Published in final edited form as:

J Nutr Biochem. 2014 April ; 25(4): 483–488. doi:10.1016/j.jnutbio.2014.01.002.

Reduction of the Body Burden of PCBs and DDE by Dietary Intervention in a Randomized Trial^{☆,☆☆,★}

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Abstract

Serum polychlorinated biphenyls (PCBs) in Anniston, Alabama residents have been associated with hypertension and diabetes. There have been no systematic interventions to reduce PCB body burdens in Anniston or other populations. Our objective was to determine the efficacy of 15 g/day of dietary olestra to reduce PCBs in Anniston residents. Blood PCBs and DDE were measured at baseline and 4-month intervals in a double-blind, placebo-controlled, one-year trial. Participants with elevated serum PCBs were randomized into two groups of 14, and received potato crisps made with olestra or vegetable oil (VO). Elimination rates during the study period were compared with 5-year pre-study rates. Eleven participants in the Olestra group and 12 in the VO group completed the study. Except for one participant in the VO group, reasons for dropout were unrelated to treatments. The elimination rate of 37 non-co-planar PCB congeners during the one-year trial was faster during olestra consumption compared to the pre-trial period (-0.0829 ± 0.0357 and -0.00864 ± 0.0116 years⁻¹, respectively; $p = 0.04$), but not during VO consumption (-0.0413 ± 0.0408 and -0.0283 ± 0.0096 years⁻¹, respectively, $p = 0.27$). Concentration of PCBs in two Olestra group participants decreased by 27 and 25% during the trial. There was no significant time by group interaction in change from baseline. However group main effects for total PCBs, PCB 153 were of borderline significance. This pilot study has demonstrated that olestra can safely

[☆]The study was supported by the National Institutes for Environmental Health Science (R21 ES019206) and the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant 8 UL1 TR00007. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

^{☆☆}The authors declare no conflict of interest.

[★]Author contributions to the manuscript: concept and design of the study (RJJ, JEH, DDB, JCK, WET, AS, JRO, CS, KH, SC, PT, MP); conduct of the trial (RJJ, JEH, DDB, TB, SC, CS, KH); analysis of data (RJJ, JEH, DDB, JCK, WET, AS, JRO, PT, MP, TB); writing of manuscript (RJJ, JEH, JRO, JCK, MP); responsibility for final content (RJJ, JEH, MP).

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Supplemental online material has been submitted.

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reduce body burdens of PCBs and supports a larger intervention trial that may also determine whether reduction in PCBs will reduce the risk of hypertension and diabetes.

Keywords

PCBs DDE; olestra; dietary intervention

INTRODUCTION

Polychlorinated biphenyls (PCBs) are persistent, environmental toxicants and/or carcinogens. PCBs were manufactured for 40 years in Anniston AL, resulting in environmental contamination and high body-burdens of PCBs that were associated with increased risk of hypertension and diabetes as assessed by the Anniston Community Health Study (ACHS)(1–3). No systematic interventions have been made to reduce PCBs in Anniston residents.

In addition to the studies in Anniston, the analysis of NHANES data disclosed a strong association between the serum level of non-coplanar PCB 153 and diabetes (4). Although there is an apparent relationship between risk of disease and level of PCBs, there is minimal evidence that reducing the levels of PCBs will alter this risk. To our knowledge, only a single case report study has demonstrated that reducing PCBs will reduce the markers of disease, specifically blood glucose and lipid levels (5). Presumably this paucity of data is the result of not having a suitable method for removing PCBs from the body. We therefore undertook the study to determine if it is possible to reduce PCB levels as a first step toward determining whether disease risk might then be altered.

PCBs are lipophilic and associated with stored triglycerides and serum lipids. The concentration of PCB levels in serum lipids thus reflects the total body burden as an estimate of the concentration in adipose tissue (6–8). The measurements of PCBs in Anniston residents noted above have utilized lipid-corrected serum levels as a measure of exposure. Although direct measurements of concentration in adipose tissue and total body fat would have provided a more exact determination of body burden, we opted to use the lipid-normalized serum levels because of concerns about participant compliance in this exploratory trial.

