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Review

Unraveling the Molecular Pathways of Cadmium-Induced Aging

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Cadmium (Cd) is a toxic heavy metal widely recognized for its detrimental effects on human health, particularly due to its long biological half-life and ability to accumulate in tissues over time. Chronic exposure to Cd, whether through environmental, occupational, or dietary sources, has been implicated in accelerated aging and age-related pathologies. Increasing evidence from diverse model systems, including yeast, *Caenorhabditis elegans*, *Drosophila melanogaster*, mammalian cell cultures, rodents, and population studies, suggests that Cd disrupts key cellular processes such as oxidative stress response, mitochondrial function, DNA repair, and epigenetic regulation. These disruptions contribute to cellular senescence, tissue degeneration, and systemic aging phenotypes. By examining findings across different biological models, this review aims to elucidate the conserved and model-specific mechanisms by which Cd influences the aging process.

Keywords: cadmium, aging, molecular mechanisms, model systems

1 Introduction

The relationship between environmental pollutants and human health has become an increasingly urgent area of research, particularly in the context of aging and age-related diseases. Among these pollutants, Cd, a highly toxic heavy metal introduced into the environment through industrial emissions, mining, and agricultural runoff, has garnered significant attention due to its persistence, bioaccumulation, and systemic toxicity (Ankush et al., 2024). Once absorbed, Cd accumulates in tissues such as the liver and kidneys, where it can remain for decades, exerting long-term detrimental effects on cellular and physiological functions (Thévenod & Lee, 2013). Notably, Cd toxicity is mostly associated with its ability to increase oxidative stress and disrupt cellular repair processes. These stress-induced changes mimic and intensify the molecular mechanisms normally associated with age-related decline.

Aging is a universal, multifactorial, and irreversible biological process characterized by the gradual decline in function at molecular, cellular, tissue, and organismal levels. It is driven by the cumulative effects of both endogenous metabolic processes and exogenous environmental stressors, leading to homeostatic imbalance and increasing susceptibility to chronic diseases and mortality (Yang et al., 2020). Despite significant advancements in medicine that have extended life expectancy and healthspan, the period of life spent in good health has not improved at the same rate (Garmany et al., 2021). This discrepancy underscores the importance of understanding the mechanisms underlying aging and how environmental exposures may accelerate these processes.

At the core of many aging-related changes is oxidative stress, a state of imbalance between reactive oxygen species (ROS) and the body's antioxidant defense systems (Navrátilová et al., 2021). Although Cd is not redox-active, it indirectly promotes ROS generation by depleting glutathione, disrupting mitochondrial function, activating inflammatory pathways, and mobilizing iron, which catalyzes further radical formation (Cuypers et al., 2010). Acute Cd exposure can lead to oxidative damage

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through the generation of radicals, including superoxide (O_2•–), hydrogen peroxide (H_2O_2), and hydroxyl radicals (•OH), which damage DNA, proteins, and lipids. Chronic low-dose exposure, on the other hand, has been linked to epigenetic alterations, apoptosis resistance, and dysregulated gene expression, all of which contribute to cellular dysfunction and premature aging.

The hallmarks of aging, a conceptual framework proposed by (López-Otín et al., 2013), include genomic instability, telomere attrition, epigenetic changes, mitochondrial dysfunction, cellular senescence, and more. Many of these hallmarks are directly influenced by oxidative stress, making it a central player in aging and age-related pathologies, including cardiovascular disease, Alzheimer's disease, diabetes, and chronic kidney disease. Epidemiological studies further support this association, with diseases such as dementia, stroke, and ischemic heart disease showing a strong, age-related increase in incidence (Leyane et al., 2022).

Despite increasing recognition of these mechanisms, therapeutic strategies targeting oxidative stress remain limited, often hindered by poor specificity, bioavailability, and delivery efficiency. Novel interventions, such as caloric restriction, antioxidant therapy, senolytic agents, and stem cell treatments, offer promising avenues but require further investigation to determine their efficacy in mitigating environmental stress-induced aging (Z. Li et al., 2021).

This review provides a comprehensive synthesis of current research on Cd toxicity and its impact on aging, using various model organisms, with a focus on oxidative stress, molecular signaling, and cellular dysfunction. By highlighting key mechanisms and identifying knowledge gaps, we aim to shed more light on understanding the mechanisms of direct or indirect Cd-mediated premature aging.

