Vitamin D as a shield against sewage sludge contaminants

Vitamin D appears to offer measurable protection against several major classes of toxins found in sewage sludge — particularly heavy metals and pathogens — though the evidence varies sharply by contaminant. For cadmium and lead, animal and human studies show vitamin D supplementation activates antioxidant pathways, induces metal-binding proteins, and reduces organ damage. For PFAS, a landmark 2020 study revealed that PFOA directly competes with vitamin D for its own receptor, effectively creating functional vitamin D deficiency even when blood levels appear normal. PubMed Central Endocrine disruptors like phthalates and BPA are inversely associated with circulating vitamin D, suggesting a bidirectional harm loop. PubMed Central PubMed Central Biosolids — applied to over 40% of U.S. agricultural land PubMed Central — contain all of these contaminants simultaneously, nih yet no study has examined vitamin D's protective role against this combined exposure cocktail.

Biosolids contain a staggering array of contaminants

The EPA has identified **726 chemical pollutants** in biosolids, yet its Part 503 rule (1993) regulates only ten inorganic metals, pathogens, and vector attractiveness. PubMed Central nih A 2025 review found 229 contaminants of emerging concern positively detected in biosolids from 419 samples analyzed. Frontiers The contaminant categories with documented health effects are extensive.

Heavy metals represent the longest-studied threat. Cadmium (an IARC Group 1 carcinogen) causes kidney tubular dysfunction and bone demineralization. Taylor & Francis Online PubMed Lead is neurotoxic at any detectable level, impairing brain development in children AMS Samplers and causing hypertension in adults. Arsenic drives skin, bladder, and lung cancers. Frontiers Mercury damages the nervous system, while hexavalent chromium causes DNA damage via oxidative stress. Taylor & Francis Online EPA ceiling concentrations for land-applied biosolids allow cadmium up to **85 mg/kg** and lead up to **840 mg/kg** — limits set in the early 1990s gov.scot and widely criticized as outdated.

PFAS contamination has emerged as the most politically charged issue. The first nationwide inventory (Venkatesan & Halden, 2013) found PFOS at **403 ± 127 ng/g** dry weight in U.S. biosolids — more than 10× levels found in Spain and Germany. PubMed Central EPA's January 2025 draft risk assessment US EPA concluded that human health risks may exceed acceptable thresholds when biosolids contain as little as **1 ppb of PFOA or PFOS**, ASDWA a threshold most biosolids exceed. Wastewater Digest PFAS exposure is linked to kidney and testicular cancers, immune suppression, elevated cholesterol, and reduced vaccine response in children. Colorado Department of P… EWG

Pathogens in biosolids include *Salmonella*, *E. coli* O157:H7, *Cryptosporidium*, *Giardia*, norovirus, and hepatitis A virus. While Class A biosolids are treated to near-sterility, Class B biosolids retain significant pathogen loads. PubMed *Ascaris* roundworm ova can survive in soil for up to a decade. Virginiabiosolids Risk modeling estimates bacterial and viral infection rates of **1–29%** within 100 meters of spray-application sites. National Academies

Endocrine disruptors — including nonylphenol (up to 12.3 μg/g), BPA, PubMed phthalates (DEHP at near-100% detection), Frontiers and synthetic estrogens — persist in treated sludge. Anaerobic digestion can paradoxically increase overall estrogenicity. ResearchGate **Microplastics** accumulate in biosolids at **70–98%** of incoming wastewater loads, ALGA nih reaching concentrations of 240 particles per gram. The UK applies an estimated **2.7×10^{15} microplastic particles** to agricultural soils annually via biosolids. Frontiers Pharmaceutical residues and antibiotic resistance genes round out a contaminant profile that creates compounded, poorly understood exposure risks. Springer

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Strong evidence that vitamin D counters heavy metal toxicity

The most robust evidence for vitamin D's protective role against biosolid contaminants involves cadmium and lead, where multiple animal studies and some human data converge on clear protective mechanisms.

