Biomedical Research 2020; 31 (6): 164-175

ISSN 0970-938X
www.biomedres.info

Quantification of PCB in the serum of patients with breast cancer and its correlation in the soil of their place of residence.

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Abstract

Polychlorinated biphenyls (PCB) are highly lipophilic compounds and persistent in the environment, which converts them into substances able to accumulate in the food chain and persistent contaminants in soil, air, and water. Our objective was to determine the concentration of PCB in the serum of patients with Breast Cancer (BC) and its correlation with PCB in the soil of their homes in different areas of the Comarca Lagunera region in Mexico. With non-probabilistic sampling, we selected the homes of subjects with and without BC. In 20% of cases, the diagnosis was carried out 25 and 39 years of age. Sample analysis was by Gas-mass Chromatography (GC). The concentration of the different congeners was similar between the samples of household soil in cases and controls, with a sole exception with marginal significance (p=0.056), that is, congener 52, was greater in the cases. The highest concentrations found in soil in the study were for congeners 118 and 138. The highest risk found for BC was congener 195; however, it was not statistically significant, similar to the other congener quantified in soil. The correlation analysis between PCB serum concentrations and that of the soil exhibited a low concentration, the highest being for congener 101. The concentrations in serum of the 13 congener were significantly greater between cases and controls. No risk association was found among the individual concentrations of the 41 congeners' PCB or among total PCB neither in soil nor with BC.

Keywords: Polychlorinated biphenyls, Contamination, Industry, Public health.

Accepted on September 03, 2020

Introduction

Among the Persistent Organic Contaminants (POC), we find the Polychlorinated biphenyls (PCB), due to their great production and toxicity, their being highly lipophilic, their being substances able to accumulate in the food chain and their being soil, air, and water contaminants. In the U.S. states of Illinois and Alabama, between 1929 and 1977, more than 700,000 tons of PCB was produced [1]. The Criteria of Environmental Health evaluate the dose-response relationship of cancer for PCB [2,3]. In Japan, 59,000 tons were produced between 1930 and 1970 [4].

In 2007, Mexico developed the National Implementation Plan (PNI) of the Stockholm Accord on POC, among the Ministries of the Environment and Natural Resources (SEMARNAT) and of Agriculture, Livestock, Rural Development, Fishing, and Food (SAGARPA, México), through the National Service for the National Health for Food Safety and Food Quality (SENASICA), and organizations of the civil society, in the Mexican states of Coahuila, Jalisco, and Baja California, which are known as temporary PCB storage areas [5]. In addition, during the past 35 years, the industrialization processes of the northern Border States have generated millions of tons of dangerous residues [6]. Under certain conditions of exposure to chemical substances and inadequate management, risks can be represented for the environment and human health [7]. The estrogenic activity has been quantified of BPC detected in human tissue, including the regulation associated with the estrogen receptor with the endogenous hormone 17β-estradiol, finding the estradiol- equivalent exposure higher in air [8-10]; in fact, these have been considered endocrine disruptors [11-13]. Obesogenic properties have been attributed to exposure to bisphenol A, altering lipid metabolism [13]. Environmental contamination and the existence of PCB is a worldwide problem, with the great industrialized cities the most contaminated, among these Mexico City (CDMX) [14,15].

The industrial development in the North of Mexico leads to elevated levels of contamination in air, water, and soil, affecting the health of humans due to damage to the ecosystem. Because there is little information in Mexico on the study of PCB, it is necessary to conduct studies that support knowledge of what carcinogens are. The objective of this study was to carry out the quantification of PCB in serum in patients with Breast Cancer (BC) and its correlation in the soil of the place of residence of these patients in different areas in the North of Mexico.

Materials and Methods

The present investigation was approved by the Ethics Committee in Investigation (approval no. 123301538X0201 COFEPRIS). By means of non-probabilistic sampling, we selected the addresses of subjects with and without BC, according to the subjects included in the clinical phase of a previous study to evaluate the association of serum BPC with BC. First, we identified the participants included in the clinical study. We obtained their addresses and selected those who resided within the urban zone of the Laguna and in suburban areas. We visited the selected households and spoke with the study participants to request authorization for the sampling of the earth (soil) in their exterior and/or interior gardens/yards. Once authorized, we proceeded to take soil samples considering 20 cm in depth according to the technique described later. The serum PCB levels of the subjects were taken from the existing registries of the clinical study. We performed a correlation of the results in serum and soil. We stratified the study participants' addresses according to the distance of the households from the possible PCB-emitter sites. This distance was considered to be when the participants lived approximately 1 km in distance from these sites.

Measuring technique of the PCB

Soil sampling and analysis

Sample preparation: We took approximately 500 g of the upper soil layer (0-20 cm). The sample was collected in aluminium foil free of PCB contamination, packed, labelled with their respective name, kept in individual plastic bags, leaving these too dry for 72 h.

Screening: With the purpose of homogenizing the sample, once dry, the sample was ground in a mortar and subsequently passed through a sieve 2 mm in diameter. These samples were stored in aluminium foil at room temperature until their analysis.

Extraction: We weighed 1 g of the soil sample and placed this into Green-Chem glass flasks and LEV of the microwave oven, adding a Carboflon, the internal standard (PCB 141 C13), and 14 mL of methylene chloride. The PCB is extracted by means of the microwave program as follows: 10 min of ramp to reach 120oC, maintaining this for 30 min. On concluding the extraction time, the flasks are left to cool at 4oC for 24 h. The samples were filtered through Whatman no. 1 paper, and the filtered material was evaporated at 37oC with a soft nitrogen current up to 4 mL. In order to ensure the elimination of the methylene chloride, we added 5 mL of hexane, and this continued to be evaporated until 2 mL, three times.

