Dietary gel-forming fibers increase PFAS excretion and decrease PFAS in the body, in an organ-dependent manner

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Abstract

Background:
US Military Service Members, their families, and the American public face significant exposures to per- and polyfluoroalkyl substances (PFAS). Once in the body, PFAS do not break-down and several remain in the body long after exposure ends. This is concerning because robust epidemiological evidence shows that PFAS exposures are associated with multiple adverse health effects, including kidney and testicular cancers, liver damage, increased cholesterol and poor response to vaccines. Theses health risks can be reduced by lowering PFAS levels in the body. However, the only approaches to reducing PFAS body burden are phlebotomy or treatment with cholestyramine, neither of which are feasible on a population scale. We hypothesized that dietary fibers that form a gel in the gut will trap PFAS entering the gastrointestinal tract, disrupt their reuptake into the body, and enhance PFAS excretion in feces.

Methods:
We conducted an exposure study in which mice were administered a mixture of commonly measured PFAS and fed a diet based on the "What we eat in America" NHANES analysis supplemented with one of five insoluble or soluble fibers (cellulose, wheat dextrin, chitosan, β-glucan, or psyllium) over a 6-week period. The negative control diet contained no additional dietary fiber. The positive control diet was supplemented with cholestyramine. PFAS were measured in feces, serum, ileum, kidney and brain tissues by LC-MS/MS.

Results:
As expected, cholestyramine increased fecal concentrations of PFAS and reduced PFAS body burden. PFAS are likely to be absorbed in the ileum because of high levels of transporter proteins that can move PFAS from the gut contents into the body. β-glucan and psyllium in the diet doubled daily excretion of PFAS compared with the control diet and also resulted in 40-50% reductions in ileal tissue PFAS concentrations. Fiber effects on serum PFAS concentrations were lesser (20%) but this level of reduction was consistent with reductions in the kidney and brain in mice fed the β-glucan and psyllium diets. Patterns of reductions were PFAS-specific and for psyllium consistent across serum, kidney and brain. β-glucan had a distinct effect on PFAS in the brain.

Conclusions:
While cholestyramine is an effective treatment for individuals with high PFAS exposures, our preliminary data support the use of gel-forming, dietary fiber supplements as a feasible approach, with beneficial nutritional effects that can be applied to human populations.

Introduction

PFAS Facts:
There are at least 14,000 different PFAS compounds

- **A wide array used in consumer products, are important component of fire fighting foam, and used as mist suppressant in metal plating**

1) Exposure typically occurs as a mixture (6 PFAS are commonly found in blood of US population)
2) Resistant to biodegradation and persistent in the environment
3) Many are water-soluble!
4) PFAS are efficiently absorbed but are difficult to eliminate

Adverse health effects of PFAS:
According to recent systematic reviews by ATSDR (1), EPA (2,3) AND IARC (4) PFAS cause:

1) Renal cell and testicular cancer (PFOA)
2) Liver toxicity (PFOA, PFOS, PFHxS)
3) Increases in serum total cholesterol and low-density lipoprotein (LDL) cholesterol (PFOA, PFOS, PFNA, PFDA)
4) Decreased antibody response to vaccines (PFOA, PFOS, PFHxS, PFDA) ·
5) Pregnancy-induced hypertension/pre-eclampsia (PFOA, PFOS)
6) Decreases in birth weight (PFOA, PFOS)

Long half lives enhance PFAS toxicity
Long chain PFAS such as PFOA, PFNA, PFHxS and PFOS have elimination half-lives of 2 to 10+ years (1). While PFAS can be eliminated in urine and bile, the processes are remarkably inefficient because transporter proteins move PFAS from the urinary filtrate or from the bile contents in the gut back into the body (5-9). As a result, PFAS accumulate in the body.

Current approaches to reduce PFAS in the body:

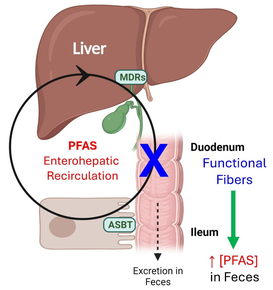
1) Phebotomy
   Studies in firefighters show that blood donation reduces PFAS body burden (10-13)
2) Bile Acid Sequestrants
   Originally shown in a rat study in 1987 (14) and now shown in three clinical trials, bile acid sequestrants (cholestyramine and colesevalam) significantly reduce PFAS body burden (13,15,16)

Question

Is there a more feasible, accessible, and economical solution to increase PFAS elimination and reduce toxicity?

Hypothesis

Dietary fibers that form a gel in the gut will trap PFAS entering the gastrointestinal tract, disrupt their reuptake into the body, and enhance PFAS excretion in feces.



Methods

Elements of human relevant model:

C57BL6/J background

♀♂

"What we eat in America" (NHANES) base diet

PFAS drinking water exposure

Exposure scenario:

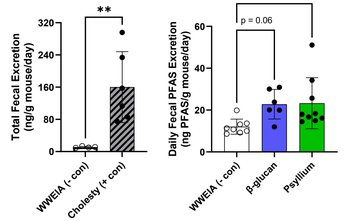
1) Mice were fed the WWEIA base diet or the base diet supplemented with cholestyramine (positive control), oat β-glucan or psyllium.
2) Mice were exposed to PFAS in drinking water (PFOA, PFHxA, PFNA, PFDA, PFUnDA, PFHxS, PFOS - prepared as a single 40 L ba˙tch). with the goal of producing an occupational level serum concentration
3) One week after acclimation to the diet, PFAS exposures were started and continued for 6 weeks. At the end of the exposure period, total serum concentrations of PFAS in animals fed the WWEIA diet was ≈ 10 µg/mL.