For **cadmium**, a human cross-sectional study of 133 subjects in cadmium-polluted areas of China (Chen et al., 2018) found that higher serum 25(OH)D was associated with lower risk of cadmium-induced renal tubular dysfunction. PLOS Animal studies have illuminated the mechanisms: vitamin D_3 injections mitigated cadmium nephrotoxicity ScienceDirect by inhibiting intestinal cadmium absorption, restoring vitamin D receptor (VDR) expression in kidneys, reducing lipid peroxidation, and decreasing apoptosis (Abdelghany et al., 2023). ScienceDirect BaSalamah et al. (2020) demonstrated that vitamin D_3 combined with calcium alleviated cadmium liver toxicity by remodeling cellular calcium pathways and reducing ER stress. PubMed Critically, cadmium itself disrupts vitamin D metabolism — studies in the Itai-itai disease region of Japan showed cadmium impairs renal conversion of 25(OH)D to active $1,25(OH)_2D$, PubMed Springer and a study in 140 Polish schoolchildren found children with high blood cadmium had **23% lower vitamin D_3 levels**. PubMed

For **lead**, the evidence is equally compelling. Refaat et al. (2018) described the first study showing molecular interactions between vitamin D and lead toxicity, finding that lead upregulates CYP24A1 (the vitamin D-degrading enzyme) while inhibiting CYP27B1 (the activating enzyme), effectively sabotaging cellular vitamin D metabolism. Vitamin D_3 supplementation reversed these effects, restored antioxidant defenses, and reduced inflammation in rat kidneys and testes. Nature BaSalamah et al. (2020) showed vitamin D protected against lead-induced neurotoxicity in the cerebral cortex via the **Nrf2 and NF-κB**

pathways — two master regulatory systems for antioxidant defense and inflammation. A NHANES analysis (Jing et al., 2025) confirmed that vitamin D-deficient individuals had significantly increased susceptibility to lead-induced early kidney injury. BMC Public Health PubMed Central Importantly, a clinical trial in children and young adults with HIV found that high-dose vitamin D_3 supplementation (4,000–7,000 IU/day for 12 weeks) did **not** increase blood lead levels, and vitamin D was negatively correlated with lead after supplementation (Groleau et al., 2013).

The underlying mechanisms are well-characterized. Vitamin D activates the **Nrf2-Keap1 antioxidant pathway**, PubMed upregulating heme oxygenase-1, glutathione S-transferases, and superoxide dismutase. A foundational 1987 study (Karasawa et al., PNAS) showed that 1,25-dihydroxyvitamin D_3 directly induces **metallothionein** gene expression Sage Journals — metallothioneins being the primary intracellular proteins for binding and detoxifying cadmium, mercury, lead, and arsenic. Wikipedia +2 Vitamin D also suppresses NF-κB-driven inflammation, restores depleted glutathione, and maintains calcium homeostasis ScienceDirect that competes with toxic metal absorption. PubMed

One important caveat deserves emphasis. Moon (1994) documented that vitamin D increases intestinal absorption of toxic metals (cadmium, lead, aluminum, cobalt) alongside essential minerals — a "double-edged sword." PubMed However, this concern appears manageable: adequate essential mineral intake (calcium, magnesium, zinc, iron) alongside vitamin D supplementation appears to resist toxic metal uptake, VitaminDWiki and the clinical trial data showed no increase in blood lead with supplementation. NCBI For arsenic, evidence is primarily epidemiological — subjects with the lowest vitamin D quartile and highest urinary arsenic had a **302% increased risk** of type 2 diabetes versus those with high vitamin D and low arsenic (Le et al.). Frontiers For mercury, direct protective evidence is minimal, though vitamin D does not increase mercury absorption (unlike other metals). Wiley Online Library

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PFAS directly sabotages the vitamin D receptor

Perhaps the most striking finding in this research landscape is that PFAS doesn't merely coexist with vitamin D — it actively antagonizes vitamin D at the molecular level.

