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RESEARCH ARTICLE

Human health risk surveillance of polychlorinated biphenyls in bovine milk from alluvial plain of Punjab, Pakistan

Saman Sana[1,2] · Abdul Qadir[1] · Neil P. Evans[3] · Mehvish Mumtaz[1] · Ambreena Javaid[4] · Amjad Khan[5] · Saif-ur-Rehman Kashif[2] · Habib ur Rehman[6] · Muhammad Zafar Hashmi[7]

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Abstract

Punjab is the leading province of Pakistan in the production of bovine milk and its consumption. Rapid industrialization, high energy demand, and the production of waste have increased the risk of polychlorinated biphenyls (PCBs) toxicity in the environment. This research work was designed to assess human dietary exposure of ∑PCBs17 congeners through ingestion of buffalo and cow's milk from eight main districts of Punjab, Pakistan. The average concentrations of ∑DL-PCBs (8.74 ng g^{-1} and 14.60 ng g^{-1}) and ∑I-PCBs (11.54 ng g^{-1} and 18.68 ng g^{-1}) in buffalo and cow milk samples were analyzed, respectively. The PCB-156 was predominantly high congener found in both buffalo (2.84 ng g^{-1}) and cow milk (2.86 ng g^{-1}). It was found that the highest PCBs in bovine milk samples were observed in close vicinities of urban and industrial areas. The estimated daily consumptions of DL-PCBs and I-PCBs, from buffalo and cow milk, were below the acceptable daily intake for both adults and children. Moreover, hazard quotients (HQ) of the ∑PCBs17 congener value were less than 1.0 in adults and greater in the case of children reflecting the high chances of cancer. Furthermore, comprehensive monitoring for childhood cancer is recommended to establish the relationship in future studies.

Keywords Cattle farming · Dioxin-like PCBs · PCB accumulation · Dairy products · Human health risk

Introduction

Throughout the world, there is increased concern about the potential health effects of persistent organic pollutants (POPs) owing to their persistence within the environment, long-range transportation, bioaccumulation, and their carcinogenic capacity (Meng et al. 2017; Sohail et al. 2018; Weber et al. 2019). Polychlorinated biphenyls (PCBs) also termed as chlorinated hydrocarbons (Johnson et al. 1964) are a broad group of organic chemicals produced by human activities like industrialization (Dai et al. 2016). These are highly toxic compounds which can pose serious health risks to both adults and kids. These were discussed in the Stockholm Convention on POPs 2001 because of their potential for adversarial effects on the health of humans and the environment (WHO 2010). PCBs were produced for their outstanding electric insulation properties and were once extensively used in transformers and capacitors as coolant fluids (Hulin et al. 2020; Kabir et al. 2015). Despite a drastic decline in their manufacture since the 1960s, due to their accessibility, low cost, and adaptability, PCBs are still used for cooling and insulation along with transformer oil, in

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✉ Abdul Qadir
aqadir.cees@pu.edu.pk

[1] College of Earth and Environmental Sciences, University of the Punjab, Lahore, Pakistan

[2] Department of Environmental Sciences, University of Veterinary & Animal Sciences, Lahore, Pakistan

[3] Institute of Biodiversity, Animal Health and Comparative Medicine, University of Glasgow, Glasgow, Scotland

[4] Department of Geography, Kinnaird College for Women University, Lahore, Pakistan

[5] Lahore Garrison University, Lahore, Pakistan

[6] Faculty of Biosciences, University of Veterinary and Animal Sciences, Lahore, Pakistan

[7] Department of Chemistry, COMSATS University, Islamabad, Pakistan

many developing countries like Pakistan (Eqani et al. 2012; Mahmood et al. 2014a). Furthermore, their use for cable insulation, as plasticizers, pigments, paints, and hydraulic equipment (EPA, 2021), means that there remains a worldwide demand for 4000 MT of PCB/year (Eqani et al. 2012). Direct or indirect production and release of new PCBs is increasing the environmental load, and its effect is increasing due to various thermal and industrial processes including incineration, metallurgy, cement production, uncontrolled burning of waste, inappropriate dumping of e-waste, leakage of oil from transformers, open electronics repair workshops, incineration sites, polluted goods, and municipal and industrial wastewater disposal (Breivik K et al. 2002; EPA, 2004; Eqani et al. 2013; Gong et al. 2017; Mahmood et al. 2014a). Despite concern about their long-term safety and restrictions in their production, PCBs are ubiquitous within the environment, PCBs are detectable in various matrices in most countries, and human exposure remains possible (Bányiová et al. 2017; Lind et al. 2019).

The 209 PCB congeners are divided into two broad groups: "dioxin-like PCBs (DL-PCBs)" and "indicator PCBs (I-PCBs)" which are often used as markers in pollution studies (Ahmadkhaniha et al. 2017; Rosinska and Karwowska 2017). There are 12 PCB congeners also called "Dirty Dozen'" whose toxicological effects are comparable to polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) (WHO 2016); because of similarities in properties with PCDDs and PCDFs, these 12 congeners are grouped together and named as dioxin-like PCBs (DL-PCBs) (ATSDR, 2014; Debela and Sheriff, 2021). The indicator PCBs (I-PCBs) are a group of 7 congeners also known as marker PCBs because of their availability and predominance in PCB mixtures (Kim et al. 2004). The congeners of DL-PCBs and I-PCBs are detected in higher concentrations in various environmental matrices including food, human fluids, and tissues (IARC 2016), indicating their potential for bioaccumulation and increasing their risk to human health. Concern about environmental levels of PCBs arises as PCBs are categorized as carcinogenic to human beings (group 1) (IARC 2012) and it has been estimated that high-fat foods, like dairy products especially milk (Costabeber et al. 2018; Roveda et al. 2006), eggs, and animal-based products, contribute 90% of human PCB exposure (EFSA CONTAM Panel et al. 2018; Fadaei et al. 2015; FAO/WHO 2018; Malisch and Kotz 2014), particularly for infants (Sarode et al. 2016) and children (Lamarche et al. 2016; Larsson et al. 2015). In 2018, 838 million tons of milk was produced globally with a significant contribution coming from India and Pakistan. Currently, Pakistan is the fourth leading milk producer globally (Ishaq et al. 2018; Perisic et al. 2015; Sana et al. 2021) and it is expected that in the coming decade, Pakistan's milk production will continue to increase (FAO 2019). PCB levels in milk have been published for many countries including France (Hulin et al. 2020), Slovakia (Toman et al. 2020), Italy (Bertocchi et al. 2015; Chirollo et al. 2018; Esposito et al. 2010; Tremolada et al. 2014), Brazil (Costabeber et al. 2018; Heck et al. 2007), Iran (Ahmadkhaniha et al. 2017), California (Chen et al. 2017), Mexico (Pérez et al. 2012), Netherlands (Baars et al. 2004), Siberia (Mamontova et al. 2007), Belgium (Focant et al. 2003), Germany (Kerst et al. 2004), Chile (Pizarro-Aranguiz et al. 2015), South Korea (Son et al. 2012), India (Vanitha et al. 2010), and the UK (Sewart and Jones 1996). While reports on PCB concentrations in other environmental matrices, including soil, air, water, and sediments (Ali et al. 2015; Baqar et al. 2017; Eqani et al. 2015; Mahmood et al. 2014a; Syed et al. 2014, 2013), and some elements of the food chain (Mahmood et al. 2014b; Mumtaz et al. 2016) within Pakistan have been published, to date, no reports are available that detail the PCB concentrations in bovine milk and relate them with human health. Acceptable limits of PCBs in milk for Pakistan have also not been defined. The objectives of the current research were, therefore, to explore the concentration, homolog, and congener distribution of DL-PCBs and I-PCBs in milk from cows and buffalo; to conduct source apportionment and analyze spatial variation in PCB concentrations in milk from various districts; and to evaluate health risks related to PCB consumption in milk by children and adults.