1.1 Studies of Cd-Induced Aging in Yeast

The toxicity of Cd has been extensively studied for its harmful effects on cellular processes, including processes related to aging, in yeast, a valuable model for understanding eukaryotic biology. There are two types of aging in yeast: replicative aging, which represents the maximum number of cell divisions before death, and chronological aging, which refers to the viability duration during the stationary phase. Notably, chronological aging in yeast parallels mammalian apoptosis (Dahiya et al., 2020).

Both acute and long-term exposure to Cd trigger stress responses, predominantly through the production of free radicals generated during cellular respiration, resulting in oxidative stress that impacts aging-related pathways. These free radicals cause cumulative damage to various cellular components, including DNA, proteins, and lipids. Oxidative stress affects both replicative and chronological aging, but in different ways. Replicative aging is primarily influenced by the damage that occurs during cell division, while chronological aging is affected by long-term metabolic and mitochondrial decline in non-dividing cells (Costa & Moradas-Ferreira, 2001).

In *Candida tropicalis* 3Aer, transcriptomic and proteomic analyses revealed that acute Cd^{2+} exposure induces cell cycle arrest at the G2/M checkpoint and activates antioxidant defense mechanisms to combat ROS accumulation. Strikingly, long-term exposure leads to redistribution and amyloid formation of GAPDH and MDH, which appear to play a role in modulating metabolic pathways such as the pentose phosphate pathway, thereby contributing to delayed cellular aging and cellular dysfunction (Khan et al., 2019). Similarly, filamentous yeast, *Trichosporon cutaneum* R57, responds to Cd-induced oxidative stress by upregulating antioxidant enzymes like superoxide dismutase (SOD) and catalase, enhancing reserve carbohydrate storage, and maintaining relatively stable growth, suggesting a robust oxidative stress adaptation mechanism (Lazarova et al., 2014).

In *Saccharomyces cerevisiae*, Cd^{2+} induces a caspase-dependent apoptotic response, dependent on the yeast caspase Yca1p and glutathione metabolism, particularly through the *gsh1* gene. Interestingly, this response is heterogeneous within the population, with only a subpopulation undergoing apoptosis, emphasizing the complexity of Cd-induced stress (Nargund et al., 2008). Genome-wide transcriptomic profiling via RNA-Seq further uncovered that Cd stress significantly alters redox balance, impacting mitochondrial membrane potential and increasing ROS levels, while upregulating genes involved in oxidative stress response and glutathione metabolism (Huang et al., 2016).

Additionally, *Schizosaccharomyces pombe* (*S. pombe*) exposed to Cd showed ionome disruption, particularly depletion of K^+ and accumulation of Ca^{2+}, Mg^{2+}, Cu^{2+}, and Fe^{3+}, indicating that ionic imbalance is a key component of Cd-induced cellular dysfunction (Pozgajova et al., 2020). Notably, the absence of Tor1, a TORC2 subunit, in *S. pombe* mitigated many of the detrimental effects of Cd, suggesting a protective role of TOR signaling modulation in metal-induced aging (Požgajová et al., 2020).

Collectively, these findings across diverse yeast species underscore that Cd accelerates aging via multiple interlinked mechanisms, including oxidative stress, DNA damage, mitochondrial dysfunction, and altered metabolic and ion homeostasis, yet also highlight

species-specific adaptive responses that can delay or counteract aging under metal stress.

1.2 Impact of Cd Toxicity on Aging, Stress Response, and Reproduction in *Caenorhabditis elegans*

C. elegans is a valuable bioindicator for toxicity tests due to its short life cycle, ease of mass culture generation, and low cost (Lu et al., 2018). In this model organism, Cd exposure consistently shortens lifespan and accelerates aging-associated physiological decline through coordinated disruptions of stress-response, metabolic, and epigenetic pathways. Cd-mediated aging involves key regulatory mechanisms, including DAF-16/FOXO signaling, mitochondrial function, and chromatin-based gene regulation (Lee & Lee, 2022).

