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**A NON-ABSORBABLE DIETARY FAT SUBSTITUTE ENHANCES ELIMINATION OF  
PERSISTENT LIPOPHILIC CONTAMINANTS IN HUMANS**

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**Abstract**

For individuals contaminated with persistent lipophilic pollutants, there is an urgent need for a therapy to enhance contaminant elimination from the body and hence reduce long term exposure. This study investigated the possibility of enhancing the excretion of native chemical via the faeces by augmenting the lipophilic properties of the faeces with the non-absorbable lipid substitute olestra. The faecal excretion of polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs), polychlorinated biphenyls (PCBs), and hexachlorobenzene (HCB) was measured in 3 volunteers. The excretion while eating an olestra-free diet was compared with the excretion while eating a diet supplemented with 25 g/d of olestra. The excretion while on the olestra diet was higher by a factor of 1.5 – 11, depending on the compound. This resulted from higher concentrations of the contaminants in the faeces and higher excretion of faeces dry mass due to the food additive. Using 2,3,7,8-Cl<sub>4</sub>DD as an example, it was estimated that ingestion of 25 g/d of olestra would more than double the overall rate of elimination of this compound from the body. It is concluded that regular consumption of olestra may provide a therapeutic approach for reducing the body burden of persistent lipophilic contaminants.

**Keywords:** PCDD/F; PCB; HCB; polysucrose ester; olestra; faecal excretion; elimination**Introduction**

Many environmental contaminants of concern for human health are very persistent in humans. Half lives of 3 – 28 years have been reported for most 2,3,7,8-substituted polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs) as well as for a variety of polychlorinated biphenyl (PCB) congeners [1,2]. Consequently, individuals who have unwittingly accumulated a large quantity of such a substance, for instance in the workplace or via an accident, are exposed to high tissue levels for decades. This long-term exposure increases the likelihood of adverse health effects [3].

There is currently no therapy available to protect individuals from the adverse effects of these compounds. Once people have become contaminated, the only way to help them is to enhance the elimination of chemical from the body. This is not easy, since metabolism is very slow, and enhancing metabolism is generally not a feasible alternative. However, there are physical mechanisms by which chemicals can be eliminated. Experiments in laboratory animals and humans have shown that lipophilic contaminants in the body are excreted via non-biliary transfer to the faeces [4,5]. The underlying mechanism is believed to be transfer of the native compound across the mucosa of the intestine [6]. This process was recently identified as the most important non-metabolic elimination mechanism for persistent PCDD/Fs in humans [7].

It has been proposed that the faecal excretion of lipophilic contaminants can be enhanced by increasing the lipophilic character of the faeces and thus enlarging their capacity to transport non-polar compounds [6]. Efforts have been made to stimulate the faecal excretion using dietary supplements that are not readily absorbed in the digestive tract such as mineral oil, hexadecane, cholestyramine and dietary fibre [8-13]. This approach has been moderately successful in laboratory and domestic animals [8-11], but in humans little stimulation has been observed [12,13]. We hypothesised that the sucrose-polyester olestra may be more effective, since it is a very lipophilic molecule that is not absorbed in the human intestine and passes the gut without being degraded [14,15]. Other studies have reported that olestra enhances faecal excretion of lipophilic compounds in laboratory animals [16,17]. Moreover, the extensive testing leading to its certification as a food additive has shown that it can be consumed in large quantities for extended periods of time by most people without side effects [15].

### Experimental

The enhancement of faecal excretion of PCDD/Fs, PCBs and hexachlorobenzene (HCB) as a result of the ingestion of olestra was investigated in three male volunteers aged 25, 37 and 54 years (abbreviated M25, M37 and M54). The volunteers were healthy and had no history of intestinal disorders.

The study consisted of a control phase and a test phase. During the control phase, which lasted 3 days, the volunteers ate a diet containing no olestra. During the test phase each volunteer ate 90 g of potato chips per day that contained 25 g of olestra. The chips were eaten in 3 portions of 30 g with meals. The test phase lasted 8 days for M25 and M54 and 10 days for M37. The volunteers ate a normal diet with the exception of M37, who ate a vegetarian diet free of meat, fish and dairy products during the first 5 days of the test phase and during a second control phase. This reduced the dietary intake of PCBs and PCDD/Fs to near zero, since these food items account for >85 % of the contamination of the German food supply with these substances [18,19].

Two markers (an iron capsule and corn kernels) were taken by the volunteers at the beginning of the first and before going to bed on the last day of each phase. All of the faeces produced during the phase itself and during the three days after the phase ended were collected directly in aluminium foil. The foil was folded over the sample, sealed in a plastic bag and frozen for later analysis.