Methodology

Materials

All chemicals used in this study were of grade that is suitable for analysis. PCB native standards, PCB-209, and Tetrachloro-meta-xylene (TCmX) were acquired from AccuStandard (America) and stored at −20 °C. Ethanol, hexane, acetone, and di-chloro-methane (DCM) were obtained from Merck. Pure N_2 was procured from a local gas-filling facility. Solid phase extraction (SPE) column used for cleanup of samples, were attained from SILICYCLE$_{\text{Inc}}$ (SPEC-R31830B-06P, Certified SiliaPrep$^{\text{M}}$ C18, 500 mg/6 mL).

Sampling strategy

Eight districts of Punjab with industrial (Eqani et al. 2015) and agricultural (Ali et al. 2015) significance were selected for the collection of samples (milk) from buffaloes (*n* = *26*) and cows (*n* = *28*) (March to December 2018). The study area map is presented as Fig. S1 and the coordinates are given in Table S1. The samples were collected from randomly selected buffaloes and cows, in their native environment, as part of normal milking, during either early morning or evening. Samples were placed in glass bottles of dark color (amber), sealed, labeled, transferred to an icebox, and taken to Environmental Toxicology Laboratory at College of Earth and Environmental Sciences, University of the Punjab, Lahore, where they were kept at − 20 °C until further analysis (Deti et al. 2014; Ibigbami et al. 2019; Sajid et al. 2016). During the sample collection, a questionnaire (Table S2) was used to record the native environment, living conditions, and demographic settings of the buffaloes and cows.

Sample preparation

Extraction and the cleanup process of PCBs were conducted with minor modifications to previously published methods (Dewan et al. 2013; Sana et al. 2021). Concisely, after maintaining a room temperature of the samples (25 mL per sample), 1 mL was spiked with 50 µL TCmX (100 ppb) (Naqvi et al. 2020; Sohail et al. 2018). Samples were incubated overnight (at 4 °C) after the addition of 6 mL of n-hexane and 3 mL of acetone. Samples were then sonicated (with sonicator: Model PS-20A) for 60 min on 3 °C before being centrifuged (Model 800 Electronic Centrifuge) at 3500 rpm for 10 min. The resulting supernatant was transferred to a separate glass vial and the residual sample was extracted two times with n-hexane and was added to the same container.

The milk extract was cleaned up by SPE with C18 silica cartridges from SILICYCLE, (Aguilera-Luiz et al. 2011). Cartridges were primed with n-hexane, before application of samples and elution of PCBs (2 × 5 mL of DCM). The eluates were concentrated using pure N_2 gas streaming (Sosan and Oyekunle 2017). Furthermore, 50 µL of 100 ng mL^{-1} strength of ^{13}C-PCB-209 was added to the 1 mL sample (final volume). The samples were filtered through a 0.22-µm filter and kept in 1.5 mL vials (glass) till further analysis.

Sample analysis

The PCB content of samples was analyzed using a gas chromatography-mass spectrometer (Agilent Technologies, 5975C inert XL EI/CI MSD using Triple Axis detector; 7890A GC System) tailored along with an autosampler (Agilent Technologies 7693), at Environmental Biotechnology Laboratory, University of Glasgow, UK. Selected ion monitoring (SIM) mode was used for the quantification of 17 PCBs (DL-PCBs including PCB 77, 81, 126, 169, 105, 114, 118, 156, 157, 167, and 189 and I-PCBs comprising PCB 28, 52, 101, 138, 153, and 180). A Varian column with specifications (CP-Sil 8CB, 50 m, 0.25 mm, and 0.25 µm) and injector port at 250 °C were used. The basic temperature of the mass spectrometric detector (MSD) was 230 °C and then lowered to 150 °C (quadruple temperature). The succeeding arrangement was used for analyzing all samples: initial 3 min temperature was 150 °C then 4 °C per minute up to 290 °C. The isothermal process was maintained for 10 min.

Quality assurance and quality control

Distilled water was used for washing glassware then it was rinsed with DCM and dried at 450 °C for almost 6 h before use. Standards of 1, 10, 20, 50, 100, 200, 500, and 1000 ng g^{-1} were used for developing calibration curves and standardization of instruments. The limit of detection (LOD) was set at 3 × the signal-to-noise ratio (S/N), while the limit of quantification (LOQ) was 10 × the S/N. The table of LOD and LOQ is given as Table S5. Samples were investigated in small groups with a procedural blank run after every 10 samples. PCB concentration was lesser than the limits in all of the field, procedural, and blanks of solvent. The range of the recovery for TCmX was 75–84 %. The spiked recovery was 88–151 % (mean = 105%). The considered relative standard deviation of the spiked replicates was 20 % (mean = 11%). Integration of peaks and data analysis was done by software (Agilent MSD productivity Chemstation).