PCBs and their metabolites enter the intestine by biliary or non-biliary secretion and are reabsorbed by enterohepatic circulation. Reducing organochlorine reabsorption hastens removal from the body as demonstrated by administering cholestyramine to remove kepone(9). Following the same strategy, we used the non-absorbable lipid, olestra, which reduces DDT absorption and enhances DDE excretion in animals (10)(11). When added to the diet of mice exposed to hexachlorobenzene (HCB), olestra increased HCB excretion 30-fold(12). Remarkably, in a study of a single patient who had high PCB exposure, a regimen of olestra decreased adipose PCBs from 3200 to 56 mg/kg over 2 years(5).

These previous preliminary studies have demonstrated that olestra can increase the rate of excretion of organochlorines from the body. However, there has not been a controlled randomized clinical trial to determine if olestra is effective in reducing the body burden of organochlorines in humans. In addition to the preliminary data that demonstrated effects of olestra on organochlorines in animals, we believed that olestra would provide a low-risk dietary intervention with high probability of compliance during a year of study. Olestra is approved by the FDA for use in foods in the US, and it is also approved for food uses in 24 other countries. Potato crisps of uniform size containing olestra, provide a readily measurable dose form. We report here the results of a one-year placebo-controlled

intervention with olestra to reduce PCBs in residents of Anniston, Alabama. In addition to the measurement of changes in serum PCBs, we measured serum DDE levels, which had been previously reported to be reduced by olestra in animals(11).

SUBJECTS AND METHODS

Study participants

Study participants from Anniston were identified from the ACHS with serum PCB levels (37 non-coplanar congeners) above the national 50th percentile reported in the 2005–2007 National Health and Nutrition Examination Survey(13). Recruitment from this pool ensured measurement of PCB levels during the trial and during the 4–6 year period prior to the trial. Recruitment took place from December 2010 to March 2011. All participants began the trial on April 27 or April 28, 2011.

The study size was based on the expected standard deviation of 4.5% for within group error for PCB analyses (14). A group size of 10, 80% power, and alpha of 0.05 predicted that we would be able to see a reduction in body burden in the olestra group of 7% relative to a 1% change in the control group in a year. We recruited 14 participants in each group with the goal of completing the parallel trial with 10 in each group.

Exclusion criteria included: pregnancy, lactation, intolerance of the test products, current use of weight-loss medications, gastrointestinal or eating disorders, history of bariatric surgery, and kidney stones. All participants were given verbal and written explanation of the study, and questions concerning its risks and details were solicited, and written informed consent statement obtained.

Test products

Crisps made with either olestra or vegetable oil (VO) were purchased commercially. Olestra crisps were Pringles® Light Original, and VO crisps were Pringles® Original. Both crisps were then produced by Procter & Gamble and are now produced by Kellogg. The daily dose of 24 olestra crisps provided 15 g of olestra. The crisps were provided in individually sealed and labelled packets that contained half of the daily dose (12 olestra crisps; six VO crisps). The dose of both crisps provided 112 kcal/day. A month's supply of crisps was packaged in a sealed opaque box, and the study coordinator who dispensed the boxes was not aware of the contents. The participants were also unaware of their treatment assignment. Participants recorded daily ingestion of crisps in diaries, and they returned boxes containing unused product. Compliance was assessed as percent of provided dose.

Study design

Participants were randomized *a priori* by the Cincinnati Children's Hospital biostatistician into VO and Olestra groups of 14 each and enrolled using a stratified design based on BMI split at 30 kg/m², and sex. Within each stratum the subjects were put in random order using a random number generator in SAS. Then group assignment was generated using random block sizes of 2 and 4, due to the small sample size.