Cleanliness: After extraction with microwaves, cleansing is conducted with florisil; the florisil cartridges (1,000 mg/6 mL Phenomenex) were added to 10 mL of hexane, with additions two different times (5 mL at the beginning and 5 mL at the end), without permitting the cartridge to dry. The sample is shaken in vortex for 30 s and then passed through the cartridge, without the application of vacuum, the tube is rinsed with 1 mL of hexane, and the florisil cartridge is added. The PCB are retained in the florisil for their later elution with 12 mL of 6% diethyl ether:hexane, adding these twice.

Concentration phase: The eluate was evaporated with soft nitrogen current at 37°C, until reaching a volume of 0.1 mL, which is placed in a vial for their injection into the chromatograph.

Chromatographic analysis

With standard solutions of individual congeners (Ultra Scientific Analytical Solutions, North Kingstown, RI, USA), we obtained a mass spectrum of the 41 PCB utilized by SCAN mode, to determine the ions and retention times of each compound, which were utilized for quantification in the samples, which was performed with Selective Ion Monitoring (SIM), employing a mixture of 41 Accustandard PCB (C-QME-01, Québec (Ministry of Environment Congener Mix) to perform the calibration curves.

Temperature ramp: The samples are injected by means of the pulsed split method, with a temperature program in the microwave oven that starts at 100oC and is maintained for 2 min, followed by a ramp of 20oC/min up to 200oC that is maintained for 0 min, after a temperature ramp of 15oC/min up to 310oC that is maintained for 5 min. Detection limits were obtained of 0.2-2.1 ppbs. The calibration curve presented a linear concentration curve of 2-100 ppbs, with which we obtained recovery percentages of 82%-119% for the EC-2 Reference Certificate Standard for the A Lake Ontario Blended Sediment for Toxic Organics of the National Water Research Institute, Canada.

Equipment: We employed a microwave oven for extraction and digestion (CEM–MARS), and a Hewlett-Packard Gas Chromatograph with the HP model 5973 Mass Selective Detector and the HP 6890® Auto-Sampler. Carboflon is utilized for the extraction of organic compounds that are non-polar solvents (transparent), heating inserts of Carboflon®, which allow for the efficient heating of non-polar solvents. Carboflon® is an inert fluoropolymer filled with an absorbent microwave material. The insert is placed in the extraction recipient to permit the use of non-polar solvents without the need to add additional solvents.

Chromatographic analysis

Study design: An epidemiological case: control study was proposed to be conducted at the Comarca Lagunera. All women complying with the study criteria, with primary BC and/or benign pathologies of the breast were invited to participate in the study. To women who voluntarily came to participate in the study, we applied a questionnaire that included sociodemographic, occupational, reproductive history, familial antecedents of cancer, and lifestyles. A sample of blood was taken from each of these women. Sample size was calculated according to the corresponding table for paired case: control studies. The parameters utilized to calculate the "n" were adjusted in the following manner: proportion of exposure of the controls 40%, an alpha of 0.05, study power at 80%, and capacity to detect an Odds Ratio (OR), 2. We utilized the Epi-Data computer program to estimate the number of participants to recruit, these being 70 cases and 70 controls.

Selection of the population: All of the patients who came to the Gynecology/Oncology Breast Clinic for a consultation due to unspecific breast tumor, at the Hospital General de Zona Nº 16 and 18 of the IMSS, Hospital General Universitario, Hospital General del ISSSTE, SSA de la Ciudad of Torreon, Coahuila, and Hospital General de Zona Nº 46 and 51 of Gómez Palacio, Durango, were invited to participate in the study. According to the anatomopathologic diagnosis, the participants were divided into two groups as follows:

Group 1 (controls): women with benign breast pathologies and whose medical treatment necessarily requires surgical intervention.

Group 2 (cases): Patients diagnosed for the first time with BC and who require surgical intervention.

In terms of the cases, we included women aged between 20 and 70 years who accepted to participate in the study. We considered controls as women similarly to their respective case, also residing in the same area (the colony for the city dwellers and the community for the rural dwellers) and who do not have previous antecedents of prior cancers or with a diagnosis of premalignant lesions.

Collection and storage of the biological serum samples

Serum: From each of the participants and prior to any medical intervention, we took 20 mL of peripheral venous blood by Vacutainer tubes for pesticides without anticoagulant. After retraction of the clot, the sample was centrifuged at 2,000 rpm for 10 min to obtain the serum. Serum aliquots were made, obtained, and deposited in amber polypropylene vials that had been previously washed with acetone/hexane and refrozen at -70ºC until their analytic processing (quantification of PCB and total lipids).

Analytic procedures

Quantification of total lipids in serum and tissue: The concentrations of total lipids were quantified by means of commercial colorimetric kits (Aldrich/SIGMA) utilizing a UV/Vis spectrophotometer (HACH model XT5000).

Quantification of PCB in biological samples: For the process of extraction and quantification of PCB, we utilized 5 mL of serum following the method proposed and validated by the U.S. Environmental Agency (EPA) (method 1668) [3]. The biological samples were fortified with marked standards, certified and assessed by the EPA (Wellington Laboratories & Accustandard, USA). The 20 congeners evaluated were those that had been related bibliographically with an increase in the risk for cancer and those most frequently found in humans (28, 52, 81, 99, 105, 114, 118, 123, 126, 128, 138, 153, 156, 169, 170, 180, 183, 187, and 157).

Extraction methodology of PCB in serum: This technique for PCB extraction is a complement of the 1668-EPA standard protocol [3]. Generally, it begins by placing 2 mL of problem serum in an assay tube measuring 13 x 100 with a screw cap. These are fortified at a concentration of 30 ppb of the standard that contains a mixture of congeners. The samples are conserved under refrigeration at 4ºC, which were also protected from light until their analysis. The analysis is performed for 20 congeners (8, 18, 28, 52, 44, 66, 101, 77, 118, 153, 105, 138, 126, 187, 128, 180, 170, 195, 206, and 209) [16]. For the calibration curve, we fortified the PCB-free serum at concentrations of 20, 30, 40, and 50 ppb with a mixture of standards; the samples were conserved under refrigeration at 4ºC, protected from light.