Cd toxicity is further exacerbated by interactions with other ions which results inthe life cycle shortening. For instance, combined exposure to 25 mM calcium (Ca) and 200 µM Cd decreases lifespan more than Cd alone (200 µM). In comparison, exposure to 1.56 mM Ca with 200 µM Cd shows no additional lifespan reduction compared to Cd alone. This combined stress elicits amplified cellular responses, such as stronger induction of *hsp-16*::gfp and elevated oxidative damage. Mitochondrial pathways are central to this vulnerability, as mutations in *mev-1*, which affects succinate dehydrogenase activity, sensitize worms to Ca/Cd co-exposure, further reduce lifespan (D. Wang et al., 2010).

Insulin/IGF-1 signaling mutants display altered sensitivity: *daf-16* mutants show enhanced susceptibility to combined Ca/Cd toxicity, while *daf-2* mutants demonstrate increased resistance, with lethal concentration (LC_{50}) values for Cd significantly higher in *daf-2* and *age-1* mutants than in wild-type worms. Moreover, *daf-2* mutants express 3-fold higher basal levels of metallothionein (MT1) mRNA, which is further induced upon Cd exposure, contributing to their resilience (Barsyte et al., 2001; D. Wang et al., 2010).

Beyond lifespan reduction, epigenetic mechanisms contribute to longer-term, transgenerational consequences, as chronic Cd exposure leads to increased germ cell apoptosis and reduced fertility across multiple generations, mediated by epigenetic changes such as histone H3K4 trimethylation and modulation of stress-responsive transcription factors like DAF-16/FOXO and SKN-1/Nrf2 (Huang et al., 2024).

Together, these findings show that Cd disrupts mitochondrial integrity, stress-resilience pathways, and epigenetic regulation in *C. elegans*, driving premature aging and compromised reproductive health.

1.3 Age-Dependent Vulnerability to Cd Toxicity in D. melanogaster: Linking Oxidative Stress, Neurodegeneration, and Epigenetic Memory

D. melanogaster is a highly relevant model for studying Cd-induced aging because its cellular stress-response pathways, detoxification mechanisms, well-defined nutritional requirements, and genetic regulators of aging are well conserved with those of mammals. Its short lifespan and powerful genetic tools enable rapid, mechanistic assessment of how Cd exposure might accelerate aging-related cellular dysfunction (Piper & Partridge, 2018).

Chronic Cd exposure in *D. melanogaster* induces premature aging characterized by reduced lifespan, cognitive impairment, and neurodegeneration, primarily through activation of stress pathways c-Jun N-terminal kinase/ stress-activated protein kinase (JNK/SAPK), increased apoptosis, and disruption of liquid–liquid phase separation (LLPS) in neuronal cells, leading to abnormal ribonucleoprotein (RNP) granule formation. Behavioral assays reveal significant deficits in learning and memory, correlating with early neuronal cell death (De Donno et al., 2025). Behavioral assays show deficits in learning and memory that correlate with these neurodegenerative changes.

Additionally, Cd alters the expression of apoptosis-related (*p53*, *caspase-3*) and epigenetic regulator genes (*dDnmt2*, *dMBD2/3*), with these effects persisting for up to three generations even after the removal of exposure. This highlights the dual impact of Cd on aging: direct neurotoxicity and heritable epigenetic modifications affecting lifespan and fertility (Yang et al., 2020). Further, age plays a crucial role in stress tolerance: older flies show significantly reduced resistance not only to Cd (a proteotoxic stress), but also to oxidative, genotoxic, osmotic, starvation, infection and heavy metal stresses, meaning that the negative effects of Cd are exacerbated by age-related declines in cellular repair and detoxification mechanisms (Belyi et al., 2020).

These results highlight *D. melanogaster* as a powerful model for unraveling the complex mechanisms of Cd-induced premature aging, revealing both immediate neurotoxic effects and heritable epigenetic changes. Future studies using this model may provide a basis for research with other model systems, enhancing our understanding and guiding interventions against Cd-related aging and toxicity.

1.4 Cd-Induced Premature Cellular Aging: Mechanisms Across Diverse Mammalian Cell Types

Cd induces premature aging and senescence in various mammalian cell lines through multiple

converging pathways. In cultured human astrocytes, Cd concentrations of ≥ 20 μM promote apoptosis and cell cycle arrest by disrupting redox homeostasis, marked by glutathione depletion and reduced expression of antioxidant enzymes (catalase, GST-A4), and activating stress signaling via the JNK and PI3K/Akt pathways. These changes are associated with a decrease in anti-apoptotic Bcl-2, an increase in pro-apoptotic Bax, DNA fragmentation, and an increased expression of cell cycle inhibitors such as *p53*, *p21*, and *p27*, indicating the pro-aging effects of Cd exposure (Ospondpant et al., 2019).