Subjects visited the Anniston clinical site monthly for 12 months. Every 2 months they were weighed, received nutritional counselling, and given a 2-month supply of crisps. At each visit participants returned diaries recording crisp consumption. At months 0, 4, 8, and 12, fasting blood samples were taken for PCB and lipid analyses. Serum glucose and insulin were measured at 0 and 12 months.

The study was approved by Institutional Review Board of the Cincinnati Children's Hospital Medical Center. This study included use of a U.S. Food and Drug Administration's Investigational New Drug Application (IND # 109 636) for olestra-containing crisps. At CDC, analyses were conducted as technical assistance and in compliance with Research Determination procedure; an exemption from the CDC IRB was obtained. Data collection in the original ACHS was approved by the University of Alabama's IRB. The study is registered with ClinicalTrials.gov (NCT01261338). Adverse events were reported to the Anniston Coordinator, and a medical consultant in Anniston was available at all times to evaluate any report of referral for medical care.

Serum measurements

Serum lipids were measured using a CDC-certified method (Medpace Reference Laboratories, Cincinnati, OH). Serum glucose (Trinder modified Emerson method), insulin (radioimmunoassay) and vitamin E (HPLC) were measured at the CTRC Core Laboratory, Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

Organochlorine analysis

Serum was analyzed for PCB non-coplanar congeners, consisting of 35 individual congeners and two sets of co-eluting peaks (congeners 138-158 and 196-203) at the CDC as described previously(14). This set of congeners was previously studied in the Anniston ACHS and allowed us to utilize pretrial concentrations from that study. The method also provided measurements of nine pesticides including DDE, and we analyzed DDE in addition to the PCBs. PCB and DDE concentrations were normalized to serum lipids as previously described ($2.27 \times \text{total cholesterol} + \text{triglycerides} + 62.3$) and expressed as ng/g lipid(6–8).

Statistical considerations

RedCap® software was used for data management and EXCEL® for data capture. SAS® version 9.3 (SAS Institute, Cary NC) was used for analysis unless otherwise noted. Outliers and distributional properties were assessed by univariate analysis. Analysis of the PCB congeners and DDE incorporated a log transformation. Baseline differences between groups were analysed using T-test and Wilcoxon Rank sum or Chi-square and Fisher's exact test, as appropriate. Analysis of the PCBs and DDE over the year used the fraction of their lipid-normalized values at the first visit. Changes over the one-year period between Olestra and VO groups were assessed with a generalized linear random-effects mixed model, to account for the repeated nature of the design. Of initial interest was the interaction between visit and group, and if this was non-significant the main effects model was examined. Baseline values of the PCBs and DDE, as appropriate were retained in the model.

Elimination rate constants were determined from the natural logarithms of these fractions (described below). Since we hypothesized that olestra crisps, relative to VO crisps and to each individual's own prior elimination rate of PCBs, would result in accelerated PCB loss, comparisons were based on one-tailed tests. Individual regression analysis plots of the logarithms of the fractions versus time were performed for each participant using Sigmaplot®. Data are presented as mean $\pm$ standard error or geometric mean (95% confidence interval (CI)), the latter reported when the data were skewed and a logarithmic transformation was used for analysis. Analysis of the PCBs included congener 153, the sum of congeners 153 180, 194, 196–203, 206, and 209 (higher chlorinated congeners), and the total of 37 congeners.

We used a first-order decay model assuming the elimination rate of PCBs from the body was proportional to the amount in the body so that $dA/dt = -kt$ and $\ln(A/A_0) = -kt$, where A_0 is the amount at time 0, and A is the amount remaining at time t . Time is expressed in years,

and the rate constant, k , as years^{-1} . The natural logarithms of A/A_0 were plotted against time to determine the elimination rate constant using linear regression analysis. Concentrations of lipid-normalized PCBs obtained four to six years before the study and at time 0 for each participant, were used to calculate individual pre-trial elimination rates, and these rates were compared with each participant's elimination rate during the trial by paired T-test. Each individual's pre-trial elimination rate was also compared with the rate during the trial by a one-tailed T-test based on the standard error calculated from the regression analysis of each individual's change during the trial. Values are presented as means and standard errors with significance determined by $p < 0.05$.