Extraction: From the fortified sample, we added 5 ml of HPLC-grade hexane. These were placed in a vortex during 2 h for their homogenation in order to extract the PCB to be analyzed. When this time was over, these were left to rest for 10 min; afterward, we proceeded to centrifuge them for 5 min at 2,500 rpm. After separating the hexane, this was placed in a clean conic tube with a cap protecting it from the light. Two mL of hexane were again added for mixing, at 2,500 rpm for 5 min and a 10-min rest. On separating the hexane from the serum, there was a final volume of 7 mL.

Concentration phase: The hexane extracts were placed in a double boiler at a temperature of 70ºC until the hexane was concentrated at a volume of 0.8 mL; then it was left to cool. The 0.8 mL was a weighed in a vial and saved at 1 mL with pesticide-grade hexane.

Gas chromatography with electron uptake detector: Chromatographic analysis. From the standard solution of congeners (Congener Mix; AccuStandard, CT, USA), we obtained the chromatograms of the 20 PCB utilized for identifying the retention times of each component that were employed for sample quantification, using Gas

Chromatography with an electron uptake detector (Auto System XL Gas Chromatograph; Perkin Elmer) with an autosampler, separating the compounds into a column of 60 m with ID 0.53 mm, carrying out calibration curves [17,18].

Temperature ramp: The samples are injected by the pulsed split method [19], with a temperature program in the microwave oven that begins at 100ºC maintained for 3 min, followed by a ramp of 25ºC/min up to 245ºC that is maintained for 20 min, after this a ramp of 1ºC/min was maintained for 0 min. We obtained detection limits of 0.65-3.16 ppb. The calibration curve presented a linear concentration interval of 1-100 ppb, with which we obtained recovery percentages of 80% for the certified standard of reference (Congener Mix; Accutandard, CT, USA).

Statistical analysis: Evaluation of the exposure was carried out by means of the quantification of serum and in soil of the chemical compounds-for-study and through the application of the questionnaire designed for this purpose. Based on the concentrations of PCB, the participants of both groups were subdivided into tertiles for their later statistical analysis. The independent and dependent variables were described according to their frequencies and means of distribution. The differences between means were established using non- parametric Mann–Whitney U tests, bivariate analysis, and the Pearson correlation. To establish the differences between the two groups of each of the dependent variables, parametric and non-parametric tests were employed according to the case. The means of crude association were calculated, the dependent mean with each of the independent means, the measurements of adjusted association, dependent vs. independent, and each Covariables. Covariables that exhibited a modification of 10% on the association measurement, in this case the Odds Ratio (OR). We calculated the best regression model for the evaluation of BC and its main risk factors. It was determined that the risk factors entertained a more important specific weight in the disease burden. The measurements that expressed the association were the OR and the 95% Confidence Intervals (95% CI).

Results

The average age of the cases was significantly higher (p<005) than that of the controls. Likewise, the cases presented a BMI higher than that of the controls (Table 1)

Table 1: *General characteristics of the women included in the study.*

Variables	Cases (n = 70)	Control (n =70)	OR	IC	p*
Age	49.71 (12.3)	42.1 (13)	1.04	1.01-1.07	0.0005
BMI**	29.0 (5.0)	27.7 (5.3)	1.04	0.9-1.1	0.03

*Mann-Whitney U test; **BMI: Body Mass Index (weight/height2).

Serum Concentrations of PCB: With respect to the level of PCB in serum, at least one congener was detected in 77% of the participants. The four most frequently found congeners were 105 (44.3%), followed by 187, 206 (43.6%), and 195 (42.9%), while those least frequently found were 8 and 18 (25%). The congers detected at high concentrations among the subjects studied were 180 (15.26 ppb), 18 (5.09 ppb), 44 (3.72 ppb), and 126 (3.47 ppb). When the concentrations of the PCB congeners were compared between the groups, it was found that 13 congeners (8, 18, 52, 105, 118, 128, 138, 170, 180, 187, 195, 206, and 209) were significantly greater (p <0.05) among the cases than among the controls (Table 2).

Table 2: *Serum PCB concentration by study group.*

Congener	Cases(n=70)	Control(n=70)	p*
8	0.561 (0.32-0.98)	0.506 (0.21-1.20)	0.032
18	0.477 (0.28-0.79)	0.551 (0.29-1.03)	0.039
28	0.368 (0.21-0.62)	0.616 (0.42-0.90)	0.239
52	0.401 (0.23-0.69)	0.469 (0.19-1.13)	0.017
44	0.437 (0.29-0.64)	0.612 (0.30-1.23)	0.383
66	0.946 (0.72-1.24)	0.749 (0.50-1.10)	0.406
101	0.649 (0.45- 0.93)	0.604 (0.44-0.81)	0.501
77	0.383 (0.24-0.59)	0.796 (0.58-1.08)	0.676
118	0.513 (0.32-0.80)	0.234 (0.11-0.49)	0.003
153	0.459 (0.28-0.74)	0.535 (0.34-0.84)	0.140
105	0.622 (0.45-0.84)	0.578 (0.33-0.98)	0.012
138	0.587 (0.42-0.80)	0.241 (0.11-0.50)	0.002
126	0.581 (0.39-0.85)	0.472 (0.30-0.72)	0.115
187	0.728 (0.48-1.08)	0.521 (0.37-0.72)	0.045
128	0.341 (0.23-0.49)	0.260 (0.09-0.68)	0.0001
180	0.579 (0.37-0.90)	0.393 (0.26-0.58)	0.0000
170	0.637 (0.45-0.88)	0.259 (0.11-0.57)	0.0000
195	0.637 (0.47-0.85)	0.445 (0.30-0.64)	0.0010
206	0.604 (0.42-0.85)	0.353 (0.20-0.61)	0.0000
209	0.524 (0.33-0.82)	0.213 (0.07-0.61)	0.0000
PCB Total	5.268 (3.50-7.90)	3.331 (2.37-4.67)	0.0167

*Mann Whitney Test. Results are expressed as geometric mean (IC 95%).