In kidney proximal tubular epithelial cells (HK-2), Cd exposure triggers cellular senescence, characterized by S-phase arrest, enhanced senescence-associated β-galactosidase activity, and elevated levels of *p53* and *p21*. This is driven by the suppression of SIRT1 (Sirtuin1), a key anti-aging deacetylase, leading to *p53* hyperacetylation and impaired cell cycle progression, effects that can be partially reversed by SIRT1 activation or *p21* silencing (Chou et al., 2022).

In bone-derived cells, Cd has profound effects on skeletal aging. In bone marrow mesenchymal stromal cells (BMMSCs), Cd induces mitochondrial dysfunction, DNA damage, and NF-κB-mediated senescence, evidenced by upregulation of *p21*/*p53*/*p16*^{INK4a}, along with impaired osteogenic differentiation and enhanced adipogenesis (Luo et al., 2021). Likewise, Cd exposure in osteoblasts promotes senescence through DNA damage response (ATM/H2AX phosphorylation), mitochondrial dysfunction, and SOD2 acetylation, all of which are attenuated by SIRT1 overexpression, highlighting its central role in modulating Cd-induced skeletal aging (Zhou et al., 2023).

Within the vascular system, low-dose Cd has been shown to increase expression and secretion of von Willebrand factor (vWF) in endothelial cells, contributing tovascular inflammation, stiffness, and atherosclerotic risk, hallmarks of vascular aging (X. Wang et al., 2023).

Collectively, these studies demonstrate that Cd accelerates cellular aging across diverse systems by targeting antioxidant defenses, mitochondrial function, DNA integrity, and key senescence regulatory pathways such as *p53*/*p21*, NF-κB, and SIRT1, offering potential targets for therapeutic intervention.

The mechanisms of Cd-mediated premature aging are depicted in Figure 1.