In the laboratory the samples were freeze-dried and those faeces were identified which were excreted after the first marker but before the second marker. For the control phase the faeces for the 3 day period were pooled. The analysis of faeces samples pooled over 3 days has been shown to give reproducible measurements of faecal excretion of PCDD/Fs and PCBs [20]. For the test phase, the faeces from M25 and M54 were pooled into 2 day composites and the faeces of M37 were analysed on a daily basis.

Each of the pooled freeze-dried faeces samples was homogenised in a blender. An aliquot of each sample was Soxhlet extracted in toluene for 16 h. An internal standard cocktail containing 12  $^{13}\text{C}_{12}$  labelled PCDD/Fs, 9  $^{13}\text{C}_{12}$  labelled PCBs and  $^{13}\text{C}_6$  labelled HCB was added to the solvent prior to extraction. The extracts were cleaned up using  $\text{H}_2\text{SO}_4$ -silica gel, a mixed acidic/basic silica gel column and an aluminium oxide column to yield a PCDD/F fraction and a fraction containing the PCBs and HCB. These were analysed using HRGC/HRMS on a VG Autospec Ultima at a mass resolution of 10,000. The quantification was conducted using the internal standards and a minimum of two chlorine isotopes per analyte. A smaller aliquot was extracted in toluene and evaporated to dryness for the determination of the lipid content of the faeces.

In addition to the faeces samples, blood samples were taken from each of the volunteers. Venous blood was taken from the arm following an overnight fast. The blood flowed directly from the cannula into a pre-washed glass bottle containing heparin. The blood was frozen and stored at  $-20^\circ\text{C}$  until analysis. The blood samples were extracted using the method of Pöpke et al. [21] and cleaned up and analysed in a similar manner to the faeces samples. Further details of the experimental procedures and analytical methods are given elsewhere [20].

### Results and Discussion

The lipid normalised concentrations of the contaminants in the volunteers' blood are published elsewhere [20]. They lie in the range typical for the German population with background exposure [22].

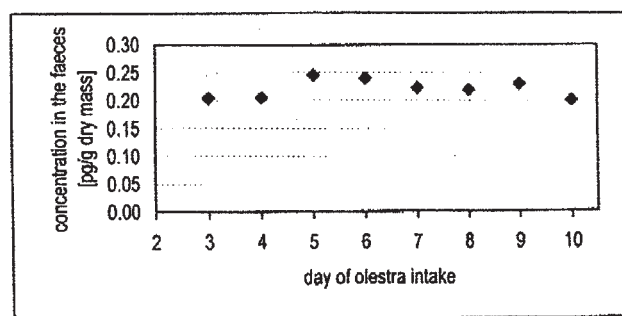
The daily excretion of contaminants during the control phase was positively related to the lipid normalised concentration in blood, i.e. volunteers with a higher blood concentration of a compound showed higher faecal excretion compared to volunteers with low blood concentrations. This is in agreement with measurements of the faecal excretion of PCDD/Fs in contaminated chemical workers, which showed the contaminant excretion rate to be linearly related to the blood concentration [7]. It also concurs with the results of a study of a people with background levels of these compounds (which included the 3 volunteers in this study) that showed that the faecal excretion was related primarily to the blood concentration and not to the dietary ingestion of contaminant [20]. Both of these papers show that the faecal excretion of these compounds originates from tissue residues and not from incomplete absorption of chemical taken up via food. This and the fact that the dietary intake of the volunteers had been well characterised in earlier studies [23] were the reasons why dietary intake was not quantified in this investigation.

In evaluating the faecal excretion during the test phase, the first two days' data were discarded to preclude possible transition effects. The excretion rates during the period of olestra ingestion were 1.5 - 11 times higher than during the control phase (Table 1). This increase was due to a combination of higher dry weight and lipid weight based concentrations of most compounds in the faeces and an approximate doubling in the quantity of faeces dry mass/tripling in the quantity of faeces lipid mass as a result of eating the non-absorbable olestra.