Half-lives cannot be calculated when elimination rate constants are 0. Therefore half-life estimates for each group were based on the mean of the group's elimination constant.

RESULTS

The baseline characteristics of the groups and final visit measurements are presented in Table 1. Eleven of 14 participants in the Olestra group and 12 of 14 in the VO group completed the trial. One participant in the olestra group started at the four-month visit and completed eight months of treatment. There were no statistically significant differences between groups at the initial visit (Table 1). Changes from baseline from the participants who completed the trial are presented in Table 2. There were no statistically significant changes in BMI, consistent with the nutritional counselling that was provided to maintain body weight during the trial.

Serum PCB levels

There were no statistically significant differences in total PCBs, PCB 153, or a group of higher chlorinated congeners (153 180, 194, 196–203, 206, and 209) at baseline between the Olestra and VO groups. The baseline values for total PCBs (geometric mean (95% CI) as ng/g lipid were 1448 (960, 2184) and 1341 (1001, 1978) for the Olestra and VO groups, respectively. For the higher chlorinated congeners these values were 709 (470, 1072) and 629 (475, 834); and for PCB 153, 247 (144, 424) and 253 (168, 381), respectively.

The percent change from baseline was used to analyze the effect of study group on serum PCBs (Figure 1). The p-value for the overall group effect was 0.06. There was no statistically significant interaction of time by group for PCB 153 or for total PCBs. The p-value for the overall group effect was 0.09. For the higher congeners the interaction was not statistically significant. The p-value for the overall group effect was 0.16. In all analyses, baseline level was retained as a covariate in the model, although not statistically significant.

The total lipid-normalized serum PCBs (37 congeners) mean (95% CI) at the beginning of the trial were 1341 (1001, 1798) and 1448 (960, 2184) ng/g lipid (parts per billion, ppb) for the VO and Olestra groups, respectively. The concentrations on a wet weight basis were 8.4 (6.4, 11.2) and 9.3 (5.9, 14.8) ng/g serum for the VO and Olestra groups, respectively.

Elimination rate constants were calculated for the 37 congeners, a group of higher chlorinated congeners (PCBs 153 180, 194, 196–203, 206, 209), and PCB 153 alone. The higher chlorinated congeners were selected because of prevalence. Congener 153 was analysed separately because of prevalence and its measurement in previous studies. Serum PCB levels (ng/g lipid) 3.7 to 6.2 years (mean of 5.2 ± 0.1 years) before the trial for each individual were compared with time 0 levels to calculate pre-trial elimination rates. Rates were calculated from values at 0, 0.33, 0.67, and 1.0 years (Table 3).

Half-lives were estimated from the mean elimination rate constants. Total PCB half-lives were 80.2 and 24.5 years for Olestra and VO groups, respectively. During the trial, these decreased to 8.4 and 16.8 years, respectively. Higher chlorinated congener pre-trial values of 280.1 and 33.4 years decreased to 8.6 and 23.4 years for the Olestra and VO groups, respectively during the trial. These values for PCB 153 were 33.3 and 23.2 years during the pre-trial period and 5.6 and 10.6 years during the trial for the Olestra and VO groups, respectively.

Percent change in body burden was calculated from elimination rate constants for pre-trial and trial periods. The predicted change during the year of the trial was determined from the pre-trial elimination rate. This predicted change compared with the observed change is presented for all PCBs during the trial for the VO and the Olestra groups in Figure 2. During the trial the VO group's PCB concentrations decreased to 96% of baseline, compared with a one-year decrease to 97% predicted by the pre-trial measurements. The Olestra group's concentration decreased to 92% of baseline, compared with a predicted value of 99%. The decrease during the trial period was significantly greater ($p < 0.05$) than that predicted from the pre-trial elimination rate for the Olestra group.