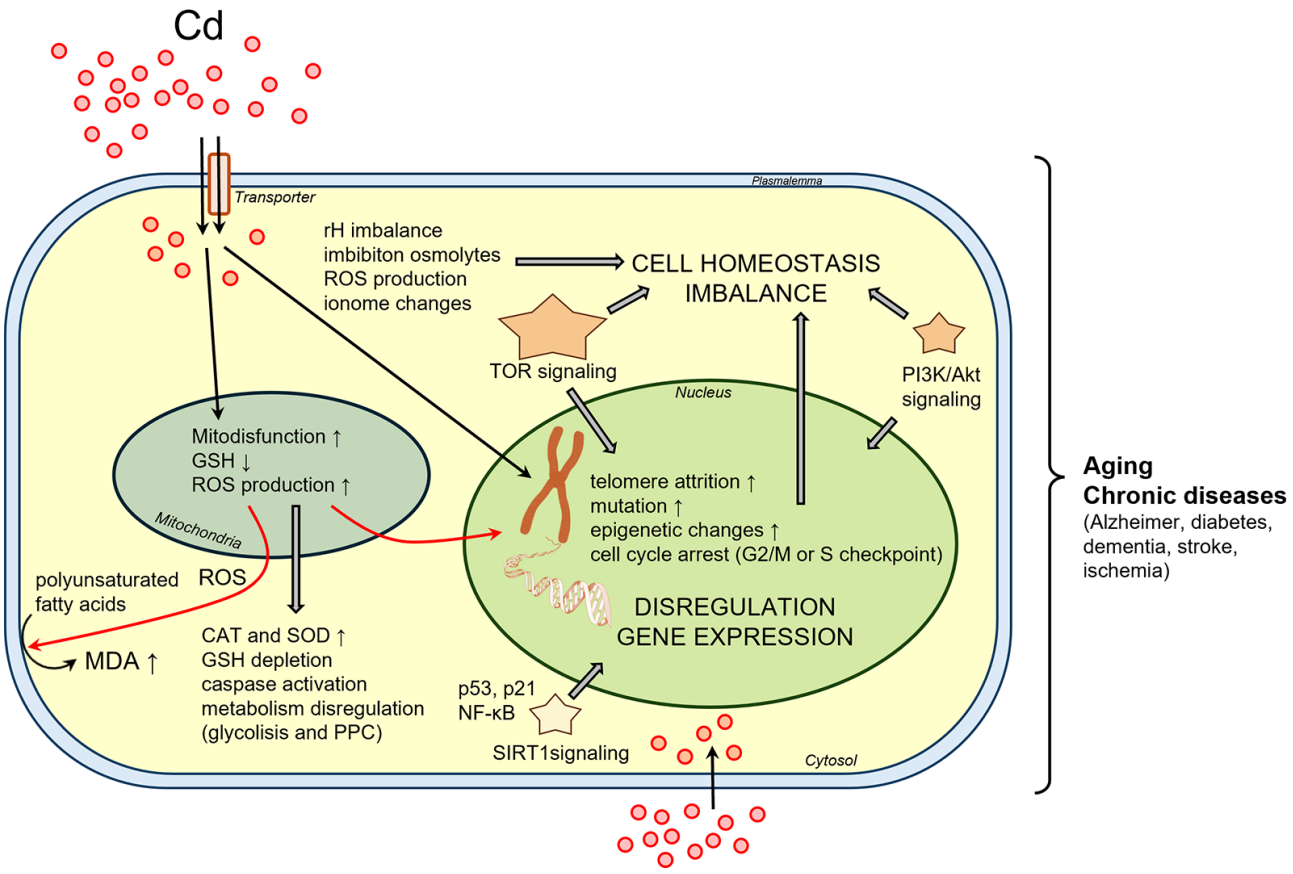

Figure 1 The mechanisms of Cd-mediated premature aging

Cd exposure accelerates biological aging through multiple, interconnected mechanisms. Cd induces excessive production of reactive oxygen species (ROS), leading to oxidative stress and lipid peroxidation. This oxidative imbalance impairs mitochondrial function, decreases ATP production, and promotes mitochondrial DNA damage. Furthermore, Cd interferes with DNA repair pathways and epigenetic regulation, resulting in genomic instability. Disruption of redox homeostasis and protein folding contributes to cellular senescence and apoptosis. Cd also alters the expression of key aging regulators, including sirtuins, mTOR, and NF-κB signaling pathways, ultimately compromising cell homeostasis and tissue integrity. Collectively, these effects drive premature aging at both cellular and systemic levels.

1.5 Multi-Organ Impact of Cd Exposure on Aging Phenotypes in Rodents

In rodent models, chronic Cd exposure is increasingly implicated in accelerating aging-related cognitive, neurogenic, and Alzheimer-like pathologies. For example, aged mice given Cd intraperitoneally at 1 mg/kg/day for three months display worsened memory and synaptic deficits. Additionally, these mice showed elevated levels of ROS, increased lipid peroxidation, and suppressed antioxidant defenses, including Nrf2 and HO-1. Moreover, activation of the stress kinase p-JNK, alongside an increase in amyloidogenic processes, has also been detected (Ali et al., 2021).

In another study, exposure of 4-week-old C57BL/6 mice to Cd in drinking water (3 mg/L) for 28 weeks impairs hippocampus-dependent learning and memory, reduces the number of adult-born neurons and their maturation in the dentate gyrus (H. Wang, 2021). A related investigation showed that Cd-induced impairment of adult hippocampal neurogenesis is dose-dependent, involves apoptosis, and is mediated by activation of JNK and *p38* MAPK signaling in neural progenitor cells (H. Wang et al., 2019).

Moreover, Cd disrupts brain and liver drug-processing genes in a sex- and ApoE-genotype-specific manner. In the livers of Cd-exposed ApoE4 males, proinflammation genes were enriched, while ApoE3 females showed enrichment in circadian rhythm and lipid metabolism genes. Cd up-regulated arachidonic acid-metabolizing Cyp2j isoforms only in ApoE3 brain, with cation transporter dysregulation being male-specific. In livers, Cd uniquely upregulated genes linked to the pregnane X receptor in ApoE4 males, and Cyp2 isoforms and Cyp7a1 in ApoE3 females, affecting mainly intermediary metabolism (H. Wang et al., 2022).

