

Global Distribution and Biochemical Effects of Trifluoroacetic Acid (TFA) in *C. elegans*



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Abstract

Background: TFA is an ultra-short-chain PFAS with rising global levels from industrial sources, PFAS degradation, and atmospheric transport.

Knowledge gap: Chronic effects and molecular mechanisms remain poorly understood.

Approach: Literature review on environmental TFA concentrations and distribution. *C. elegans* exposure assays (0.01–0.5 mM TFA; 48–60 h; no food) measuring oxidative/metabolic stress genes (SOD-3, NHR-49, GST-4, CTL-1) via qPCR.

Key findings: Low–moderate doses upregulated oxidative stress and metabolic genes. 0.5 mM caused strong downregulation and >50% lethality.

Conclusion: TFA is globally distributed and biologically active at sublethal levels, warranting greater regulatory attention.

Introduction

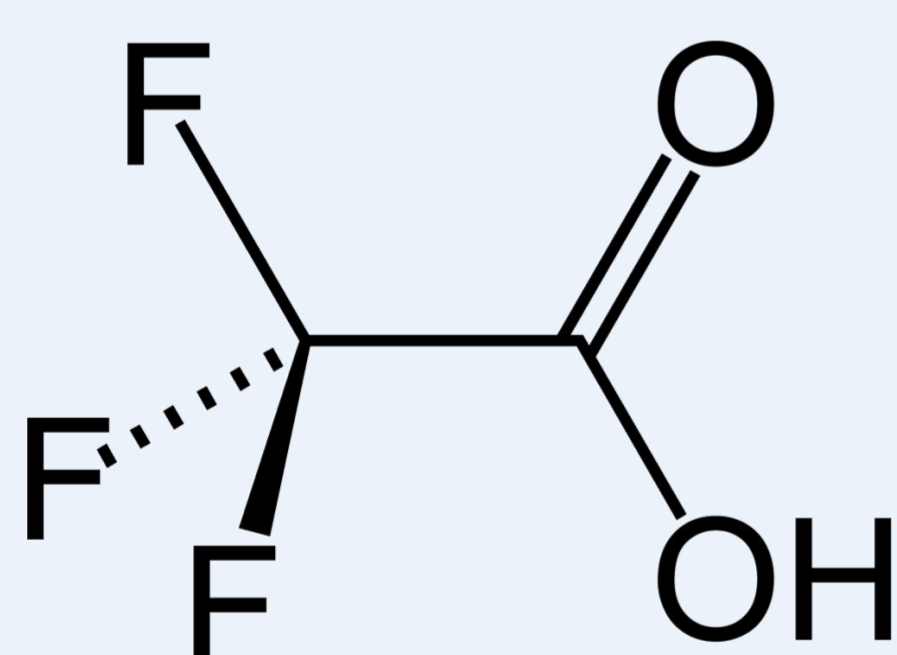
PFAS: Persistent, anthropogenic chemicals with strong C–F bonds; used in consumer & industrial products.

Long-chain PFAS: Well-documented toxicity; regulated in many countries.

TFA: Smallest perfluorocarboxylic acid; Mobile, water-soluble, resistant to degradation; Detected in rain, rivers, lakes, and drinking water.

Knowledge gap: Toxicological data for ultra-short-chain PFAS like TFA is scarce.

Study aims: Map geospatial TFA occurrence; Evaluate oxidative/metabolic stress gene responses in *C. elegans*.



Methods

1. Environmental Review

Databases: Web of Science, Scopus, Google Scholar, EPA/ECHA reports.

Inclusion: Quantitative TFA data with location, matrix, detection method.

Compiled by compartment (precipitation, surface water, groundwater, drinking water).

2. *C. elegans* Bioassay

Strain: N2 wild-type.

Exposure: L4 stage, K medium, TFA concentrations: 0.01–0.5 mM, 48–60 h, no food.

Genes measured:

- Oxidative stress: SOD-3, CTL-1, GST-4
- Metabolism: NHR-49

Analysis: $\Delta\Delta C_t$ method; triplicates; descriptive trends.

Results

1. Environmental Distribution of TFA

Global detection: Found in precipitation, rivers, lakes, groundwater, and drinking water on multiple continents.

Concentration ranges:

- Precipitation: ng/L to >6 $\mu\text{g/L}$ (highest in industrial & agricultural regions).
- Surface waters: Often elevated downstream of manufacturing zones or in watersheds with fluorinated pesticide use.
- Drinking water: Detected in municipal supplies; levels vary widely.

