dry weight for sediment. The monitoring data outlined two scenarios: standard and worst-case, with corresponding PEC values of below 0.047 and 0.1 μg/L for water and 40 and 90 μg/kg dry weight for sediment. Consequently, the ratios of PEC to PNEC were calculated as 0.16 and 0.3 for water and 1 and 2.4 for sediment [65].

CBs are managed through stringent controls to reduce their environmental discharge. Nonetheless, there was scarce data regarding their distribution and the dangers they presented in rivers throughout China. Therefore, a highly industrialized and agriculturally developed area in Southern China was chosen for a comprehensive investigation into the levels of contamination and related risks in both sediment and fish tissues. The study found that these hydrophobic pollutants primarily build up in the fish tissues, with the concentration order being liver > brain > muscle. It was also discovered that some TCBs are derived from the reductive dechlorination of more highly chlorinated benzenes. When assessing the daily human consumption of these contaminants through fish across different age categories, the results suggested that these pollutants are unlikely to constitute a significant health hazard [66].

MacLeod and Mackay [67] provided an in-depth risk evaluation of benzene and CBs that included categorization of chemicals, calculation of emission levels and environmental presence, analysis of chemical behavior, and simulations of regional mass balance, all specifically devised for the Southern Ontario area. They selected the Level III EQuilibrium Criterion model to assess the principal transport and transformation behaviors of these substances, highlighting marked differences in their volatility and hydrophobic characteristics. The environmental levels recorded correspond well with the forecasts provided by the steady-state Level III ChemCAN chemical fate model, a regional Level III fugacity model for assessing chemical fate in Canada. Furthermore, an elaborate human exposure model was created to predict the uptake of these pollutants by residents of Southern Ontario. A new technique for determining the highest allowable environmental concentrations was also introduced. According to the research findings, the acceptable daily intake of 1,2,4-TCB for the general population was established at 3.8 μg/day.

Abbreviations

TCB	Trichlorobenzene
GC	Gas chromatography
CB	Chlorobenzene
MCB	Monochlorobenzene
DCB	Dichlorobenzene
TeCB	Tetrachlorobenzene
PeCB	Pentachlorobenzene
HCB	Hexachlorobenzene
MS	Mass spectrometry
FID	Flame ionization detector
ECD	Electron capture detector
LLE	Liquid–liquid extraction
SPE	Solid-phase extraction
SPME	Solid-phase microextraction
TCP	Trichlorophenol

LD50	Lethal dose 50
NOAEL	No observed adverse effect level
LC	Liquid chromatography
MS/MS	Tandem mass spectrometry
HS	Headspace
SPM	Semipermeable membrane
TQMS	Triple quadrupole mass spectrometer
LOD	Limit of detection
LOQ	Limit of quantification
EU	European Union
PEC	Predicted environmental concentration
PNEC	Predicted no-effect concentration

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