DL-PCB toxicity equivalence

The toxicity profile of DL-PCBs was evaluated by assessing the toxicity equivalence (TEQs) by Eq. (1), where *C* represents the concentration of DL-PCB congeners and TEF denotes the toxic equivalency factor as per the World Health Organization (WHO), International Program on Chemical Safety (IPCS), 2005 (Van den Berg et al. 2006).

$$TEQ = C \times TEF \tag{1}$$

Risk assessment of human health

Guidelines from USEPA were followed for the calculation of health risks (non-carcinogenic and carcinogenic) for adults and children (Dougherty et al. 2000; Sosan, 2017). Estimated daily intake, i.e., EDI (ng kg^{-1} day^{-1}) of PCBs from milk consumption, was calculated according to the following formula (Eq. 2) (Binelli and Provini, 2004).

$$EDI = \frac{CR \times C}{BW} \tag{2}$$

CR is the rate of milk consumption (mL day^{-1}) (Pakistan Economic Survey 2018), *C* represents the measured concentration (ng g^{-1}) of PCB congeners, and BW is body weight (children = 27.7 kg and adults = 60 kg) (Adeleye 2019; Sosan 2017). The risk level posed to human beings can be represented by using all these parameters (Dougherty et al. 2000; Wang et al. 2011).

Non-carcinogenic risk assessment

To evaluate the health risks of not causing cancer, a comparison was done between EDI (PCBs in milk) and acceptable daily intake (ADI) (EU, 2011).

Carcinogenic risk assessment

The hazard ratio (HR) was found by following (Dougherty et al. 2000) (Eq. 3) where CBC (ng kg^{-1} day^{-1}) is the cancer benchmark ratio which is derived using Eq. 4.

$$HR = EDI/CBC \tag{3}$$

$$\mathrm{CBC} = (\mathrm{RL} \times \mathrm{OSF} \times \mathrm{BW})/\mathrm{CR} \tag{4}$$

Risk level (RL) is taken as 10^{-6}, and the oral slope factor (OSF) is measured by unit mg kg^{-1} day^{-1}.

Data analysis and visualization

Descriptive statistics including mean, standard deviation, range, percentage contribution, and distribution frequency were generated for the milk samples gathered from Punjab districts using Microsoft Excel version 2010. Origin (Pro 8) was used to apply the Kruskal–Wallis test and multivariate statistical analysis of differences in PCBs concentration between study areas. p-value was taken as 0.05. Arc GIS (version 10.2) was used to represent the map of the area under study.

Results and discussion

PCB profile

The concentration profile of DL-PCBs and I-PCBs of the milk samples acquired from buffaloes and cows is given in Table 1. Among all the analyzed milk samples ($n=54$) of buffaloes ($n=26$) and cows ($n=28$), the total means

Table 1 Descriptive statistics (mean ± standard deviation (SD), range values, percentage (%), and detection frequency (DF)) of PCBs in milk samples of buffaloes and cows (ng g^{-1})

DL-PCBs	Buffaloes ($n=26$)						Cows (n = 28)					
	Mean	**SD**	**min**	**max**	**%**	**DF**	**Mean**	**SD**	**min**	**max**	**%**	**DF**
Non-ortho substituted PCBs												
PCB-77	0.00	0.00	0.00	0.00	0.00	0.00	0.70	1.63	0.00	13.96	2.10	2.00
PCB-81	0.29	0.25	0.00	1.77	1.44	6.00	1.14	1.22	0.00	8.78	3.43	6.00
PCB-126	0.73	0.56	0.00	4.11	3.59	9.00	0.92	1.33	0.00	9.47	2.78	6.00
PCB-169	1.20	1.84	0.00	18.01	5.89	5.00	1.59	2.16	0.00	9.40	4.77	10.00
Mono-ortho substituted PCBs												
PCB-105	0.43	0.61	0.00	2.64	2.11	7.00	1.15	1.48	0.00	8.49	3.46	11.00
PCB-114	0.31	0.88	0.00	4.56	1.54	3.00	0.89	1.61	0.00	13.84	2.68	3.00
PCB-118	0.04	0.13	0.00	1.43	0.22	1.00	2.49	6.32	0.00	54.23	7.47	3.00
PCB-156	2.84	2.09	0.00	20.47	14.02	15.00	2.86	3.08	0.00	17.74	8.59	12.00
PCB-157	2.33	3.48	0.00	37.64	11.50	9.00	2.73	4.99	0.00	44.40	8.21	10.00
PCB-167	0.16	0.45	0.00	3.81	0.78	1.00	0.13	0.27	0.00	3.81	0.40	2.00
PCB-189	0.41	0.95	0.00	4.47	2.00	4.00	0.00	0.00	0.00	0.00	0.00	0.00
I-PCBs												
PCB-28	4.45	2.36	0.00	9.40	21.96	25.00	7.59	3.58	1.23	22.26	22.82	28.00
PCB-52	4.49	3.89	0.00	13.29	22.12	22.00	7.81	6.14	0.00	22.73	23.48	27.00
PCB-101	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
PCB-138	1.03	1.91	0.00	20.15	5.09	5.00	2.01	2.88	0.00	15.41	6.04	6.00
PCB-153	1.10	2.27	0.00	19.19	5.41	9.00	1.26	3.32	0.00	37.85	3.78	3.00
PCB-180	0.47	1.34	0.00	15.10	2.33	1.00	0.00	0.00	0.00	0.00	0.00	0.00
∑DL-PCBs	8.74						14.60					
Mean of ∑DL-PCBs	0.79		0.00	2.84			1.33		0.00	2.86		
∑I-PCBs	11.54						18.68					
Mean of ∑I-PCBs	1.92		0.00	4.49			3.11		0.00	7.81		
∑PCBs	20.28						33.28					

of detected PCB congeners were 20.28 and 33.28 ng g^{-1}, respectively.

PCB-156 was the predominant congener among the DL-PCBs for both buffaloes 14.02% and cows 8.59%, followed by PCB-157 (11.50% in buffaloes and 8.21% in cows). PCB-169 and 126 accounted for 1.20% and 0.73% of the congeners in buffalo's milk samples, respectively whereas, PCB-118 and 169 were 7.47% and 4.77%, respectively, in cows. PCB-189 was not found in investigated milk samples of the cows.