Di Nisio et al. (2020) published a multi-level mechanistic study in *Scientific Reports* demonstrating that PFOA competes with calcitriol (active vitamin D) for the **same binding site on the vitamin D receptor**. PubMed Central +2 Using molecular docking, surface plasmon resonance, and cell culture experiments, they showed PFOA caused approximately a **10% reduction** in calcitriol binding to VDR, altered expression of vitamin D-responsive genes including CYP24A1 in osteoblast-like cells, and reduced bone mineralization. Nature In a small human cohort of young men from PFAS-contaminated Veneto, Italy, the PFAS-

exposed group showed elevated parathyroid hormone (suggesting compensatory secondary hyperparathyroidism) despite comparable 25(OH)D levels — evidence of **functional vitamin D deficiency** even when standard blood tests appear normal. PubMed Central Nature

This receptor-level interference was dramatically expanded by Azhagiya Singam et al. (2023), who computationally screened **5,206 PFAS compounds** against VDR. They identified 14 PFAS predicted to bind VDR as strongly as natural ligands, PubMed and of 256 commercially important PFAS, **83 (32%) were predicted to be stronger VDR binders than PFOA**. PubMed This suggests the problem extends far beyond the most-studied PFAS compounds.

Epidemiological evidence on PFAS and vitamin D levels is growing but inconsistent. The strongest inverse associations come from studies of postmenopausal women (NHANES 2003–2018, n=2,114), where PFOS exposure was associated with **2.5-fold increased odds** of vitamin D deficiency and PFOA with **3.1-fold increased odds**. ScienceDirect Zhao et al. (2024) found negative associations exclusively in older females. Environmental Health However, a study in 442 pregnant African American women (Chang et al., 2021) found mostly positive associations between PFAS and vitamin D — possibly reflecting shared protein binding or confounding by fish consumption. PubMed ScienceDirect A study in the highly PFAS-exposed Veneto region of Italy found mostly null results for vitamin D but positive associations with serum calcium independent of vitamin D, suggesting PFAS may disrupt calcium metabolism through non-vitamin D pathways. ScienceDirect

No clinical trial has tested vitamin D supplementation to counteract PFAS effects. Di Nisio et al. explicitly recommended that "PFAS-exposed communities would benefit from assessment of vitamin D status and consequent VD supplementation to counteract PFOA antagonism on VDR." PubMed Central However, given PFOA's mechanism as a VDR antagonist, simple supplementation to raise serum 25(OH)D may not fully overcome receptor-level blockade — higher doses or VDR agonist analogs might be necessary.

Vitamin D powerfully supports pathogen defense and gut barrier integrity

The evidence for vitamin D's role in defending against the types of pathogens found in biosolids is among the strongest in this entire research area, supported by mechanistic, animal, and clinical data.

The foundational discovery is that vitamin D directly controls production of **cathelicidin (LL-37)**, a potent antimicrobial peptide. Oxford Academic Springer The human cathelicidin gene contains a vitamin D response element in its promoter, and Liu et al. (2006) showed in a landmark *Science* paper that macrophages from vitamin D-deficient individuals had impaired antimicrobial responses — responses that were rescued when 25(OH)D was

added. LL-37 has demonstrated activity against *E. coli*, *Salmonella*, *Staphylococcus*, *Pseudomonas*, and multiple viruses. Vitamin D also induces **β-defensin 2**, (European Review) activates the **NOD2 intracellular pathogen receptor**, (Wiley Online Library) and enhances autophagy for clearing intracellular bacteria. (Springer) (PubMed)

For *Salmonella* — a primary biosolid pathogen concern — the evidence is particularly strong. Wu et al. (2016) showed active vitamin D enhanced autophagic clearance of *Salmonella* from intestinal epithelial cells via VDR-mediated Atg16L1 expression. Cheng et al. (2022) demonstrated that vitamin D-deficient laying hens had significantly higher *Salmonella enteritidis* loads and more severe intestinal damage. A clinical study of 70 hospitalized children found those with vitamin D below 30 ng/mL had **threefold increased odds** of culture-confirmed *Salmonella* infection. (MDPI)

Equally important is vitamin D's role in maintaining **gut barrier integrity** — the first line of defense against ingested biosolid contaminants. VDR-knockout mice develop severe colitis when exposed to even mild insults. Vitamin D upregulates tight junction proteins (ZO-1, claudin-1, occludin, E-cadherin) in intestinal epithelial cells, and a human randomized trial showed that vitamin D_3 supplementation (1,000 IU daily for one year) increased tight junction protein expression in rectal mucosa. Vitamin D-deficient mice infected with *Citrobacter rodentium* (a model for pathogenic *E. coli*) suffered lethal infection, higher bacterial loads, and greater translocation of bacteria to internal organs. Vitamin D sufficiency maintained the ILC3/IL-22 axis essential for mucosal immunity, and deficiency was rapidly fatal.