Table 1: Average daily faecal excretion with and without olestra intake

volunteer diet	no intake of olestra				intake of 25 g olestra per day			
	M25 normal	M37 vegetar.	M37 normal	M54 normal	M25 normal	M37 vegetar.	M37 normal	M54 normal
faeces collection (days)	3	3	3	3	6	3	5	6
faeces excretion	[g/d]							
dry mass	34	49	39	47	70	101	90	76
lipid mass	8	13	13	10	37	41	38	31
excretion of PCDD/F	[pg/d]							
2,3,7,8-Cl <sub>4</sub> DD	4.2	2.5	3.1	9.7	19.4	22	20	46
1,2,3,7,8-Cl <sub>5</sub> DD	16.9	10.8	10.8	25	55	59	56	99
1,2,3,4,7,8-Cl <sub>6</sub> DD	13.2	8.2	9.1	21	23	34	33	42
1,2,3,6,7,8-Cl <sub>6</sub> DD	52	58	57	128	105	220	203	330
1,2,3,7,8,9-Cl <sub>6</sub> DD	14.0	8.5	11.1	26	26	29	31	35
1,2,3,4,6,7,9-Cl <sub>7</sub> DD	24	38	34	40	115	101	95	76
1,2,3,4,6,7,8-Cl <sub>7</sub> DD	126	120	141	220	240	340	337	360
Cl <sub>8</sub> DD	1220	1480	1450	2300	1840	2700	2900	3600
2,3,7,8-Cl <sub>4</sub> DF	1.86	< 3.5	< 1.85	< 2.0	5.7	8.1	7.7	11.7
1,2,3,7,8-Cl <sub>5</sub> DF	< 1.78	3.3	1.75	1.89	4.9	8.1	7.0	5.1
2,3,4,7,8-Cl <sub>5</sub> DF	44	23	18.8	66	144	133	129	300
1,2,3,4,7,8-Cl <sub>6</sub> DF	19.0	16.8	11.4	23	39	46	47	62
1,2,3,6,7,8-Cl <sub>6</sub> DF	14.7	11.4	9.0	17.1	36	39	37	55
2,3,4,6,7,8-Cl <sub>6</sub> DF	11.4	8.8	7.3	9.3	24	31	28	24
1,2,3,4,6,7,8-Cl <sub>7</sub> DF	27	39	40	48	46	98	82	62
1,2,3,4,6,8,9-Cl <sub>7</sub> DF	7.7	10.7	10.3	18.1	13.5	24	22	15.3
1,2,3,4,7,8,9-Cl <sub>7</sub> DF	1.87	2.9	1.51	2.1	2.9	3.7	4.2	3.7
Cl <sub>8</sub> DF	17.3	43	33	29	33	54	53	47
excretion of PCB/HCB	[ng/d]							
PCB 28	6.3	3.5	5.2	10.8	40	59	49	74
PCB 52	2.7	1.41	2.4	4.1	11.0	11.9	8.9	15.5
PCB 99	6.6	6.5	6.5	12.5	55	65	65	110
PCB 101	2.7	1.38	1.96	4.9	21	16.8	13.9	29
PCB 105	1.73	1.08	1.24	3.4	12.4	11.2	10.9	27
PCB 118	12.2	8.2	8.9	28.6	110	81	83	230
PCB 138	58	42	38	130	350	370	380	930
PCB 153	106	69	65	270	590	560	560	1790
PCB 170	29	11.8	11.5	73	88	93	91	260
PCB 180	56	28	29	151	240	210	210	730
PCB 202	0.36	0.69	0.63	1.38	2.1	4.5	4.3	7.9
PCB 209	0.60	0.55	0.66	8.7	3.1	2.7	3.6	19.8
HCB	80	97	82	320	770	890	870	2400

The effect of olestra on contaminant excretion was very reproducible. For instance, the concentrations of 2,3,7,8-Cl<sub>4</sub>DD in the faeces of M37 varied by only  $\pm 10\%$  over the 8 days of sampling (Fig. 1). This is also evidence of the reproducibility of the experimental protocol and analytical methods employed. The increase in the faecal excretion during the olestra phase was significant at the 95 % level in 70 % of the cases (one-side t-test).



**Figure 1:** Concentrations of 2,3,7,8-Cl<sub>4</sub>DD in the faeces of M37 during days 3 – 10 of the test phase.

During days 1 – 5 M37 consumed a vegetarian diet; during days 6 – 10 he consumed a normal diet.

It is notable that changes in contaminant uptake and faeces composition caused by switching from the vegetarian to the normal diet on day 6 resulted in no change in the faeces concentrations of M37 (Fig. 1). Since previous work had shown that for most chemicals the daily intake via the vegetarian diet of M37 was <20 % of the intake via the normal diet [23], this is evidence that the enhancement in faecal excretion does not originate from reduced absorption of ingested contaminant.

Figure 2 shows the faecal excretion during the olestra phase divided by the daily intake of the contaminants measured in another study using the same volunteers on a comparable diet [20]. The quotients are plotted for those compounds that clearly bioaccumulated in the volunteers, i.e. for those compounds that were quantifiable in blood. The quotient was greater than one in all cases. This confirms that the enhancement in faecal excretion during the olestra phase did not only originate primarily from reduced absorption of ingested contaminant. For most chemicals it must have originated largely from excretion of residues stored in the body.