Proportionally PCB-52 and PCB-28 represented 22.12% and 21.96%, respectively, of the I-PCBs in buffaloes' milk. In cows, PCB-52 and PCB-28 showed almost equal contribution to the I-PCB load with 23.48% and 22.82%, respectively. The percent contribution of PCB-138 to the total I-PCBs for buffaloes and cows' milk was 5.09% and 6.04%, respectively. PCB-101 was not detected in the samples examined.

The PCB pollution trend of the present study indicates that congeners from the group of I-PCBs including PCB-52 and 28 are predominant followed by PCB-156 from the group of DL-PCBs. The reason for the highest values of I-PCBs might be sources of these pollutants which include old contaminated buildings (Andersen et al. 2021), sealants used in construction (MECF 2022), iron and steel making plants (Odabasi et al. 2009), paints (Hu and Hornbuckle 2010), pigments, dyeing and chemical industry, various thermal processes (Lee et al. 2005), waste incineration (Kim and Osako 2004), e-waste (Fu et al. 2011), and agricultural activities (Mao et al. 2021), whereas PCB-156 has been used widely for insulation of various electrical equipment and as plasticizers (Agbo and Abaye, 2016). Plastic pollution is in itself a big issue in Pakistan (Mukheed and Khan 2020); hence, it supports the results of this present study.

Concentration profile of DL-PCBs in buffaloes and cow's milk

Calculation of DL-PCB profile for the milk samples (buffaloes and cows) indicated that mono-ortho congeners (PCB-105, PCB-114, PCB-118, PCB-156, PCB-157, PCB-167, and PCB-189) showed higher values than the non-ortho PCB congeners (PCB-77, PCB-81, PCB-126, and PCB-169). $\sum_{11}$DL-PCBs in buffaloes was 8.74 ng g^{-1} with an average (0.79 ng g^{-1}). Congener with the highest mean concentration was PCB-156, i.e., 2.84 ng g^{-1} (range LOD to 20.47 ng g^{-1}). High concentrations of PCB-156 point to the possible use and discharge of commercial PCBs as it is an important component of technical mixtures of Aroclor and Kanechlor (Kim et al. 2009; Malik et al. 2014). It was reported in a study conducted in New York that exposure to Aroclor 1254 was only related to PCB-156 (Seegal et al. 2011). The next highest concentrations of congeners were PCB-157 and PCB-169 with mean concentrations of 2.33 ng g^{-1} and 1.20 ng g^{-1}, respectively. DL-PCB congeners are mainly thought to be produced from industrial activities including coal-burning for sintering iron ore and steel manufacturing. The average concentration of PCB-126 in buffaloes' milk samples is 0.73 ng g^{-1} ranging between LOD and 4.11 ng g^{-1}. The potency of PCB-126, however, means that it is often the main contributor (up to 90%) to the toxicity of common PCB mixtures (Bhavsar et al. 2008; Chirollo et al. 2018; Zhang et al. 2012), and so its presence may have toxicological implications, even though it only made a small contribution in the overall PCB mixtures detected in the samples of the current study. PCB-77 was not detected in any sample. The PCB profile observed in the current study contrast with previous research conducted in Italy (Bertocchi et al. 2015) where PCB-118, PCB-105, and PCB-167 were reported to be present in bovine milk samples at higher concentrations, i.e., 3.00 ng g^{-1}, 0.85 ng g^{-1}, and 0.21 ng g^{-1}, respectively, whereas PCB-126, PCB-169, PCB-114, PCB-156, PCB-157, and PCB-189 were present in lower concentrations, i.e., 0.03, 0.00, 0.07, 0.41, 0.10, and 0.05 ng g^{-1} compared to the present work. Another Italian study conducted in 2010 also reported lower average concentrations of DL-PCBs in bovine milk, except for PCB-118 as compared to current work (Esposito et al. 2010). In a study from Chile surveyed for 3 years, the reported mean values for DL-PCBs were 0.1113, 0.079, and 0.070 ng g^{-1} in each year. All reported PCB congener values were also lesser than the mean of buffalo milk samples in this study (Pizarro-Aranguiz et al. 2015). This may be explained by the previous and current exposure of PCBs to various environmental matrices of the area under study (Naqvi et al. 2018; Syed et al. 2013) and calls for action against PCBs.

In cows, the $\sum_{11}$DL-PCBs was 14.60 ng g^{-1}, range LOD to 54.23 ng g^{-1}. All analyzed milk samples were predominantly polluted with PCB-156 with the average concentration being 2.86 ng g^{-1}. Congeners with the next highest mean concentrations were PCB-157 and PCB-118 with an average 2.73 ng g^{-1} and 2.49 ng g^{-1}, respectively. Other DL-PCBs which contributed significantly to cows' milk samples were PCB-169, 105, 81, 126, 114, 77, and 167 with mean concentrations 1.59, 1.15, 1.14, 0.92, 0.89, 0.70, and 0.13 ng g^{-1}, respectively. The concentration of PCB-126 was detected between LOD and 9.47 ng g^{-1} in milk samples of cows. PCB-189 was not found in milk samples collected under this study. A comparison of results of the present study with work done in Iran in 2017 indicates that the level of PCBs in the cows' milk in Iran is much higher (Ahmadkhaniha et al. 2017). However, these studies contrast with reports from Slovakia in 2020 where the values of the 7 types of PCBs analyzed were below LOQ (Toman et al. 2020). The comparison of all congeners in the present study with previous literature for $\sum$DL-PCBs has been shown in

Table S3 so that trends of contamination could be assessed which could provide preliminary data for making remedial plans in future.