Together, these animal studies highlight that Cd promotes premature aging of the brain via oxidative stress, impaired neurogenesis, synaptic deficits, and amyloid pathology. Additionally, genetic background and developmental timing (e.g., adolescent exposure) significantly modulate vulnerability to Cd-induced neurodegeneration.

Cd exposure in rodent models also induces premature aging phenotypes beyond the nervous system, affecting organs such as the kidney and liver via mitochondrial dysfunction, metabolic disruption, inflammation, and impaired organ regeneration. In rat kidney, long-term exposure (80 weeks) to 1 mM $CdCl_2$ causes reduced mitochondrial number in proximal tubular cells, decreased cytochrome c oxidase activity, and accumulation of oxidized mitochondrial lipids, suggestive of progressive mitochondrial damage (Takaki et al., 2004). In mice, chronic exposure to moderate Cd levels (100–200 ppm) over 16–24 weeks induces renal fibrosis that is exacerbated in the absence of Nrf2, an antioxidant master regulator, correlating with elevated blood urea nitrogen (BUN) and neutrophil gelatinase-associated lipocalin (NGAL), confirming oxidative stress and impaired repair mechanisms (C. Chen et al., 2023).

Similarly, low dose Cd intake (10 mg/L via drinking water over 16 weeks) produces liver changes akin to early non alcoholic fatty liver disease (NAFLD), including altered lipid metabolism, diminished mitochondrial oxidative phosphorylation, increased apoptosis, and elevated liver enzymes (Go et al., 2015). Additionally, long-term Cd exposure in mice results in hepatic iron deficiency, depressed body weight, and elevated ALT, indicating chronic hepatotoxic stress (Tokumoto et al., 2023). Finally, even during puberty, Cd can trigger inflammatory responses in liver tissue: gavage with $CdCl_2$ (5 mg/kg) for multiple days produces hepatocyte infiltration, raised pro-inflammatory cytokines (TNF-α, MCP-1, IL-1 family), and activation of the NLRP3 inflammasome (X. Li et al., 2021).

Collectively, these studies reinforce that Cd accelerates aging-related dysfunction in non-neural tissues, compromising metabolism, organ structure, and regenerative capacity, especially under long-term or developmental exposure, and highlight critical roles for antioxidant pathways (e.g., Nrf2), mitochondrial integrity, and inflammatory regulation.

1.6 Population-Based Studies

Cd exposure is increasingly recognized as a significant environmental risk factor that accelerates biological aging and contributes to adverse health outcomes in human populations. Environmentally occurring Cd is

present at concentrations capable of entering the human body and reaching target tissues, making population-based studies crucial for risk assessment. Cd levels in non-polluted soils typically range from 0.01–1 mg/kg, and most European agricultural soils fall below 0.07 mg/kg, though a minority exceed 1 mg/kg. Dissolved Cd in groundwater is generally < 1 µg/L, and drinking water is typically below this threshold except in industrially affected areas, where levels may approach ~10 µg/L. Cd accumulates in plants, with crops from uncontaminated soils containing < 1 µg/kg, but substantially higher levels occurring in polluted regions (Kubier et al., 2019). Given Cd's mobility and bioavailability, chronic dietary and drinking-water exposure contributes to long-term body burden and accumulation in organs such as the kidney and liver.

1.6.1 Aging Biomarkers

Research studies indicate that Cd accelerates aging via cellular senescence pathways, such as telomere attrition, which partially mediates pulmonary function decline in chronic obstructive pulmonary disease (COPD) patients, as blood Cd was inversely correlated with telomerase reverse transcriptase (TERT) activity, accounting for up to 37.5 % of the decline in lung function metrics (Lv et al., 2023). This mechanism aligns with findings linking Cd exposure to epigenetic age acceleration measured through DNA methylation clocks, where older adults with higher blood Cd levels exhibit significantly greater epigenetic age than expected for their chronological age (Ryoo et al., 2025). Beyond its impact on pulmonary aging, Cd-related biological aging processes extend to multiple organ systems, highlighting its broader role in age-associated disease risk.