DDE

Of nine analyzed pesticides, the most prevalent was DDE, DDT's principal metabolite. Baseline lipid-normalized levels were elevated relative to the general population, with 383 (171, 857) ng/g lipid in the Olestra group and 466 (279, 779) ng/g lipid in the VO group, corresponding to the 75th to 90th percentile values for the U.S. population over 20 years(13). The change in DDE levels during the pre-trial period was extremely variable. In the Olestra group, there was a mean increase of 84.3 ± 66.2 % in DDE and in the VO group, an increase of 17.3 ± 46.6 %. This high variance is consistent with highly variable exposure during the pre-trial period, which prevents a comparison of the elimination rate during the pre-trial with that during the trial. During the trial the mean elimination rate constant for the DDE in the VO group was -0.053 ± 0.0460 year⁻¹, and that for the Olestra group was -0.175 ± 0.064 year⁻¹ ($p=0.067$).

Changes from baseline

No difference in PCB concentrations was found between the Olestra and VO groups at baseline. For PCBs the analysis examined the percent change from baseline. The visit by group interaction was not significant, $p=0.70$, and the baseline term was borderline ($p=0.06$). The main effects model showed a significant group effect ($p=0.02$) and the baseline level was of borderline significance ($p=0.06$). Baseline (geometric mean, 95% CI, ng/g) concentrations of DDE were 383 (171, 857) and 466 (279, 779) for the Olestra and VO groups, respectively. At 12 months the concentrations were 84.1 ± 4.0 % and 94.9 ± 3.6 % of the baseline values for the Olestra and VO groups, respectively.

Adverse Events and Dropouts

Five participants dropped out of the study: two in the VO group and three in the Olestra group. In the VO group, one was due to weight gain and diarrhea, and the other due to hypertension. In the Olestra group: one was hospitalized during the first month of the trial with diabetic complications; one was lost to follow up; and one had an infection. Four participants reported adverse events that may be related to the trial. Two participants in the Olestra group and one in the VO group reported loose stools. For one participant in the Olestra group, crisp consumption was temporarily discontinued, the symptoms stopped, and the participant continued the study regimen without recurrence of loose stools. One participant in the olestra group reported gas and bloating.

Compliance

Returned containers were checked and found to be consistent with the diaries that were kept by the participants. The VO group consumed 96.7 ± 1.2 % of provided crisps, and the Olestra group, 92.9 ± 2.2 %.

Discussion

In this placebo-controlled trial, intervention with 15g of olestra per day for one year significantly reduced lipid normalized PCBs more than that predicted by pre-trial measurements. These results are consistent with olestra increasing the rate of reduction of the body burden of PCBs, and they suggest a feasible intervention to reduce associated health risks.

There was high variance in the response to olestra. For example, total PCB levels in Participants 13 and 19 decreased by 27 and 25%, respectively, during the trial, yielding half-lives of 2.2 and 2.4 years, values that are markedly greater than their respective reductions of 0.2% and 0.9% per year in the pre-trial period. PCB elimination rates during the trial were significantly different from pre-trial rates ($p < 0.05$) for Participants 13 and 19 and for five of 11 Olestra group participants. In the VO group the rates during the trial differed from pre-trial rates in only two of 12 participants.

Wide variations in serum concentration and elimination rates are typical of PCB biomonitoring. PCB half-life estimates varied considerably within treatment groups, among pre-test and in-test estimates, as well as when compared between pre-test and in-test estimates. Given these realities, we acknowledge that even more variability is likely to be observed when determining half-lives based on a 1-year timeframe for biomonitoring (as done in this study), compared to estimations based on longer timeframes. This analytical consideration indicates the value of a longer trial.

