PFAS Contamination and Cancer: An Emerging Concern

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What are PFAS?[1]

Per- and polyfluoroalkyl substances (PFAS) are a group of man-made chemicals with widespread use since the 1940s. There are >9,000 PFAS chemicals; however, the most common include the long-chained Perfluoro-octane Sulfonate (PFOS) and Perfluorooctanoic Acid (PFOA).

- PFAS is characterized by their carbon-fluorine bond, making them highly stable and resistant to degradation.
- Long-chain PFAS are eliminated slowly, over a period of years, and they tend to bioaccumulate in protein-rich compartments. In contrast, short-chain PFAS are eliminated within days.

Their persistence and potential health effects, including an association with cancer, have raised concerns.

Figure 1: PFAS sources. They are found in drinking water, soil, air, and in a variety of useful products such as nonstick cookware, firefighting foam, and waterproof clothing.[1,2]

Methods

- Critically review and examine the emerging concerns regarding PFAS contamination and exposure and its positive correlation with cancer using published literature that would highlight directions for future research.
- Conducted a comprehensive literature search encompassing various published sources that influence the relevance and applicability of study findings using PubMed, CDC, Cochrane Library, and Elsevier through the year 2023.

Findings

Potential Mechanism of Action PFAS Carcinogenesis:[3]

PFAS has a high affinity to serum protein due to their structural similarity to fatty acids. Evidence suggests that PFAS are not directly mutagen; however, several mechanisms are proposed:

- Epigenetic modifications: alterations in DNA methylation, histone modifications, and non-coding RNA expression, which can contribute to the development of cancer.
- Alterations in cellular metabolism: studies showed associated changes in glucose metabolism and pyruvate production in prostate cancer cells.
- Endocrine disruption: research studies have demonstrated a link between PFAS exposure and reduced testosterone levels in male neonates. This association is attributed to the ability of PFAS to cross the placenta and exhibit estrogenic and antiandrogenic effects.[4]
- Transcriptional dysregulation: associated with changes in gene expression patterns in various tissues, including the liver, prostate, and testes.

However, it is important to note that the mechanisms of PFAS, especially in relation to cancer, are poorly understood.

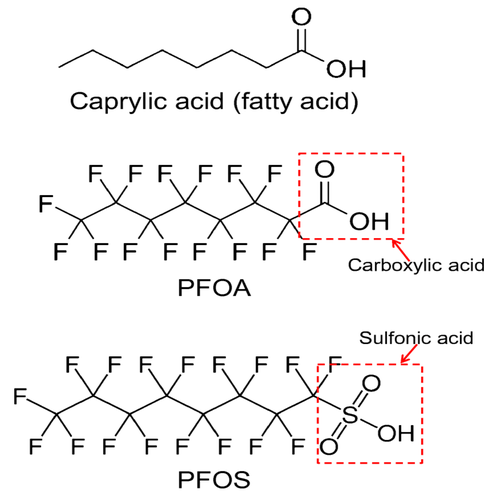
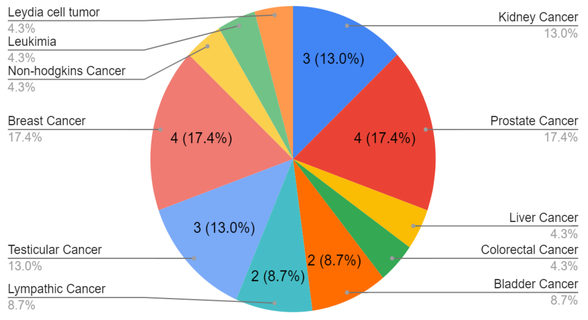


Figure 2: The structure of linear isomer of PFOA and PFOS and Caprylic acid for comparison, DOI: 10.1007/s00125-022-05695-5 2022/Diabetologia

Correlation Findings:[5,7]

- A scoping review identified 16 cohort (or case-cohort) studies, 10 case-control studies (4 nested within cohorts and 6 non-nested), 1 cross-sectional study, and 1 ecologic study. The cancer sites with the most evidence of an association with PFAS were testicular and kidney cancer.
- Evidence suggests a potential connection between PFAS exposure and cancer in both animal studies and in humans with higher PFAS concentrations. However, it is important to consider the limitations inherent in these studies, which may provide alternative interpretations of the findings.
- Some main study limitations include inaccurate self-reporting, lack of information on the timing and duration of PFAS exposure, difficulty in accurately assessing PFAS exposure levels, lack of information on potential confounding factors, potential exposure misclassification, and lack of information on the time windows when PFAS exposure might be most likely to lead to cancer. It was challenging to establish definitive findings regarding PFAS exposure.

Positive Correlation Between PFAS Exposure and Types of Cancer Studies



PFAS & Chemotherapy Resistance[6]

One study revealed that exposure to specific PFAS can cause resistance to carboplatin in ovarian cancer cells in vitro. It demonstrated that PFAS exposure resulted in reduced carboplatin-induced cell death and decreased mitochondrial membrane potential, which indicates compromised cell health. These findings imply that PFAS exposure may diminish the efficacy of carboplatin chemotherapy in individuals with ovarian cancer.

Conclusion

The association between PFAS exposure and cancer is an area of ongoing research and scientific investigation. While numerous studies have suggested an increased risk of certain types of cancer with PFAS exposure, establishing a definitive causal relationship is complex due to varying factors and limitations in the available evidence.

- The evidence suggests that PFAS exposure may contribute to the development or progression of cancer by potentially disrupting key biological processes, including hormonal regulation, immune function, and DNA damage repair mechanisms. However, further research is needed to fully understand the underlying mechanisms and establish a clear cause-and-effect relationship.
- Given the potential health risks associated with PFAS, it is important to prioritize prevention of exposure, mitigation of environmental contamination, and public awareness. Efforts should focus on reducing exposure to PFAS through regulation, monitoring, and the development of safer alternatives. Additionally, continued research is necessary to better understand the long-term effects of PFAS exposure and to inform policies and guidelines aimed at protecting public health.

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