1.6.2 Clinical Aging Outcomes

Cd exposure is also implicated in cognitive decline among older adults. Elevated blood Cd correlates with poorer working memory capacity, partially mediated by reduced antioxidant defense abilities, underscoring oxidative stress as a critical pathway in Cd-related neurodegeneration (Souza-Talarico et al., 2017). Moreover, epidemiological studies demonstrate a robust association between Cd exposure and increased risk of osteoarthritis, with biological aging markers mediating up to 69.4 % of the effect of metal on disease progression (L. Chen et al., 2022).

Exposure to Cd correlates with frailty, a geriatric syndrome marked by increased vulnerability to stressors and mortality. Studies have found that urinary Cd levels strongly predict frailty onset and mortality in middle-aged and older adults, with Cd, cobalt, and tungsten identified as major contributors (Zheng et al., 2024).

1.6.3 Mortality and Systemic Impact

Population studies consistently show that Cd exposure increases mortality risk. In a prospective cohort including nearly 40,000 US adults, those in the highest quartile of blood Cd exhibited a 73 % increased risk of all-cause mortality, and elevated risks for cardiovascular and cancer-specific mortality were also observed (Z. Li et al., 2022). Notably, these effects continued to be observed in never-smokers, suggesting significant exposure routes beyond tobacco, such as environmental contamination, with exposure occurring through food and water (Nawrot et al., 2008). Similarly, among patients with type 2 diabetes, high blood Cd levels were associated with increased all-cause and cardiovascular mortality hazards, emphasizing the increased vulnerability of populations with metabolic comorbidities (Zhu et al., 2022).

These findings suggest that Cd accelerates aging processes both at the molecular and systemic levels, compounding chronic disease risks and reducing longevity.

1.6.4 Synthesis and Broader Context

Multiple large-scale studies using data from the National Health and Nutrition Examination Survey (NHANES) and other cohorts have elucidated the multifaceted impact of Cd on aging and mortality (Moon et al., 2023). For example, a study analyzing over 10,000 participants demonstrated a positive association between urinary Cd (U-Cd) levels and whole-body aging, quantified by phenotypic age, a composite biomarker integrating chronological age and molecular parameters, revealing that each 1 ng/g increase in U-Cd corresponded to an approximate 2.13-year increase in phenotypic age(Zhang et al., 2023). This relationship was modulated by sex, age, and smoking status, highlighting the complex interplay between Cd exposure and demographic factors.

Extensive epidemiological and mechanistic evidence underscores Cd as a potent accelerator of biological aging in humans, acting through pathways including telomere shortening, epigenetic alterations, oxidative stress, and systemic inflammation. Given the widespread environmental presence of Cd and its association with increased morbidity and mortality, public health strategies aiming to reduce Cd exposure, beyond smoking cessation, are urgently needed to mitigate its deleterious effects on aging and population health. Cd-mediated multiorgan disorders are depicted in Figure 2.

Evidence from diverse experimental models, including cultured cell lines, yeast, *C. elegans*, and animal studies, as well as population-based research, demonstrates that Cd exposure leads to multiorgan dysfunction contributing to premature aging and decreased longevity. In cell studies,