Endocrine disruptors and microplastics lower vitamin D and may be countered by it

The relationship between endocrine-disrupting chemicals and vitamin D is bidirectional: EDCs lower vitamin D, and adequate vitamin D may mitigate EDC damage.

Johns et al. (2016) published the landmark NHANES analysis of 4,667 adults showing that DEHP phthalate metabolites were **consistently inversely associated** with total 25(OH)D. (PubMed Central) BPA showed an inverse relationship specifically in women. (Healio) A prospective study of 477 pregnant women confirmed these findings, with DEHP metabolites and BPA associated with approximately **20% increased odds of vitamin D deficiency** at 10 weeks' gestation. The proposed mechanisms include disruption of cytochrome P450 enzymes involved in vitamin D metabolism, direct interference with VDR signaling (given VDR's membership in the same nuclear receptor superfamily as estrogen and androgen receptors), and secondary effects through EDC-promoted weight gain (obesity sequesters vitamin D in adipose tissue). (PubMed Central +2)

A comprehensive 2025 review (Furdui-Linţa et al.) concluded that adequate vitamin D may provide reciprocal protection against EDC damage through its anti-inflammatory, antioxidant, and immunomodulatory properties, recommending that "ensuring sufficient plasma level of vitamin D could represent one approach to mitigate the health risks associated with exposure to EDs." Springer

Emerging research on **microplastics** — which constitute 70–98% of biosolid mass from wastewater nih — is particularly intriguing. Li et al. (2023) exposed zebrafish to polystyrene nanoplastics and found that a high vitamin D diet reduced nanoplastic accumulation by **20% in the brain and 52–59% in intestinal tissues**, while significantly reducing neurotoxicity and anxiety-like behavior. PubMed This is the first evidence that vitamin D may directly reduce microplastic accumulation in tissues, potentially through enhanced gut barrier function and altered gut virome composition. PubMed

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Conclusion: a plausible but unproven integrated defense

The research paints a picture of vitamin D as a broadly relevant — but far from complete — defense against the contaminant cocktail in sewage sludge. The strongest evidence exists for **heavy metals** (particularly cadmium and lead), where vitamin D activates metallothionein production, Wikipedia Nrf2 antioxidant pathways, PubMed Central and anti-inflammatory signaling across multiple organ systems. For **pathogens**, vitamin D's role in cathelicidin induction, Springer gut barrier maintenance, and autophagy makes it a critical component of the mucosal immune defense Springer most relevant to biosolid exposure. Springer For **PFAS**, the discovery that PFOA acts as a VDR antagonist nih creates a disturbing positive feedback loop — the very contaminant impairs the receptor needed for vitamin D's protective effects — and suggests that standard supplementation alone may be insufficient. Nature PubMed Central For **endocrine disruptors**, the evidence of bidirectional interference is growing, with EDCs lowering vitamin D and vitamin D potentially countering EDC-driven inflammation and oxidative stress. PubMed Central Springer

Three critical gaps stand out. First, **no clinical trial** has tested vitamin D supplementation specifically in populations exposed to biosolid contaminants. Second, the **"double-edged sword"** of vitamin D increasing intestinal absorption of some toxic metals PubMed means supplementation should be paired with adequate essential mineral intake (calcium, magnesium, zinc, iron). VitaminDWiki Third, the cumulative and synergistic effects of simultaneous exposure to heavy metals, PFAS, pathogens, EDCs, and microplastics — the reality of biosolid exposure — remain entirely unstudied. Given that PFAS alone may create functional vitamin D deficiency at the receptor level even when blood levels appear normal, communities near biosolid application sites may benefit from both vitamin D status monitoring and supplementation strategies that account for receptor-level interference, though this hypothesis urgently requires clinical validation. PubMed Central