Concentration of PCB in Soil: The three most frequently found congeners were 18, 118, and 105 (52.4%) and those not found in any of the samples analyzed were congeners 206 and 209 (0%). The highest concentrations found in the study were for congeners 118 (62.27 ppb) and 138 (63.23 ppb). When the concentration of the congeners of PCB were compared between groups, these were not different (p >0.05) (Table 3).

***Table** 3: Concentration of PCB in soil by study group.*

Congener	Cases(n=29)	Control(n=32)	p*
18	2.43 (1.13-5.23)	2.32 (0.953-5.67)	0.219
17	0.53 (---)	0.56 (---)	0.943
31	1.39 (0.874-2.23)	1.01 (0.408-2.54)	0.183
28	0.514 (0.358-0.738)	0.573 (0.152-2.14)	0.526
33	2.6142 (1.26-5.40)	1.38 (0.018-04.83)	0.898
52	0.582 (0.248-1.36)	0.956 (0.229-3.99)	0.056
49	0.309 (0.067-1.43)	1.47 (0.258-8.38)	0.351
44	0.955 (0.446-2.04)	1.80 (0.528-6.18)	0.734
74	2.14 (1.90-2.40)	3.68 (2.13- 6.33)	0.285
70	0.350 (0.151-0.815)	0.807 (0.140-4.65)	0.525
95	1.52 (0.643-3.61)	2.29 (0.266-19.84)	0.399

101	1.26 (0.239-6.72)	1.47 (0.198-10.95)	0.848
99	1.02 (0.079-13.24)	0.809 (0.016-9.07)	0.875
87	1.31 (0.077-22.16)	2.34 (0.002-691.7)	0.568
110	0.657 (0.266-1.62)	0.967 (0.210-4.44)	0.294
151	0	4.47 (---)	0.301
82	0.407 (0.192-0.864)	0.619 (0.232-1.64)	0.977
149	1.19 (0.257-5.56)	1.35 (0.013-32.22)	0.623
118	2.63 (2.03-3.41)	2.92 (1.75- 4.88)	0.405
153	1.09 (0.529-2.26)	0.880 (0.151-3.36)	0.082
132	1.46 (0.573-3.73)	6.17 (0.0001-3.63)	0.151
105	1.69 (1.32-2.16)	1.75 (1.09-2.80)	0.278
138	2.30 (1.03-5.11)	2.23 (0.694-7.18)	0.689
158	0.767 (0.375-1.56)	1.13 (0.393-3.24)	0.168
187	0	0	0.0
183	0.708 (0.068-7.37)	0	0.251
128	0	0	0.0
177	2.58 (1.18-5.61)	3.37 (1.66-6.85)	0.384
171	2.56 (0.955-6.88)	1.79 (0.534-6.02)	0.524
156	0.700 (0.109-4.49)	0.613 (0.148-2.52)	0.460
180	0.528 (0.221-1.26)	1.45 (0.332-6.37)	0.329
191	0	1.39 (0.059-32.65)	0.597
169	2.33 (1.52-3.56)	2.21 (1.14-4.29)	0.791
170	3.24 (1.39-7.58)	2.48 (1.19-5.17)	0.770
201	0	0	0
208	1.65 (0.279-9.77)	0.658 (0.006-5.03)	0.385
195	0.704 (0.104-4.75)	0.49 (---)	0.138
209	0	0	0
194	0.406 (0.033-4.91)	1.33 (0.296-6.04)	0.988
205	1.05 (0.283-3.91)	0.751 (0.196-2.87)	0.959
206	0	0	0
PCB Total	16.49 (10.72-25.38)	22.55 (11.26-5.14)	0.197

*Mann Whitney Test. Results are expressed as geometric mean (IC 95%).

No association of risk was found among the individual concentrations of the 41 congeners of PCB in soil or with total PCB with BC (Table 4). Table 5 shows the correlation coefficients between the concentrations of the 10 common congeners in serum and soil in the studied population. The highest correlation found was in the case for congener 101, and the lowest, for 52. In the PCB concentrations, significance (0.03) was found for congener 177 between living and not living near an emitter industry (Table 6).

Table 4: *Risk for each congener and total PCB in soil.*

Congener	OR (Odds Ratio)	IC (95%)
18	1.02	0.926-1.13
17	1.27	0.009-178.90
31	1.30	0.805-2.12
28	0.752	0.343-1.64
33	0.971	0.657-1.43
52	0.954	0.792-1.14
49	0.933	0.672-1.29
44	0.824	0.548-1.23
74	0.956	0.675-1.35
70	0.758	0.361-1.59
95	0.935	0.771-1.13
101	0.962	0.864-1.07
99	0.870	0.584-1.29
87	0.918	0.721-1.16
110	0.961	0.860-1.07
151	0.533	0.078-3.63
82	0.713	0.306-1.66
149	0.914	0.140-1.17
118	0.896	0.884-1.06
153	0.952	0.819-1.10
132	0.906	0.652-1.25
105	0.952	0.813-1.11
138	0.968	0.882-1.06
158	0.967	0.596-1.57
187	0	0
183	1.18	0.291-4.79
128	0.823	0.485-1.39
177	0.883	0.724-1.07
171	0.946	0.770-1.16
156	0.753	0.419-1.35
180	0.833	0.493-1.40
191	0.300	0.008-11.29
169	0.920	0.695-1.21
170	1.01	0.919-1.12
201	1.44	0.247-8.44
208	1.17	0.679-2.03
195	8.50	0.154-468.56
209	0	0
194	0.496	0.095-2.57
205	0.980	0.685-1.40
206	0	0
PCB Total	0.996	0.988-1.00

*Mann Whitney Test. Results are expressed as odds ratio (OR) and IC 95%.

