

Polystyrene Microplastics Impair Bone Homeostasis via Oxidative Stress, Inflammatory Microenvironment, and Osteocyte Senescence

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Abstract

The pervasive distribution of polystyrene microplastics (PS-MPs) in ecosystems has raised substantial concerns regarding their potential impacts on human health, yet their specific effects on skeletal system integrity remain inadequately characterized. This review consolidates current evidence from epidemiological investigations, in vivo animal models, and in vitro cellular systems to delineate the pathogenic pathways through which PS-MPs compromise bone homeostasis. Following systemic entry via gastrointestinal absorption, pulmonary deposition, or transdermal routes, PS-MPs navigate biological barriers and preferentially localize within bone marrow and mineralized matrix, facilitated by the skeletal system's high vascular permeability and the adsorptive properties of hydroxyapatite. At the subcellular level, PS-MPs initiate a cascade of deleterious events beginning with excessive reactive oxygen species production, which subsequently drives mitochondrial depolarization, calcium overload, and energy deficit. This oxidative insult engages multiple stress-responsive signaling cascades, including NF- κ B, MAPK, and NLRP3 inflammasome assemblies, culminating in amplified secretion of inflammatory mediators that disrupt the delicate equilibrium between bone-resorbing osteoclasts and bone-forming osteoblasts. Concurrently, PS-MPs skew macrophage polarization toward the pro-inflammatory M1 phenotype via TLR4-dependent pathways, perpetuating a self-sustaining inflammatory milieu. Notably, internalization of PS-MPs by osteocytes provokes G1-phase cell cycle arrest, DNA double-strand break accumulation, and premature senescence through COX2-prostaglandin E2 axis hyperactivation, thereby compromising the osteocyte network's essential regulatory functions in mechanotransduction and remodeling coordination. Additional systemic contributions arise from gut barrier compromise and microbiome dysbiosis, which potentiate endotoxin translocation and fuel low-grade systemic inflammation that secondarily impacts skeletal integrity. Toxicological evidence from vertebrate models demonstrates that PS-MP exposure diminishes bone mass, disrupts cancellous bone architecture, and retards longitudinal skeletal development, with phenotypic consequences extending to unexposed offspring in multigenerational studies. Notwithstanding these mechanistic insights, critical knowledge gaps persist, particularly regarding environmentally realistic exposure scenarios, chronic low-dose accumulation kinetics, and the absence of longitudinal human cohort data. This synthesis positions PS-MPs as plausible osteotoxic agents and underscores the imperative for enhanced biomonitoring, standardized analytical methodologies, and mechanism-guided preventive strategies to mitigate potential

skeletal health burdens.

Keywords

Microplastics, Polystyrene, Bone Metabolism, Oxidative Stress, Osteocyte Senescence, Macrophage Polarization, Osteoporosis