A large adipose mass limits the proportion of the body's PCBs that are available to the blood for direct intestinal excretion. The half-life of 2,3,7,8-tetrachlorodibenzodioxin (TCDD) has been shown to double when body fat increased from 20 to 30 kg, suggesting that an individual will more likely respond to olestra when the adipose tissue compartment is small(15). Consistent with this possibility is the observation that the BMIs of Participants 13 and 19, who experienced large increases in elimination rates, were 24.1 and 27.6, respectively, which were less than that of the group mean (32.8) and were maintained during the study. It seems likely that health benefits that may result will be determined by the mass of adipose tissue that stores these compounds. A large adipose depot may limit the fraction of PCBs that are available for removal through interruption of enterohepatic circulation.

Ideally this trial would have measured adipose tissue mass throughout the study along with adipose concentrations of PCBs, so that body burden would be the product of adipose tissue mass and PCB concentration. However, given this trial's exploratory nature and our concerns about participant compliance, we opted to measure serum PCB concentrations. It has been shown, that lipid-normalized serum organochlorine concentrations are good approximations of the adipose tissue levels(16, 17). Our "window" on PCB body burden was PCBs in the blood serum lipid fraction coupled with constant body weight.

The VO was not an inert placebo since it provided dietary fat, and this might have accounted for the observed decrease in the half-life of blood PCBs in some VO individuals. Partial malabsorption of dietary fat can reduce the absorption of organochlorines in enterohepatic circulation(18).

Previous studies of the effects of olestra on organochlorine metabolism in humans have been reported. Blood levels of organochlorines were measured during three months of weight loss to determine olestra's effect on increases in blood organochlorines that accompany weight loss(19). In that trial olestra altered β -hexachlorocyclohexane but not other organochlorines. The subjects lost body weight during that trial, so that total organochlorine body burdens were not measured. Geusau reported a "relatively small effect" of olestra in on another organochlorine, the dioxin, TCDD, in two subjects(20). The small effect of olestra was attributed to the short half-life of TCDD, and poor compliance with the olestra dose during the three-year trial. Moser and McLachlan reported enhancement of fecal excretion rates of dioxin when olestra was fed to four subjects(21).

Increases in total and LDL cholesterol in the Olestra group at 12 months observed during the trial were unexpected since olestra has previously been reported to modestly reduce these levels(22–24). There was not, however, a significant increase in these lipids based on regression analysis of their concentration over time.

Minimal risk resulted from treatment with 15 g/day of olestra. Modest and transient gastrointestinal effects were reported by only two participants in the Olestra group. With the regimen of a daily normal multivitamin supplement, there was no effect on fat-soluble vitamin status based on serum α -tocopherol levels.

Our findings suggest that non-absorbable dietary lipid can hasten the removal of PCBs. Because the trial was exploratory in nature, the sample size was small and the duration was short in terms of PCB half-lives. Finally, we do not know if exposure to PCBs in foods continued in some individuals during the trial.

Conclusion

Interruption of enterohepatic circulation of PCBs and their metabolites by a non-absorbable lipid can reduce body burdens of PCBs. Modest, transient adverse events related to the regimen were observed, consistent with a low risk to benefit ratio. Extension of this study to a cohort within normal ranges of BMI, and to subjects who are undergoing weight loss will expand our understanding of this novel and potentially useful treatment strategy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We appreciate the advice on the manuscript provided by Dr. Stephen Woods and the clinical services of Kim Craven. We also appreciate the assistance of the West Anniston Foundation personnel and board members.

Abbreviations

DDE	1,1- <i>bis</i> -(4-chlorophenyl)-2,2-dichloroethene
PCB	polychlorinated biphenyl
ACHS	Anniston Community Health Survey

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Figure 1. Change from baseline for total PCBs (A), higher chlorinated congeners (B), and PCB 153 (C) for the Olestra group (solid line) and the VO group (dotted line). Standard errors are indicated by the vertical bars.

Figure 2.

A comparison of the observed (dotted line) and predicted (solid line) changes in total PCB body burden based on elimination rate constants calculated for the VO and Olestra groups. The decrease during the trial period was significantly greater than the change predicted from the pre-trial elimination rate for the Olestra group.