Table 5: *Correlation between serum and soil PCB concentrations in the studied population.*

Congener Serum/ Soil	Case *	Control *
18	0.05	-0.17
28	-0.12	-0.03
52	0.02	0.09
44	-0.09	0.14
101	0.37	0.10
118	0.32	-0.03
153	0.32	-0.05
105	0.32	-0.06
138	0.24	-0.08
180	0.31	-0.06
PCB total	0.22	-0.05

*Pearson

Table 6: *Concentrations of each congener with respect to subjects living near and far from a potential emitting industry.*

Congener	Live near	Live far	p*
18	0.709 (0.069-7.24)	3.07 (1.83-5.14)	0.350
17	0.58 (0)	0.56 (0)	0.271
31	1.32 (0.380-4.59)	1.19 (0.716-2.00)	0.944
28	0.212 (0.007-6.22)	0.681 (0.453-1.02)	0.890
33	2.81 (0.098-80.16)	1.56 (0.157-15.5)	0.374
52	0.614 (0.199-1.88)	0.749(0.288-1.95)	0.090
49	0.178 (0.043-0.738)	0.753(0.214-2.65)	0.763
44	1.54 (0.146-16.22)	1.25 (0.565-2.80)	0.681
74	2.01 (1.56-2.59)	2.94 (2.16-3.99)	0.500
70	0.239 (0.064-0.896)	0.724(0.246-2.12)	0.272
95	1.75 (0.055-55.96)	1.85 (0.631-5.45)	0.954
101	1.61 (0)	1.33 (0.357-5.00)	0.791
99	1.14 (0)	0.861 (0.105-7.01)	0.845
87	0(0)	1.75 (0.224-13.70)	0.247
110	0.637 (0.069-5.86)	0.823 (0.329-2.05)	0.875
151	0(0)	1.35 (0)	0.617
82	1.03	0.486 (0.267-0.88)	0.150
149	0.74	1.37 (0.191-9.91)	0.666
118	2.18 (1.34-3.55)	2.93 (2.12-4.05)	0.813
153	0.763 (0.068-8.47)	1.54(0.576-4.13)	0.817
132	1.36 (0.003-557.46)	3.11(0.502-19.28)	0.280
105	1.60 (1.11-2.32)	1.75 (1.29-2.37)	0.761
138	2.39 (0.965-5.94)	2.23 (1.01-4.95)	0.990
158	0.811(0.041-15.85)	0.918(0.507-1.66)	0.812
187	0(0)	1.99 (0)	0
183	0.26 (0)	0.843 (0.135-5.24)	0.814
128	0.21 (0)	4.69 (0.409-53.80)	0.590
177	0.28 (0)	3.43 (2.24-5.26)	0.037
171	0.18 (0)	2.70 (1.56-4.65)	0.158
156	0.26 (0)	0.747 (0.266-2.09)	0.581
180	0.407 (0.018-8.91)	0.923(0.394-2.16)	0.763
191	0(0)	1.12 (0.189-6.69)	0.378
169	2.52 (0.809-7.90)	2.19 (1.40-3.44)	0.689
170	2.10 (0.336-13.14)	2.99 (1.67-5.35)	0.723
201	0(0)	1.59 (0)	0.475
208	1.42 (0)	1.07(0.211-5.42)	0.801
195	0.46 (0)	0.704 (0.104-4.75)	0.984
209	0 (0)	0	0
194	0.13 (0)	1.04 (0.519-2.10)	0.762
205	0.64 (0)	0.89 (0.365-2.17)	0.28
206	0(0)	0	0
PCB Total	9.32 (3.37-25.75)	23.47 (15.98-4.48)	0.807

*Mann Whitney Test. Results are expressed as geometric mean (IC 95%).

In Table 7, the mean concentrations are presented of the 41 congeners of the PCB evaluated and of the total PCB registered between the subjects (cases and controls), whose home was localized more than 1,000 m from a potentially PCB-producing industry. When these concentrations between cases and controls were analyzed, no statistical difference was found. The number of congeners not detected in the cases and controls was similar.

Table 7: *Concentration in soil by study group that lives far from a potential emitting industry.*

Congener	Cases Live far(n=21)	Control Live far(n=27)	p*
18	3.49 (1.84-6.63)	2.68 (0.97-7.38)	0.334
17	0	0.56 (---)	0.386
31	1.43-0.754 (2.742)	0.930-0.330 (2.62)	0.661
28	0.488 (0.32-0.745)	0.900-0.385 (2.10)	0.949
33	2.26 (---)	1.38 (0.01-04.8)	0.469
52	0.504 (0.124-2.03)	0.773(0.163-3.64)	0.574
49	0.386 (0.033-4.45)	1.30 (0.104-16.38)	0.730
44	0.666 (0.260-1.70)	1.39 (0.376-5.16)	0.498
74	2.22 (1.89-2.70)	3.24 (1.82-5.78)	0.933
70	0.583 (0.064-5.25)	0.479 (0.108-2.11)	0.472
95	1.41 (0.276-7.28)	1.21 (0.199-7.36)	0.940
101	1.12 (0.059-21.27)	0.799 (0.152-4.19)	0.608
99	0.14 (---)	0.299 (0.004-21.39)	0.644
87	1.31 (0.077- 22.16)	0	0.722
110	0.669 (0.179-2.50)	0.582 (0.186-1.82)	0.961