Concentration profile of indicator PCBs in milk of buffaloes and cow

The Stockholm Convention for POPs recommended the investigation of 6 I-PCBs (PCB-28, 52, 101, 138, 153, and 180) to characterize the contamination in milk samples (IARC 2016). None of the samples investigated in this study surpassed the provisional value for the total concentration of I-PCBs, set by the European Union (EU), of 40 ng g^{-1} of raw milk (EU 2011). ∑I-PCB mean concentration in the milk samples of buffaloes is 1.92 ng g^{-1} ranging between 0.00 and 4.49 ng g^{-1}. Congener profile in buffaloes showed that PCB-52 and PCB-28 were present at the highest average values 4.49 ng g^{-1} and 4.45 ng g^{-1}, respectively, with percentage contribution of 22.12% and 21.96%. These high values may be indicative of nearby waste dumping sites, agricultural activities, and pigment industries as these are probable main sources of environmental PCB-52 and PCB-28 contamination (Hu and Hornbuckle 2010; IARC 2016). The next highest I-PCB congener concentrations were PCB-153, 138, and 180 with mean concentrations 1.10 ng g^{-1}, 1.03 ng g^{-1}, and 0.47 ng g^{-1}. These higher chlorinated PCB stay in the environment for long durations as they are difficult to degrade; hence, they might be considered as indicators of past exposure (Komprda et al. 2019). Manufacturing plants of iron and steel were also reported as potential sources for I-PCBs (Baek et al. 2010). PCB-101 was not found in the buffaloes' milk samples of the present study. ∑I-PCB average in cows was 3.11 ng g^{-1} range LOD to 7.81 ng g^{-1}. In the cows' milk samples, PCB-52 showed the highest mean value 7.81 ng g^{-1} tailed by PCB-28 with a mean concentration of 7.59 ng g^{-1}. The percent contribution of these congeners was 23.48% and 22.82%, respectively. PCB-138 and 153 show mean values of 2.01 ng g^{-1} and 1.26 ng g^{-1}, respectively. PCB-101 and PCB-180 were not detected in the cows' milk samples of the study areas tested in this study.

Research work done in California in 2017 presented lower values of I-PCBs when compared with the present study except for PCB-101 which was not detected in current work but was found (mean = 0.67 ng g^{-1}) in California. In the California study, of all of the analyzed I-PCBs in the milk samples, PCB-138 PCB-101 and 118 concentrations were the highest (Chen et al. 2017). The differences in I-PCB levels reported in the present study in comparison to previously published literature might be due to differences in season; rainy conditions are known to change PCB levels in soil and fodder crops; also, the feeding practices of buffaloes and cows differ greatly between countries and this might have impacted on levels and detection of PCB congeners. Another important factor that could influence the PCB contamination levels in milk is the days in lactation of the buffaloes and cows (Chen et al. 2017; Pérez et al. 2012; Roger Wabeke and Weinstein 1995). Table S4 shows the current study and previously published literature comparison for I-PCBs.

Toxic equivalency of dioxin-like PCBs

PCB congeners could be characterized concerning their extent of chlorination, substitution tendency, and affinity for binding to receptors. PCBs that show high attraction to aryl hydrocarbon receptor (AhR) are termed as DL-PCBs (Van den Berg et al. 2006). The toxic equivalency factor (TEF) is assigned to congeners after comparing with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) which is extremely noxious among all dioxins; hence, a toxic potency 1, i.e., TEF 1, is assigned (Chirollo et al. 2018). The concentration value of each congener was multiplied with its corresponding TEF and resulting TCDD equivalents express toxic equivalents validated through the WHO (Van den Berg et al. 2006). According to regulation (EC) No 1881/2006, milk and other dairy products should not contain more than 0.0055 ng TEQ g^{-1} fat DL-PCBs (Ahmadkhaniha et al. 2017). TEQ values are investigated for DL-PCBs (PCB-77, 81, 105, 114, 118, 126, 156, 157, 167, 169 and 189) (Table 2). The sum of DL-PCBs expressed as WHO TEQ_{2005} for buffaloes (0.11 ng g^{-1}) and cows (0.14 ng g^{-1}) sampled for the current study exceeded the recommended maximum. In the milk samples of both buffaloes and cows, PCB- 126 has the highest TEQ values i.e., 0.07 ng g^{-1} and 0.09 ng g^{-1} TEQ_{2005}, respectively. PCB-169 has a value at the second highest level in buffaloes and cows, i.e., 0.03 ng g^{-1} and 0.05 ng g^{-1} TEQ_{2005}, respectively. These values exceed the given limit of 0.0055 ng g^{-1} by EU (2011). The PCB TEQ values seen in the current study are higher than previous reports such as 0.00051 ng g^{-1} in Polish milk samples taken from cows (Piskorska-Pliszczynska et al. 2012) and 0.00389–0.00595 ng TEQ g^{-1} fat for DL-PCBs in Italian buffaloes' milk samples (Chirollo et al. 2018). `

Spatial dispersal patterns and sources of PCBs in bovine milk

The distribution patterns of PCBs in buffaloes and cows' samples from the 8 districts of Punjab, Pakistan, included in the current study are depicted in Fig. 1, whereas percentage contributions of ∑DL-PCBs and ∑I-PCBs in different districts of Punjab are shown in Fig. 2a and b, respectively. The PCB profiles differed significantly ($p < 0.05$) among the studied districts. Owing to the multiple uses of PCBs as dielectric fluids, plasticizers, flame retardants, adhesives, and electric insulation, they may be intentionally manufactured

Table 2 TEQ values for dioxin-like PCBs (DL-PCBs) (ng TEQ g^{-1}) in milk samples of buffaloes and cows

		Buffaloes		Cows	
DL-PCBs	TEF (2005)*	Mean	TEQ	Mean	TEQ
PCB 77	0.0001	0.00	0	0.70	6.99354E – 05
PCB 81	0.0003	0.29	8.75E – 05	1.14	0.000342439
PCB 126	0.1	0.73	0.072727	0.92	0.092482168
PCB 169	0.03	1.20	0.035859	1.59	0.047621126
PCB 105	0.00003	0.43	1.28E – 05	1.15	3.45763E – 05
PCB 114	0.00003	0.31	9.35E – 06	0.89	2.67133E – 05
PCB 118	0.00003	0.04	1.34E – 06	2.49	7.4557E – 05
PCB 156	0.00003	2.84	8.53E – 05	2.86	8.57733E – 05
PCB 157	0.00003	2.33	7E – 05	2.73	8.19604E – 05
PCB 167	0.00003	0.16	4.76E – 06	0.13	3.94991E – 06
PCB 189	0.00003	0.41	1.22E – 05	0.00	0.00
Sum		8.74	0.11	14.60	0.14
Mean		0.79	0.01	1.33	0.01
Min		0.00	0.00	0.00	0.00
Max		2.84	0.07	2.86	0.09

* Van den Berg M et al. (2006)

by industries (Perugini et al. 2012). PCBs are emitted into the atmosphere by production, storage, and disposal facilities, but they can also leak accidently (Schmid et al. 2003). The released PCBs may deposit and accumulate in the plants, soil, and water, which act as natural sinks. The presence of PCBs in water, soil, and plants makes these contaminants available for animals to eat when grazing (Esposito et al. 2010).