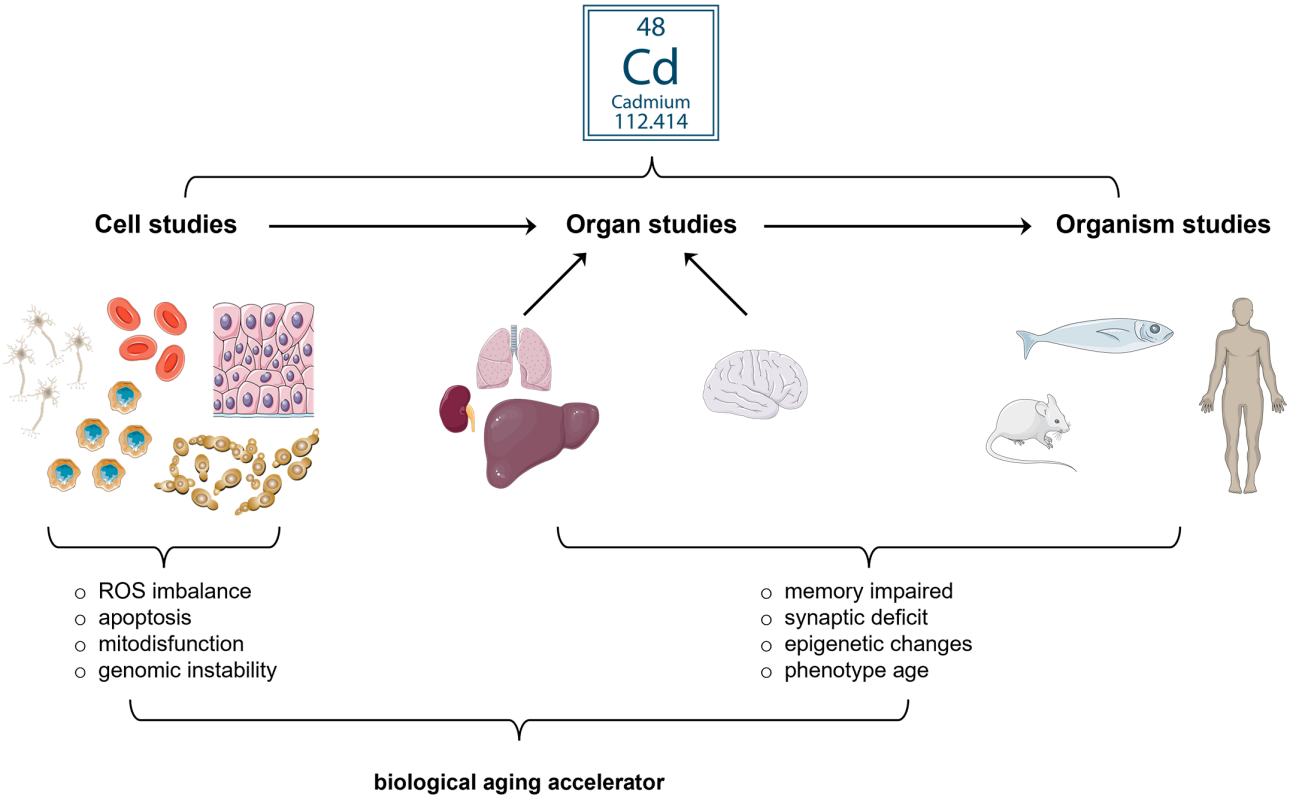

Figure 2 Cd exposure results in multiorgan disorders related to reduced life span

Cd induces oxidative stress, mitochondrial impairment, and causes genomic instability, resulting in apoptotic events, which collectively accelerate cellular senescence. Chronic Cd exposure in mammals harms the liver, kidneys, cardiovascular system, and lungs, as well as cognitive functions. Epidemiological studies further associate Cd body burden with age-related diseases, including cardiovascular disorders, neurodegeneration, diabetes, and cancer. Altogether, findings across biological systems highlight Cd as a potent environmental toxin that shortens lifespan through cumulative, systemic damage.

2 Conclusions

Cd is a widespread environmental toxicant that accelerates biological aging through several major pathways, such as oxidative stress, mitochondrial dysfunction, DNA damage, and disruption of key aging regulators. Evidence across model organisms, including Drosophila, *C. elegans*, yeast, and mammalian systems, shows that Cd shortens lifespan, promotes cellular senescence, impairs neurogenesis, and disrupts reproduction and metabolism. These effects are exacerbated with age and can be transmitted across generations via epigenetic changes. In humans, epidemiological studies link Cd exposure to accelerated phenotypic and epigenetic aging, cognitive decline, frailty, and increased mortality, even among non-smokers. This highlights the urgent need for strategies to limit environmental exposure and develop targeted interventions. Together, these findings position Cd as a significant and underrecognized driver of premature aging, with broad implications for public health and aging-related disease prevention. Understanding the impact of Cd on aging is crucial, given its widespread environmental presence and its profound effects on cellular function and organismal health. Despite significant progress, many molecular mechanisms underlying Cd-induced premature aging remain unclear, underscoring the urgent need for further research to unravel these pathways and develop effective interventions.

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

Author Contributions

Miroslava Požgajová: Writing – original draft, Supervision, Funding acquisition. Marek Kovár: Conceptualization, Writing – review & editing. Alica Navrátilová: Conceptualization, Writing – review & editing. Lucia Klongová: Conceptualization, Writing – review & editing, Hossein Zakariapour Bahnamiri: Writing – review & editing.

AI and AI-Assisted Technologies Use Declaration

AI-assisted technologies were utilized for controlling English grammar.

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