151	0.41 (---)	0	0.859
82	0.357 (0.157-0.80)	0.487 (0.190-1.24)	0.817
149	1.40 (0.087-22.47)	0	0.973
118	2.68 (1.84-3.90)	2.53 (1.91-3.37)	0.991
153	1.31 (0.474-3.62)	0.908 (0.097-8.45)	0.383
132	0	2.6 (---)	0.798
105	1.64 (1.13-2.37)	1.50 (1.16-1.93)	0.949
138	2.25 (0.486-10.41)	1.47 (0.682-3.16)	0.594
158	0.746 (0.291-1.91)	0.776 (0.443-1.35)	0.620
187	0	0	0.0
183	0	0.17 (---)	0.765
128	2.59 (---)	2.74 (---)	0.697
177	2.58 (1.18-5.61)	4.93 (3.00-8.11)	0.687
171	2.45 (0.759-7.93)	3.16 (1.51-6.61	0.673
156	1.35 (0.546-3.34)	0.432 (0.111-1.68)	0.180
180	0.586 (0.145-2.35)	0.878 (0.442-1.74)	0.709
191	0	0.673 (0.064-7.02)	0.443
169	2.15 (1.41-3.29)	2.21 (1.14-4.29)	0.223
170	3.45 (1.17-10.10)	2.45 (1.09-5.48)	0.717
201	14.19 (---)	0.18 (---)	0.813
208	0	0	0.0
195	0.812 (0.023-8.20)	0.46 (---)	0.173
209	0	0	0.0
194	0.718 (0.072-7.07)	1.33 (0.296-6.04)	0.832
205	1.16 (0.212-6.39)	0.544 (0.146-2.03)	0.774
206	0	0	0.0
PCB Total	17.80 (9.81-32.30)	25.40 (17.42-37.05)	0.719

*Mann Whitney Test. Results are expressed as geometric mean (IC 95%).

In Table 8 are presented the concentrations of the means of the 41 congeners of the PCB evaluated and of the total PCB registered between the subjects (cases and controls) whose homes were localized less than 1,000 m from a potential PCB-producing industry. The only significant difference found ($p=0.046$) in the concentrations between cases and controls was for congener 52. In the controls, only six were quantifiable, while in the cases, 34 congeners were detected in the soil samples. When the congeners were grouped according to their chemical structure, biological effects, and persistence in the environment, differences were not found in the concentrations registered in soil between cases and controls. The highest concentration registered for the groups studied was for group 2A, and the lowest, for group 4 (Table 9). No difference was found ($p>0.05$) in the concentrations by group of PCB between cases and controls whose homes were found localized at a distance of more than 1,000 m of distance from the potentially PCB-producing industries. The average concentration of the highest PCB group was for group 2A, and the lowest, for group 4 (Table 10). When the concentrations by PCB group of the cases and controls whose homes were found within a radius of 1 km from some potential PCB-producing source, a statistical difference was found ($p<0.05$) in two groups and in total PCB (Table 11). The risk was analyzed (OR) between the groups of PCB and BC; an elevated risk was found for group 4. However, the 95% CI was not statistically significant (Table 12).

Table 8: *Concentration in soil by study group that lives near an emitting industry.*

Congener	**Cases Live near (n=8)**	**Control Live near (n=4)**	**p***
18	0.824 (0.028-24.25)	0.39 (---)	0.343
17	0.58 (---)	0	0.479
31	1.32 (0.380-4.59)	0	0.079
28	0.590 (0.098-3.52)	0.1 (---)	0.479
33	2.81 (0.098-80.16)	0	0.296
52	0.702 (0.194-2.54)	0.24 (---)	0.046
49	0.178 (0.043-0.738)	0	0.296
44	1.54 (0.146-16.22)	0	0.180
74	2.01(1.56-2.59)	0	0.105
70	0.239(0.064-0.896)	0	0.105
95	1.75(0.055-55.96)	0	0.296
101	0	0	0.296
99	0.14 (---)	0	0.479
87	0	0	0.0
110	0.637(0.069-5.86)	0	0.105
151	0	0	0.0
82	1.03 (---)	0	0.479
149	0.74 (---)	0	0.479
118	2.54 (1.72-3.74)	1.03 (---)	0.123
153	0.763 (0.068-8.47)	0	0.181
132	0	0	0.0
105	1.81(1.39-2.35)	0.88 (---)	0.123
138	2.39 (0.965-5.94)	0	0.181
158	0.811 (0.041-15.85	0	0.181
187	0	0	0.0
183	0.26 (---)	0	0.479
128	0.21 (---)	0	0.479
177	0	0.28 (---)	0.157
171	3.49 (---)	0	0.695
156	0	0	0.0
180	0.407 (0.018-8.91)	0	0.296
191	0	0	0.0
169	2.52 (0.809-7.90)	0	0.105
170	0	0	0.0
201	0	0	0.0
208	1.42 (---)	0	0.479
195	0.46 (---)	0	0.479
209	0	0	0.0
194	0.13 (---)	0	0.479
205	0.64 (---)	0	0.479
206	0	0	0.0
PCB Total	14.17 (7.03-28.57)	0	0.010

*Mann Whitney Test. Results are expressed as geometric mean (IC 95%).

Table 9: *Concentration of PCBs in soil in the total population, classification according to their chemical structure and biological effects in humans.*

Group	Cases	Control	p*
1ª	1.61(0.700-.71)	2.02 (0.738-5.53)	0.343
1B	2.85 (1.03-7.87)	5.35 (2.26-12.66)	0.855
2ª	5.26 (3.74-7.41)	7.16 (4.21-12.17)	0.632
2B	4.29 (2.47-7.47)	3.08 (1.39-6.81)	0.605
3	0.847 (0.436-1.64)	1.13 (0.290-4.43)	0.115
4	0.704 (0.104-4.75)	0.46 (0)	0.129
5	3.16 (1.80-5.53)	2.83 (1.14-7.00)	0.454
PCB Total	16.49 (10.72-25.38)	22.5(11.26-45.14)	0.197

*Mann Whitney Test. Results are expressed as geometric mean (IC 95%).

Table 10: *Concentration of PCBs in soil in the total population, classified according to their chemical structure and biological effects in humans, and living far from an emitting industry.*

Group	Cases Live far	Control Live far	p*
1ª	1.45 (0.387-5.48)	2.38 (0.852-6.65)	0.964
1B	3.23 (0.964-10.8)	6.99 (3.49-14.02)	1.000
2ª	5.22 (3.23-8.44)	7.78 (4.55-13.30)	0.643
2B	4.71 (2.09-10.63)	3.39 (1.47-7.82)	0.732
3	0.978 (0.349-2.73)	1.13 (0.290-4.43)	0.433
4	0.81 (0.023-28.20)	0.46 (---)	0.173
5	3.85 (2.10-0.706)	3.33 (1.33-8.32)	0.546
PCB Total	17.80(9.81-32.30)	30.4(18.07-51.3)	0.719

*Mann Whitney Test. Results are expressed as geometric mean (IC 95%).