The highest average ∑PCB concentrations after analyzing all samples from buffaloes and cows were observed in the Okara district. The investigated high levels of PCBs in the milk of this area might be due to adjacent highway and the industries (cotton, pharmaceutical, marble and granite, plastic, zari, and agro factories) present within 5 km of the dairy farm sampled (maps 2021). Being an agricultural area, past usage of PCB-based pesticides, wood, and solid waste burning practices may also have added to the PCB level of this site (Naqvi et al. 2020). The second highest values in buffalo contaminated milk were observed in Multan making up 15.44% of the total ΣPCB concentration. In cows' milk, the second place was held by Sialkot making up 18.19% of total ΣPCB concentrations for cow milk samples in the current study. Lighter PCB homologs (mono- to hexachlorobiphenyls) are linked to few common practices including the burning of agricultural waste, cow dung, and wood (Balasubramani et al. 2014; Weber et al. 2018).

In milk samples of buffaloes, ∑DL-PCBs were predominant at district Lahore with a 21.39% contribution. It might be due to heavy traffic and dense population (Mumtaz et al. 2016). Another study highlighted the adverse PCB contamination in this site especially near industrial and waste dumping areas (Syed et al. 2014). A study conducted on the indoor environment of district Lahore also reported high levels of PCBs as compared to other parts of the country (Aslam et al. 2021). It was followed by Multan and Faisalabad with 17.45% and 16.86% contributions. In cows, the highest ∑DL-PCBs were found in Sialkot followed by Gujrat and Okara with the contribution of 21.65%, 21.17%, and 20.34%, respectively. Many industrial setups are present in the city and surrounding areas of the Sialkot district, and they might release PCBs into the surrounding environment which could be a reason for high results (Mahmood et al. 2014b). Among I-PCBs (Fig. 2b), predominant values were detected at district Okara which was followed by Gujrat by percentages of 23.06% and 19.59% in the milk of buffaloes; in the same way, cows' milk also showed predominant values in district Okara tailed by Kasur and Sialkot by percentage contribution 21.08%, 16.68%, and 15.49%, respectively. A generalized view is that bovines take up PCBs primarily from the feed but there are other known and unknown sources as well which might contribute towards the PCB levels (McLachlan 1993). District Multan also contributed significantly with 14.26% and 14.52% of I-PCBs in buffaloes and cows in the province Punjab. This is strengthened by another study, which showed air samples from Multan urban areas with the highest PCB values (Ali et al. 2015). Urban activities in the cities could also be a major source of atmospheric PCB emissions (Ali et al. 2015) and PCB atmospheric deposition may affect plants and livestock feed greatly (Toman et al. 2020). In the Sahiwal district, within a 20-km distance of the sampled dairy farm, no industrial area or other large-scale commercial activity was identified. Unintentional sources of PCB emissions including wood and coal combustion (Gullett et al. 2003; Lee et al. 2005), steel plants (Odabasi et al. 2009), e-waste (Wang et al. 2016), and incineration of domestic solid waste (Kim and Osako 2004) could be the reason of contamination of the milk samples. The difference between values observed in buffaloes and cows could be due to the variation in food sources and the surrounding environment. Moreover, eating practices of buffaloes and cows differ between locations by their probable impacts on various levels and PCB exposure. Dumping of residential waste, combustion of waste, electric equipment, PVS, vehicle fuel openly, and other chemical processes may be practiced in the majority part of the study areas. PCBs found in human beings greatly depend upon lifestyle and the degree of industrialization. In a study conducted on the Indus River basin, the highest soil PCB concentrations were observed at the agricultural sites (Ali et al. 2015). When the main sources of emissions like incinerators, dumpsites, and dielectric fluids are not present in the study area (Pérez et al. 2012), then the levels of PCB should fall in the permissible limit range. Nevertheless, the current results point towards