Analyses:

1) Metabolic cages were used to determine daily fecal output for each diet.
2) At euthanasia, body weight was measured. Blood was collected by cardiac puncture and serum prepared. Organs were collected and weighed. Feces were collected from the large intestine. All samples were stored at -80°C.
3) For PFAS analyses, samples were spiked with internal standards followed by extraction and cleanup. PFAS were quantified by liquid chromatography tandem-mass spectrometry in an Applied Biosystems API4000 triple quadrupole mass spectrometer.

Results

Figure 1: Oat β-glucan and psyllium increase the fecal excretion of PFAS
Daily fecal output was measured using metabolic cages. PFAS concentrations were measured in feces collected from the large intestine. N = 6-10 (from both sexes). * p<0.05, ** p<0.01. ANOVA. Dunnett's.



Results

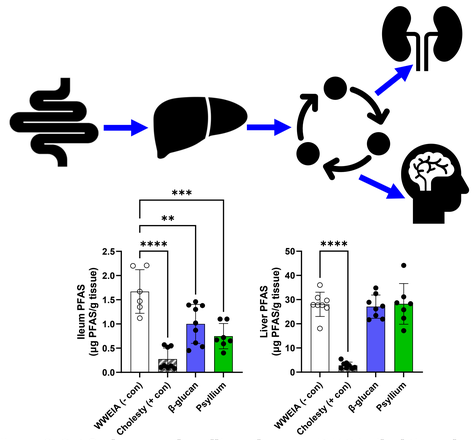


Figure 2: Oat β-glucan and psyllium decrease PFAS in ileal tissue but not liver N = 6-10 (from both sexes). ** p<0.01. *** p<0.001. **** p<0.0001. ANOVA. Dunnett's.

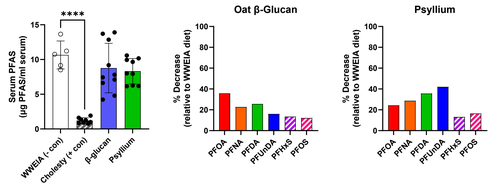


Figure 3: Oat β-glucan and psyllium decrease PFAS in serum ≈ 20%
N = 6-10 (from both sexes). **** p<0.0001. ANOVA. Dunnett's.

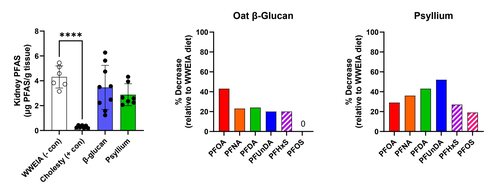


Figure 4: Oat β-glucan and psyllium decrease PFAS in kidney ≈ 20%
N = 6-10 (from both sexes). **** p<0.0001. ANOVA. Dunnett's.

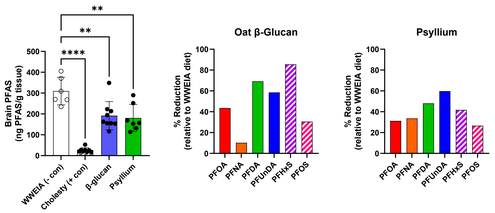
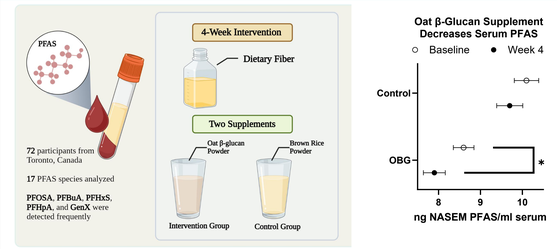


Figure 5: Oat β-glucan and psyllium decrease PFAS in brain
N = 6-10 (from both sexes).). ** p<0.001. **** p<0.0001. ANOVA. Dunnett's.

Applicability in People



- Serum samples were obtained from a previously conducted clinical trial (NCT03911427) that was designed to test if oat β-glucan (OBG) supplementation could reduce LDL in adults 18-65y with elevated LDL levels at baseline.
- In the randomized, double-blind, placebo-controlled, parallel-arm design clinical trial, participants consumed sachets of oat β-glucan or brown rice powder mixed with water three times per day immediately before or within 10 min of each main meal.
- Samples from men (chosen because men have higher PFAS level than women) were analyzed for 17 PFAS of multiple structural classes.
- We compared the serum PFAS concentrations between baseline and 4 weeks of intervention. Schlezinger et al., 2025. PMID: 40089764

Conclusions

1) The strong effect of cholestyramine confirms its utility as a front-line therapeutic for people with high PFAS exposures
2) Gel-forming dietary fibers can:
   - Increase fecal elimination of PFAS
   - Reduce PFAS in circulation and distribution to distal organs
3) Intervention can be feasibly and economically applied as a dietary supplement.
4) BUT …
   - PFAS reductions are likely caused by different/unexpected mechanisms (i.e., β-glucan is fermentable.).
   - Efficacy can be improved.

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The authors of this study declare that they have no conflict of interest, financial or otherwise, related to the research presented herein. The findings and conclusions are based solely on the data and analysis and are not influenced by any external factors or interests.