Table 11: *Concentration of PCBs in soil in the total population, classified according to their chemical structure and biological effects in humans, and living near an emitting industry.*

Group	Casos Live near	Controles Live near	p*
1ª	1.93 (0.8778-4.27)	0.24 (---)	0.026
1B	0 (---)	0.28 (---)	0.823
2ª	5.34 (2.84-10.02)	1.91 (---)	0.030
2B	3.50 (1.75-6.96)	1.48 (---)	0.597
3	0.654 (0.253-1.69)	0 (---)	0.057
4	0.46 (---)	0 (---)	0.479
5	1.74 (0.023-12.74)	0.4 (---)	0.343
PCB Total	14.17(7.03-28.57)	1.75 (0)	0.010

*Mann Whitney Test. Results are expressed as geometric mean (IC 95%).

Table 12: *Risk in total population and classification according to its chemical structure and biological effects on humans.*

Group	OR (Odds Ratio) *	IC 95%
1A	0.964	(0.872-1.06)
1B	0.962	(0.884-1.04)
2A	0.979	(0.927-1.03)
2B	0.987	(.944-1.03)
3	0.965	(0.866-1.07)
4	8.285	(0.137-499.10)
5	1.00	(0.913-1.11)
PCB Total	0.996	(0.987-1.00)

*Mann Whitney Test. Results are expressed as odds ratio (OR) and IC 95%.

Discussion

The general objective of the present investigation was to determine the concentration of PCB in blood serum in patients in patients with BC and its correlation in the soil of the place of residence in different areas of the Comarca Lagunera. Exposures to chemicals present in the environment, generated by humans, exert adverse effects on the environmentally exposed population. Among the gamma of effects that cause these, cancer is highlighted. Diverse types of neoplasms have been associated by occupational and environmental exposure to persistent organic compounds. A study was conducted in Torreon, Coahuila, in Mexico, in which an association was reported between BC and PCB; however, in this study, the possible sources of these compounds were not evaluated, and one of these (soil) comprises the reason for the present work. The average age of the studied population was 49.7 years. According to national and international statistics, the average range at presentation or diagnosis of the pathology is 35-50 years [20]. This reveals that the natural history of the disease in our population is similar to that reported. In addition, in 20% of the cases, diagnosis was performed between 25 and 39 years of age, and in this age group, PCB concentrations were the highest, suggesting that in this age group, PCB are already playing an important role in the development of the neoplasm at early ages, added to the previously known risk factors.

Overweight and obesity have been associated with BC. Central obesity is that which is most related with the pathology; in addition, there are indices that diverse environmental factors could be associated with this metabolic syndrome [21]. In fact, there are epidemiological studies that relate certain COP, denominated obesogenes, with the development of obesity [22,23]. The average BMI of our studied population was 27. According to our results, the two participants with the highest BMI had the two highest concentrations of serum PCB. Controversy exists in the literature concerning the BMI relation and the PCB concentration: on the one hand, Noren et al. report a positive relationship [24]. These results that support the fact that, due to these compounds being lipophilic, a direct relation is to be expected between the BMI (fatty tissue)

[21] and the bio concentration of same [25].

These results of this study also suggest that the BMI–PCB represents a risk factor for contracting BC. PCB enters into our organism by inhalation, by contact with the skin, and by the gastrointestinal pathway. After their entry, these PCB are transported by the blood to the liver, and are later redistributed to the adipose tissue [26]. Quantification of the congeners of PCB in blood is a direct and indirect form by means of exposure these compounds. The concentration of the congeners evaluated is found more specifically in the high concentrations among the cases. The congener found at the greatest concentration was congener 180. Demers et al. and Rusiecki et al. in their respective studies, also found this congener at very high concentrations in serum as well as in adipose tissue [27,28]. Because of its chemical properties and biological effects, this congener is highly lipophilic and is classified as biologically persistent and as an inducer of CYP1 and CYP2B [29], which are involved in the bioactivation of xenobiotics, with the subsequent cytotoxic and genotoxic effects. When the concentrations of the congeners were compared between the groups, it was found that for 13 congeners of the total 20 analyzed, total PCB were significantly higher in cases than in controls. These data suggest that women with BC can be more exposed to PCB and/or that women with BC can be presenting alterations in the metabolism of these compounds and that they tend to accumulate more or eliminate fewer compounds than the controls. Several studies have been published that have associated PCB with BC, and the results are controversial. The majority of these studies do not find a positive association; however, these results, and after carrying out multivariate analyses with the significant variables and with biologically plausible variables (known risks) for the development of cancer, a positive association was found and an increase in the risk for cancer. The total concentration of PCB revealed in our study was found below the concentration recommended by the EPA for soil of residential use, that is, below 50 ppm; thus, it can be considered that soil contamination with PCB is low and admissible. The concentration of the different congeners evaluated was similar between the soil samples of the domiciles of cases and controls, with only one exception with marginal significance (p=0.056), that of congener 52, and was greater in the cases. The highest concentrations found in soil in the study were for congeners 118 and 138. With respect to the three most frequently found, these were 18, 118, and 105; those not found in any of the samples analyzed were congeners 206 and 209. In the study conducted by Costilla et al. the congeners found by these authors at a greater concentration in soil were 101 and 105, and those of least concentration were congeners 28 and 118 [30]. The difference between the frequency and concentration of the congeners reported in the literature and ours can basically be the difference of congeners emitted by the different sources in each of the studies mentioned. The congeners found in common were 105 and 118. The greatest risk for BC was found with congener 195; however, it was not statistically significant. A significant risk was not found either with any of the other congeners quantified in soil.