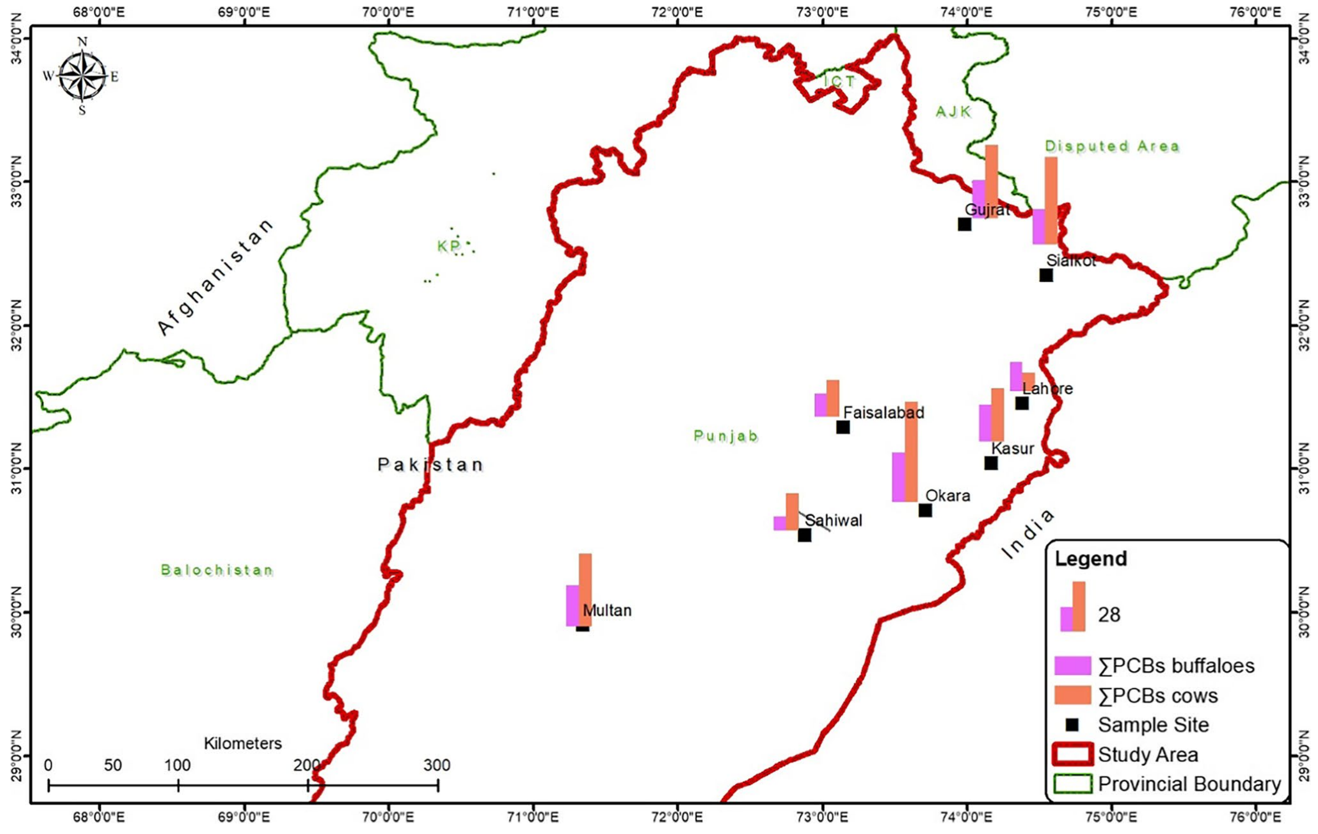

Fig. 1 Spatial distribution of ∑PCBs in buffaloes and cows

the existence of other unintended sources and emissions. Thus, it is recommended to maintain surveillance on products used for agriculture and continuous monitoring.

Health risk assessment

Non-carcinogenic risk

None of the milk samples shows EDI exceeding the corresponding ADI limits for both children and adults. For each investigated analyte, the EDI values were higher in children than adults for all milk samples. Among DL-PCBs, PCB-126 showed the highest EDI values 0.72 and 1.57 ng kg^{-1} day^{-1} (for adults and children) using buffaloes' milk whereas 0.92 and 2.00 ng kg^{-1} d^{-1} (adults and children) using cows' milk, respectively, but lower than ADI 5.5 ng kg^{-1} throughout this work (Table 3). This high value of PCB-126 may be because of its non-metabolic degradation and these results were also following a study conducted on buffaloes in Italy (Chirollo et al. 2018). ADI of DL-compounds in Dutch people aged between 20 and 25 years, 2.3 and 2.0 pg TEQ kg^{-1} BW day^{-1} males and females, respectively, was found by Patandin (1999). Two groups of children were studied (1–5 years and 6 and 10 years), and the EDI was higher than in young ones. Similar results were presented by Wittsiepe et al. (2001) in a similar study conducted in Germany with children 14 to 47 months of age.

No sample in the current study crossed the ADI limits of 40,000 ng/kg for the I-PCBs under study. PCB-28 and 52 in buffaloes' milk showed EDI values of 44.53 and 44.86 ng kg^{-1} day^{-1} in adult people and 96.45 and 97.17 ng kg^{-1} day^{-1} in children, whereas cows' milk 75.94 and 78.14 ng kg^{-1} day^{-1} in adults and 164.49 and 169.26 ng kg^{-1} day^{-1} in children, respectively. PCB-138 showed a value (43.54 ng kg^{-1} day^{-1}) aimed at kids consuming cows' milk (Table 3). PCB-28 are reported to cause developmental neurotoxicity in humans above the ADI (Leijs et al. 2019). In two studies conducted in Brazil on I-PCBs, the EDI value of ∑I-PCBs in raw milk was 1.21 ng kg^{-1} and in milk powder was found to be 110 ng kg^{-1}; both results were lower than the present study values for I-PCBs (Costabeber et al. 2018; Heck et al. 2007).

Carcinogenic risk

The potential of PCB-contaminated milk to cause cancer is based on cancer benchmark concentration (CBC). Cancer risk, categorized to be one in a million and hazard ratio