The enhancement of the faeces excretion was comparable between the three volunteers, but varied widely from compound to compound. For comparison of the compounds' behaviour, an excretion enhancement factor was calculated for those compounds that bioaccumulated. The excretion enhancement factor was defined as the quotient of the average daily excretion of contaminant when consuming 25 g of olestra daily divided by the average daily excretion when there was no olestra supplement. Figure 3 shows that the excretion enhancement factor decreased with the logarithm of the n-octanol/water partition coefficient ( $K_{ow}$ ), a measure of the lipophilicity of the compound. One possible explanation is that the enhancement of the solubility of the chemicals in olestra compared to normal faeces is less for the higher  $K_{ow}$  compounds;

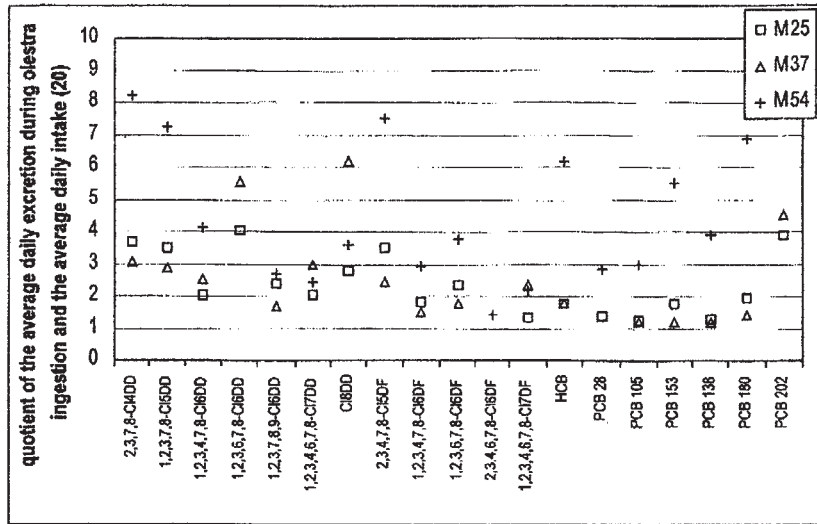


Figure 2: Quotient of the average daily excretion of chemical during the olestra phase and the average daily ingestion of chemical as measured for the same volunteers in another study [20]

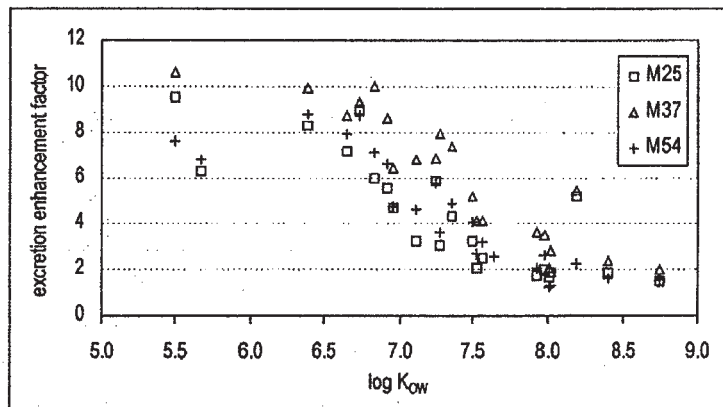


Figure 3: Excretion enhancement factor plotted against the *n*-octanol/water partition coefficient  $K_{ow}$ .

The  $K_{ow}$  values were taken from references 26-28.

i.e. olestra acts like a somewhat more polar solvent than the faeces constituents that sorb SOC. Alternatively, it could have been the result of kinetic limitations on transport across the wall of the digestive tract into the lumen. Other studies have found the digestive tract absorption of organic contaminants to decrease with increasing  $K_{ow}$  and have proposed that this is caused by either an aqueous resistance that is difficult for more hydrophobic compounds to overcome or by a membrane barrier that cannot be easily passed by larger molecules [24,25]. These same factors that influence dietary uptake may also limit the transport in the reverse direction from the tissue reservoirs into the lumen.

Faecal excretion has been estimated to contribute 40 % of the overall elimination of 2,3,7,8-Cl<sub>4</sub>DD from contaminated factory workers [7]. If this faecal excretion was increased by the average amount measured in this study (a factor of 5.7 for 2,3,7,8-Cl<sub>4</sub>DD), then the overall rate of elimination would be more than doubled. The efficacy of olestra in increasing overall elimination may be even greater for compounds with greater faecal excretion enhancement factors or for compounds that are metabolised more slowly than 2,3,7,8-Cl<sub>4</sub>DD. Further study is warranted to investigate whether modifying the olestra dose could further enhance excretion.

### Conclusions

Although this study was conducted with only 3 volunteers, it demonstrates that ingestion of olestra can decidedly increase the elimination of persistent lipophilic contaminants such as PCDD/Fs, PCBs and HCB in some people. This opens the possibility of developing the first effective therapy to reduce the body burden of contaminated individuals. Since olestra is an approved food additive in the USA, the adverse effects of such a therapy can be expected to be small. Nevertheless, because a potential therapy would extend over years and large quantities of olestra would be consumed daily, caution should be exercised.

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