Geospatial patterns:

- Higher near PFAS manufacturing hubs and regions with high HFC use.
- Detected in remote areas \rightarrow indicates long-range atmospheric transport.

2. Gene Expression Responses in *C. elegans*

Low concentration (0.01 mM):

- SOD-3: $\sim 1.5\text{--}2\times$ upregulation (mitochondrial antioxidant defense).
- CTL-1: $\sim 1.2\text{--}1.5\times$ upregulation (hydrogen peroxide detoxification).
- NHR-49: $\sim 1.3\times$ increase (metabolic adaptation).
- GST-4: Minimal change.

Moderate concentration (0.025–0.1 mM):

- SOD-3 & CTL-1 plateau; still elevated.
- NHR-49 shows a biphasic response: dip at 0.025 mM, recovery by 0.1 mM.
- GST-4 induction ($\sim 1.3\text{--}1.6\times$), suggesting detoxification pathway activation.

High concentration (0.5 mM):

- All target genes suppressed below control levels.
- Mortality exceeded 50%.
- Measured pH ~ 3.3 ; likely compounded toxicity from acidity.

3. Observed trend: pH dropped progressively with higher TFA levels (5.0 \rightarrow 3.3).

High acidity likely contributed to lethality at 0.5 mM, but gene-specific responses at lower concentrations suggest direct TFA-induced oxidative stress, not just acid stress.

4. Key Takeaways

Sublethal exposures \rightarrow activation of antioxidant and metabolic defenses.

High exposures \rightarrow system-wide transcriptional collapse and mortality.

Environmental data show some real-world TFA concentrations approach those tested in the lab.