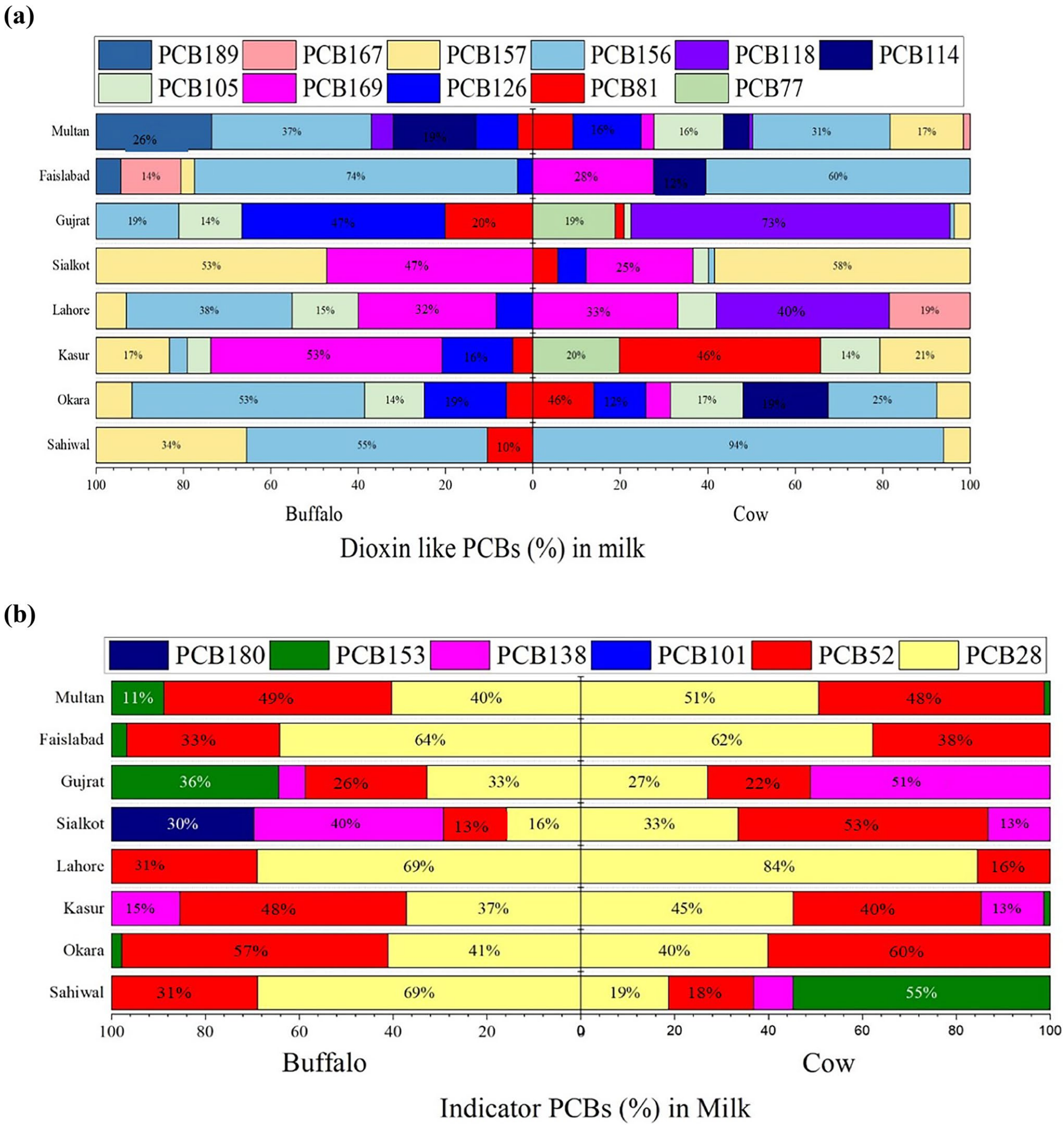

Fig. 2 Spatial distribution of **a** DL-PCBs (%) in buffaloes and cows and **b** I-PCBs (%) in buffaloes and cows

(HR > 1), is estimated from CBC for analyzing cancer-causing effects in humans (Dougherty et al. 2000). For detailed analysis, vulnerable groups especially children should be included in the process of assessment of the risk. The uptake of the pollutants may vary with age. The food and body weight ratio of children is higher than adults so a large amount of DL-PCBs could be ingested. As the children grow up, the dose per unit body weight decreases whereas the consumption per day increases and remains almost the same over 20 years of age (WHO 2000).

Table 4 represents the results calculated for carcinogenic risk based on the current study. The consumption of milk from different areas of the Punjab province that is contaminated with the ∑DL-PCBs does not pose a cancer threat to adults and kids as the HQ calculated was less than 1. But the results for ∑PCBs including both ∑DL-PCBs and ∑I-PCBs

Table 3 EDI (ng kg^{-1} day^{-1}) for dioxin-like PCBs (DL-PCBs) and indicator PCBs (I-PCBs) in milk samples of buffaloes and cows

	Buffaloes		Cows		Standard
	Adults	Children	Adults	Children	
DL-PCBs					
PCB-77	0.0000	0.0000	0.0007	0.0015	5.5 ng kg^{-1}
PCB-81	0.0009	0.0019	0.0034	0.0074	
PCB-126	0.7273	1.5753	0.9248	2.0032	
PCB-169	0.3586	0.7767	0.4762	1.0315	
PCB-105	0.0001	0.0003	0.0003	0.0007	
PCB-114	0.0001	0.0002	0.0003	0.0006	
PCB-118	0.0000	0.0000	0.0007	0.0016	
PCB-156	0.0009	0.0018	0.0009	0.0019	
PCB-157	0.0007	0.0015	0.0008	0.0018	
PCB-167	0.0000	0.0001	0.0000	0.0001	
PCB-189	0.0001	0.0003	0.0000	0.0000	
I-PCBs					40,000 ng kg^{-1}
PCB-28	44.53	96.45	75.94	164.49	
PCB-52	44.86	97.17	78.14	169.26	
PCB-101	0.00	0.00	0.00	0.00	
PCB-138	10.32	22.36	20.10	43.54	
PCB-153	10.97	23.77	12.58	27.26	
PCB-180	4.72	10.22	0.00	0.00	

Table 4 Hazard ratio for carcinogenic risk

	Buffaloes		Cows	
	Adults	Children	Adults	Children
DL-PCBs	0.01	0.03	0.01	0.04
∑PCBs	0.58	2.73	0.94	4.42

showed a cancer risk for kids in milk samples collected from both buffaloes and cows as the HQ was greater than 1. The HQ values exceeded one for PCBs indicating a high risk for infants (Devanathan et al. 2011).

Hence, it could be said that milk from Punjab, Pakistan, is safe to use for adults but it may cause risks for children. Previously, carcinogenic risk due to consumption of rice contaminated with PCBs was also reported in Punjab province (Mumtaz et al. 2016). As the significant level of PCBs is reported and detected in Pakistan's environmental matrices, therefore, implementation of educational and awareness activities in the study area might increase the knowledge of local people about the risks and hazards associated with the release of PCBs into the environment, including aspects like major emission sources and how exposure of these could be avoided.

Conclusion

The current study was conducted on buffaloes and cows for evaluating the prevalence of DL-PCBs and I-PCBs in their milk and the health risk assessment of human beings who consumed the contaminated milk. This research work has not been conducted previously up to the best of our knowledge in Punjab, Pakistan. Results of the study are also important as they reveal that the consumption of milk of Punjab, Pakistan, with high levels of DL-PCBs might lead to adverse health effects in children. The current study showed TEQ values of ∑DL-PCBs for buffaloes and cows' milk samples to be 0.11 ng g^{-1} and 0.14 ng g^{-1}, respectively. These investigated values are higher than the standard 5.5 pg g^{-1} given by the EU commission regulation. Current findings indicate the complexity and regional variability of PCB profiles and sources in bovine milk. The potential non-carcinogenic adverse health effects were calculated and should be emphasized in the sampling areas. The possible cancer risk posed to children is significant. Intentional and unintentional emission of PCBs from industries, burning of wood, coal, and poor waste disposal techniques appear to be the main source for PCBs in bovine milk in most sampling areas. The authors recommend continuous monitoring and reduction of PCBs in the environment to minimize exposure.

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Author contribution Saman Sana: conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, resources, roles/writing — original draft, and writing — review and editing; Abdul Qadir: conceptualization, funding acquisition, investigation, methodology, project administration, supervision, resources, validation, visualization, roles/writing — original draft, and writing — review and editing; Neil P. Evans: funding acquisition, methodology, resources, analytical support, software, validation, visualization, and writing — review and editing; Mehvish Mumtaz: investigation, data curation, formal analysis, visualization, review, and editing; Ambreena Mubashir: methodology, data curation, GIS analysis; map development, visualization, review, and editing; Amjad Khan: visualization, sample collection, review, and editing; Saif-ur-Rehman Kashif: visualization, methodology validation, sample collection, review, and editing; Habib ur Rehman: visualization, methodology, validation, review, and editing. Muhammad Zafar Hashmi: visualization, methodology, validation, review, and editing.

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Data availability Datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

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Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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