Table 1

Baseline characteristics of the participants who started the study. Data are presented as mean $\pm$ sem or n(%)

Variable	Olestra N=14	VO N=14	p-value
Age (years)	59.9 $\pm$ 2.6	61.0 $\pm$ 1.5	0.70
Female	8 (57.1%)	9 (64.3%)	0.70
Race/Ethnicity			
African American	11 (78.6%)	10 (71.4%)	
White	2 (14.3%)	4 (28.6%)	0.65
Native American	1 (7.1%)	0 (0%)	
BMI	31.3 $\pm$ 1.9	35.6 $\pm$ 2.9	0.23
Total Cholesterol (mg/dL)	175.2 $\pm$ 9.3	191.5 $\pm$ 10.8	0.26
LDL Cholesterol (mg/dL)	96.9 $\pm$ 8.6	111.0 $\pm$ 9.6	0.29
HDL Cholesterol (mg/dL)	54.4 $\pm$ 4.5	58.7 $\pm$ 3.5	0.47
Triglycerides (mg/dL)	119.1 $\pm$ 12.4	109.4 $\pm$ 12.9	0.59
Glucose (mg/dL)	111.4 $\pm$ 10.3	118.0 $\pm$ 13.1	0.70
Insulin (units/mL)	24.4 $\pm$ 4.5	23.2 $\pm$ 3.4	0.82
α -Tocopherol (μ g/mL)	14.2 $\pm$ 1.2	15.3 $\pm$ 2.5	0.68

Table 2

BMI and serum measurements at the end of the one-year trial and change from baseline.

Variable	Olestra N=11*		VO N=12	
	Final Visit	Change from Baseline	Final visit	Change from Baseline
BMI kg/m ²	32.8 ± 2.0	-0.07 ± 0.31	35.0 ± 3.3	-0.27 ± 0.43
Total Cholesterol (mg/dL)	213.1 ± 15.8	35.7** ± 8.8	190.0 ± 11.2	-1.4 ± 6.0
LDL Cholesterol (mg/dL)	124.5 ± 15.7	28.3** ± 8.0	109.4 ± 10.0	0.42 ± 5.11
HDL Cholesterol (mg/dL)	60.0 ± 4.8	5.9 ± 3.3	59.9 ± 4.3	-0.33 ± 2.92
Triglycerides (mg/dL)	143.1 ± 14.9	8.5 ± 16.7	104.0 ± 9.1	-6.8 ± 8.1
Glucose (mg/dL)	117.1 ± 14.7	7.4 ± 9.3	105.5 ± 9.6	-4.0 ± 6.4
Insulin (units/mL)	37.8 ± 8.4	9.9 ± 6.1	31.6 ± 6.7	8.1 ± 6.5
α-Tocopherol (µg/mL)	15.4 ± 1.1	0.32 ± 1.00	13.0 ± 1.1	-2.5 ± 1.8

* one subject in the Olestra group started late so final visit was at 8 months

** statistically significant change from baseline

Table 3

Elimination rate constants for total PCBs (37 congeners), higher chlorinated congeners, and PCB 153 in the VO and Olestra groups for the pre-trial and trial periods.

Period	Measurement	Olestra (years ⁻¹)	VO (years ⁻¹)
Pre-trial	Total PCBs	-0.00864 ± 0.0116	-0.0283 ± 0.0096
Trial	Total PCBs	$-0.0829^a \pm 0.0357$	-0.0413 ± 0.0408
Pre-trial	Higher congeners	-0.00247 ± 0.0110	-0.0208 ± 0.0062
Trial	Higher congeners	$-0.0809^b \pm 0.0356$	-0.0296 ± 0.0425
Pre-trial	PCB 153	-0.0282 ± 0.0146	-0.02987 ± 0.0084
Trial	PCB 153	$-0.1234^c \pm 0.0566$	-0.06546 ± 0.0404

Letters indicate significant difference from pre-trial value:

^a
p=0.04;

^b
= 0.03;

^c
p = 0.06.