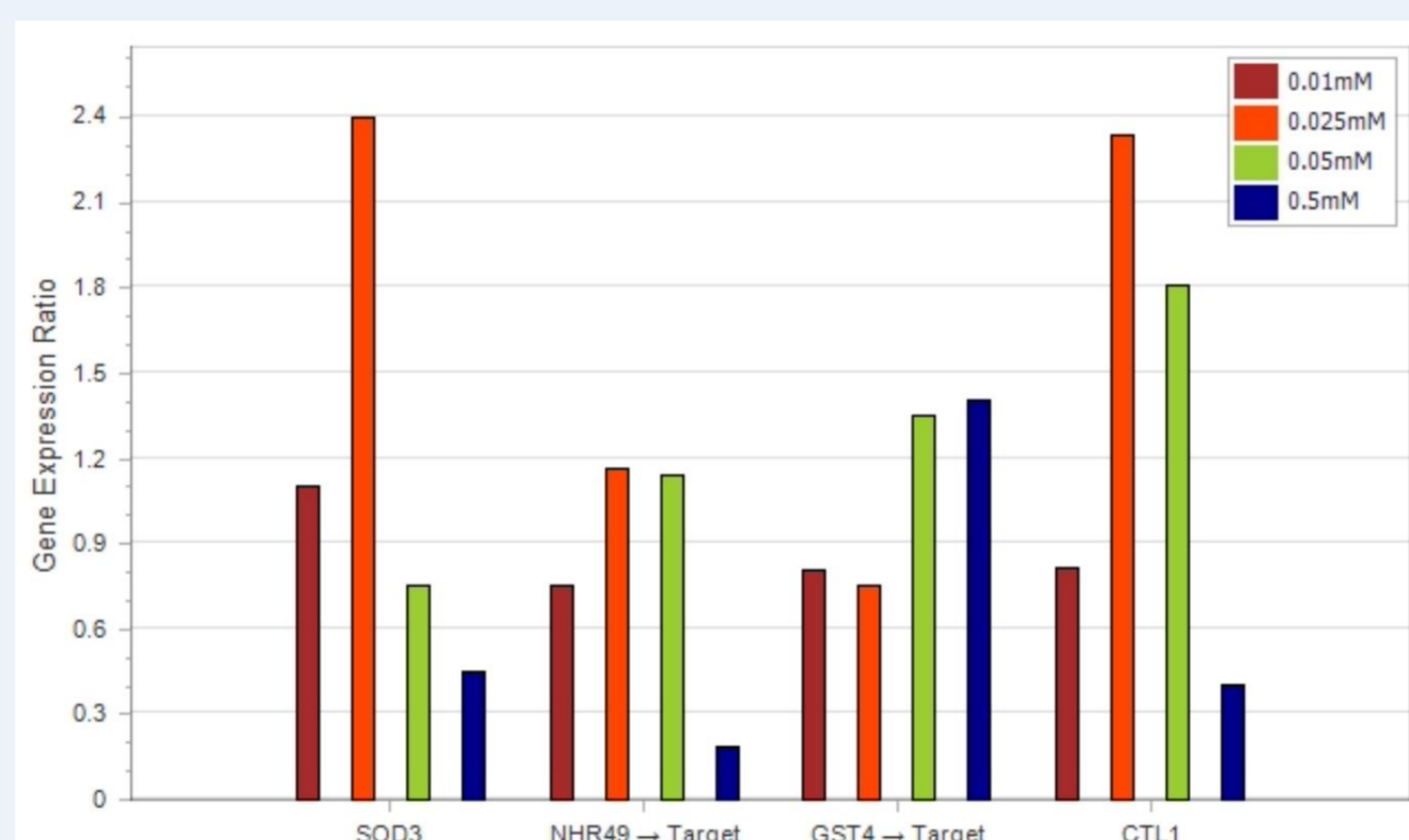


Figure 1. The effects of various TFA concentrations on SOD3, NHR49, GST4, and CTL1 gene expressions

System	Medium	Region (Year)	TFA Concentration	Concentration $\mu\text{g/L}$	Concentration $\mu\text{mol/L}$	Source (Ref)
Atmospheric Precipitation	Global	Global	0.0–100 ng/L	0.000–1.0 ng/L	0.00000–0.00001	Geometric et al. 2021
Atmospheric Rain, Rivers, Lakes, Drinking Water	China	China	10–100 ng/L	0.010–0.100 ng/L	0.00001–0.00010	Geometric et al. 2021
Atmospheric Rainwater	India, China	India, China	1–10 ng/L	0.001–0.010 ng/L	0.000001–0.00001	Geometric et al. 2021
Atmospheric Rainwater	Germany	Germany	0.1–1 ng/L	0.0001–0.001 ng/L	0.0000001–0.000001	Geometric et al. 2021
Atmospheric Drinking Water, Surface Water	Germany	Germany	10–100 ng/L	0.010–0.100 ng/L	0.00001–0.00010	Geometric et al. 2021
Atmospheric Rainwater	Switzerland	Switzerland	0.1–1 ng/L	0.0001–0.001 ng/L	0.0000001–0.000001	Geometric et al. 2021
Atmospheric Rain	USA	USA	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Rainwater	USA	USA	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Rain & Fog	USA (CA, WA, MI, NE)	USA (CA, WA, MI, NE)	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Drinking Water, Surface Water	USA	USA	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Rain	France	France	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Rain	Spain	Spain	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Rain	Italy	Italy	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Rain	Austria	Austria	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Rain	Switzerland	Switzerland	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Surface & Tap Water	Switzerland	Switzerland	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Surface Water	Germany	Germany	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Surface/Drinking Water	Germany	Germany	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Drinking Water	France	France	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Drinking Water	India, USA (2020)	India, USA (2020)	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Drinking Water	Switzerland	Switzerland	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Drinking Water	Switzerland	Switzerland	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Drinking Water	Switzerland	Switzerland	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Surface Water	Switzerland	Switzerland	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Atmospheric Surface Water	Switzerland	Switzerland	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Other	Switzerland	Switzerland	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Other	France	France	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Other	Germany	Germany	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Other	China	China	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021
Other	USA	USA	0.0–1 ng/L	0.000–0.001 ng/L	0.0000000–0.0000001	Geometric et al. 2021

Discussion

Mechanism: Likely mitochondrial ROS production \rightarrow antioxidant defense activation.

Environmental relevance: Field levels in some areas approach those causing lab-detected stress.

Regulatory implications:

TFA often excluded from PFAS regulations despite persistence & bioactivity. Data supports including ultra-short-chain PFAS in oversight.

Limitations: Acute exposure only; pH effects; single-species model.

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Conclusions

TFA is a global contaminant with potential biological impacts at environmentally relevant levels.

C. elegans data shows oxidative stress activation at low–moderate doses, toxicity at high doses.

Policy recommendation: Include TFA in PFAS monitoring and risk assessment frameworks.

Next steps: Chronic exposure tests, cross-species assays, mixture effects studies.

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