The correlation analysis between the serum concentrations of PCB and that of the soil demonstrated a low correlation, this being greatest for congener 101. This mentioned lack of correlation can be due to the timing of the taking of the blood sample and of the soil. Similarly, it can be due to the differences in the metabolism of these compounds in blood and in soil. The environmental characteristics of the city (temperature, humidity, winds) and soil (pH, hardness, organic matter, etc.) can favour rapid degeneration, thus the low concentration and poor correlation with that of the soil. Finally, another factor that can exert an influence the half-life of each congener is that there is a great deal of knowledge on the correlation of serum and adipose tissue sampling with regard to PCB, but a very limited number of studies in which serum and soil correlate. Garabrant et al. report that, in the population in which they analyzed the concentration of PCB in serum, this was lower than that found in soil; however, these authors did not carry out a correlation between both samples evaluated [31]. Humans comprise a sensitive objective of COP bioaccumulation, in particular PCB, and pesticides have been utilized widely by farmers due to their bioavailability and their simplicity of application. Therefore, this exposure route is relevant and risky [32]. Turrio-Baldassarri et al. conducted a study in which the authors correlated contaminated soil with PCB in an urban zone and another in agricultural soil, reporting a very good correlation (0.99) [33]. On the other hand, Altshul et al. reported an acceptable correlation (0.6) for congener 180 between the levels of PCB in equine and human serum [34]. Due to the low correlation found in our study and the low concentrations of PCB in soil, it is convenient to consider other possible sources of these to explain the concentrations in serum. Another important pathway of entry of these chemical products is the diet [35]. In Japan and Sweden, investigators detected PCB in whole milk for human consumption in concentrations of 5.5 ppb and 4.01 ppb, respectively [24]. Prado et al. proved in their study that the consumption of egg, meat, milk, and salmon favored elevated concentrations of PCB [20]. Another route of exposure is water; Westbom et al. [36] analyzed potable water and treated water, finding low levels of 0.25 ppb for potable water and high levels (1 ppb) for treated water, the authors concluding that, despite that minimal concentrations levels were found the potable water, the latter does not stop being a source of exposure for humans and other life forms [36]. In this respect, recently in the East Lake of China, residues of PCB and of Polybrominated Diphenyl Ethers (PBDE) were detected on the surface of the collected sediment; it is probable that these originated from urban the drainage of the local hydrographic basins, from contamination, or by environmental deposition [37]. The potential eco-toxicological risk caused by PCB was of 5% from the sampling sites, and PBDE were found in 80% of the sampled sites.

Likewise, substantial amounts of Polychlorinated Dibenzofurans (PCDF) have been detected as generated in the presence of O2 during the thermal treatment of contaminated soil [38]. Bahía Guánica in the southeast

of Puerto Rico has, since 1960, has experienced great discharges of contamination and, in its coral reefs and sediments, elevated concentrations of PCB have been found [39]. Fish for human consumption and sediment were sampled; the former showed high concentrations of PCB. River otters have also been utilized as bio monitors of organ chlorine pesticides, organ halogen compounds, dihedron, heptachloride and epoxide, PCB, and PBDE [40] in rivers in the U.S. state of Illinois; the range of the concentrations obtained from organ halogens is a risk factor for the fauna and humans that are found permanently exposed. In Mexico City, one of the most contaminated places in the world. bio monitoring was carried out for the vigilance of the population in general in terms of volatile organic compounds, among these PCB, finding, in blood samples, concentrations of up to 350 n/g of PCB, indicating that residents are exposed to contaminants [41]. Programs should be generated of the bio monitoring of these metabolites in other matrixes such as soil [42,43]. In our study, we did not find statistical significance in the entire population studied between whether they did or did not live near a possible emitter source. When the results were compared between the study groups and living near an industry, the sole congener that was significantly higher in the cases rather than in the controls was 52. Therefore, a potential source of PCB is the fact of living near industries that are potential producers of PCB.

When the congeners were grouped according to chemical structure and biological activity, including Groups 1A, 2A, and A3 and total PCB, the concentrations of these were significantly higher in cases than in controls living near a potential emitter source. Among these groups in which the greatest concentration was found was group 2A and which have estrogenic activity. Risbridger et al. note that it is important to visualize, in a general context, the effects on health that lead to metabolic and hormonal alterations due to exposure to PCB [44]. Because the mechanisms of action are not yet clear, it is necessary to investigate whether this exposure can exert a potential harmful effect. This has permitted the identification of a number of antiandrogenic contaminants present in the placenta, including plastics, surfactants, cosmetics, and pesticides [45]. Estrogens are recognized as hormones that potentially favor cancer; this group of congeners can be participating in the development of the neoplasia due to its estrogenic activity. No group of PCB was significantly associated with BC. There is no study in soil in the literature, to our knowledge, in which congeners are classified by group; therefore, we are unable to compare our results in soil with those of another study. However, this project generates new queries for analysing the effect of PCB on Mexican population and their concentration in food destined for human and animal consumption, in that these contaminants emanating from industrial activity, because of their physicochemical properties, remain in the environment.

Conclusion

It is concluded that quantification of PCB in blood serum and soil is possible by means of the CG method with an electron uptake detector. The serum concentrations of 13 congeners were significantly higher among cases than in controls. The congener concentrations of PCB in soil were not different between cases and controls. No risk association was found between the individual concentrations of the 41 congeners neither of PCB nor with total PCB in soil with BC. No correlation was found in the concentrations of the 10 common congeners between serum samples and soil samples. Only the concentration of congener 177 in soil was significantly greater in subjects who lived near a potential emitter industry than in those who did not live near these industries. The risk factor lies the fact of living near an emitter industry. When the congeners were grouped according to their chemical structure, biological effects, and persistence in the environment, differences were not found for the concentrations registered in soil for the studied population, but these were high for groups 1A, 2A, 3A, and total PCB in the population and living near the emitter sources. There exists soil contamination with PCB; however, these are not correlated with congeners in serum, suggesting that the source of these compounds in the studied participants can derive from another source and not from the soil of the place of residence of the congeners.

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