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Research Article

Inflammatory Effects of Microplastic Exposure: A Review of Il-6 and Cytokine Responses

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ABSTRACT
Background: Plastic particles have become a prevalent environmental contaminant with growing evidence of harmful impacts on human health. Plastic particles smaller than 5mm in diameter are called Microplastics (MPs). Human exposure occurs through contaminated food, drinking water, and inhalation of airborne particles, leading to the accumulation of MPs in several tissues, such as blood, lungs, placenta, and liver, which cause immunological dysregulation, oxidative stress, and chronic inflammation in the organism. Interleukin-6 (IL-6) receives considerable attention among inflammatory mediators for its important role in regulating immune responses and the pathophysiology of chronic inflammatory diseases.
Method: To identify peer-reviewed articles published primarily between 2015 and 2026, a thorough literature search was conducted in PubMed, Scopus, ScienceDirect, Google Scholar, and Web of Science. Among the search terms were inflammation, oxidative stress, nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), mitogen-activated protein kinase (MAPK), and environmental pollution. A comprehensive evaluation and synthesis of original research papers, systematic reviews, and meta-analyses evaluating the molecular mechanism of MP-induced inflammation and IL-6 signaling were conducted
Review findings: MP exposure causes oxidative stress, mitochondrial dysfunction, and immunological dysregulation, which raises the production of IL-6 and other proinflammatory cytokines, according to experimental and epidemiological research. Animal and cell culture studies have repeatedly shown elevated IL-6 concentrations, and new human data now prove a link between MP exposure and systemic inflammation. Other cytokines, such as Interleukin-1 beta (IL-1β) and tumour necrosis factor-alpha (TNF-α), are often dysregulated by MP exposure. The oxidative stress pathway, NF-κB, MAPK, and toll-like receptor (TLR) are all activated in these inflammatory reactions. However, significant variation in polymer type, particle size, experimental design, exposure concentration, and analytical techniques makes risk evaluation more difficult and restricts direct comparison between studies.
Conclusion: According to available data, IL-6 plays an essential role as a key mediator connecting exposure to microplastics to chronic inflammation and the emergence of inflammatory disorders; however, there are significant gaps in understanding of the dose-response relationship, long-term impact on human health, environmentally relevant exposure limits, and standardised analytic techniques for microplastic identification. To clarify the role of MPs in chronic inflammatory disorders and to support evidence-based public health policies, future research should focus on harmonised exposure protocols, large-scale longitudinal epidemiological studies, and mechanistic investigations that integrate molecular biology, toxicology, and clinical research.

Keywords: Inflammation, Oxidative Stress, NF-Kb, MAPK, Environmental Pollution.

INTRODUCTION

Plastics are long-lasting synthetic polymer materials that have significantly changed modern life since the early 20th century. Currently, hundreds of millions of tons of plastic are manufactured each year globally, and inadequate recycling contributes to massive environmental waste accumulation. [1] The rapid growth of plastic production has resulted in widespread environmental pollution. [2] Environmental weathering, mechanical degradation and ultraviolet radiation cause larger plastic debris to break down into microplastic (MP) particles.[3]

Microplastics (MPs) were first introduced in 2004 by Richard C. Thompson and colleagues, who described microscopic plastic debris accumulating in the marine ecosystem. [3,4] MPs are defined as plastic fragments and particles smaller than 5mm in diameter. They can be found in marine water, freshwater, air, soil, food products and drinking water. [5] Human exposure to MPs through ingestion, inhalation, and skin contact is considered unavoidable. [6] Recent studies have detected MPs in various human biological samples, such as blood, placenta, lung tissue, liver, breast milk and reproductive organs, suggesting a systemic distribution following exposure. [7]

MPs are classified into two types based on origin: primary and secondary MPs. Primary MPs are manufactured in microscopic sizes for industrial and commercial uses, including industrial abrasives, resin pellets, cosmetics, and pharmaceuticals. In contrast, secondary MPs are produced through the degradation of larger plastic products such as bags, bottles, wrapping materials, synthetic textiles, tyres, and fishing nets. [2,8]

MPs possess physicochemical characteristics, including size, shape and polymer type, which significantly influence their environmental behaviour and can be harmful to living organisms. The chemical components, degradation rates, and ability to absorb environmental pollutants of common polymers such as polyethylene, polystyrene, polypropylene, polyvinyl chloride polyethylene tetraphthalate, polyurethane, polyamide exhibit significant variability. It facilitates interaction with the biological membrane and immune cells. Following their uptake by cells, MPs activate the inflammatory signalling pathways, contribute to oxidative stress, induce mitochondrial dysfunction, and cause lysosomal damage. [2,7,8,9]

Interleukin-6 (IL-6) is the most consistently elevated inflammatory mediator after MP exposure. It plays a central role in regulating inflammation, haematopoiesis, immune response, metabolic homeostasis and tissue repair. Under normal circumstances, IL-6 is produced by various cell types, including macrophages, monocytes, epithelial cells, endothelial cells, dendritic cells, fibroblasts, adipocytes, and T lymphocytes in response to tissue damage and infection. On the other hand, prolonged exposure to MPs in the environment may result in continuous production of IL-6, which would increase various inflammatory illnesses, cardiovascular conditions, metabolic disorders, and immunological dysfunction. [9,10]

Further experimental research shows that exposure to MP modifies several cytokines, such as Tumour Necrosis Factor-α (TNF-α), Interleukin-1β (IL-1β), Interleukin-8 (IL-8), interleukin-10 (IL-10), interferon-gamma (IFN-γ), and Model Context protocol-1 (MCP-1), by activating nuclear factor kappa B cell (NF-κB), Mitogen Activated Protein Kinase (MAPK), Toll-like receptor (TLR), and NOD-like receptor pyrin domain containing protein 3 (NLRP3) inflammasome pathways. The development of chronic diseases may be linked to environmental MP exposure through these inflammatory pathways. [9,11]

While MP toxicity has been extensively investigated in experimental models, a detailed synthesis of evidence focusing on IL-6 as the primary inflammatory mediator, while integrating findings on other cytokine responses, is still lacking. This review aims to evaluate the existing literature on MP-induced inflammatory processes, summarising both experimental and clinical data, identifying research gaps, and proposing future directions for mechanistic and translational research.

SEARCH STRATEGY

This review utilises a narrative literature review methodology, drawing on peer-reviewed publications from 2016 to 2026. The sources for this review include PubMed, Scopus, Science Direct, Google Scholar and Web of Science. The following Keyword combinations were used: microplastics, IL-6, cytokines, inflammation, immune response, oxidative stress, NF-κB, NLRP3 inflammasome. The Information extracted from each study includes details such as the characteristics of MPs, including particle size, polymer type, and exposure duration. It also encompasses the measured inflammatory biomarkers, the investigated signalling pathways, and the reported outcome. To further enhance understanding of MP-induced inflammation, additional cytokine responses, including IL-6, were considered. [12]

MECHANISM OF MICROPLASTIC- INDUCED INFLAMMATION

According to emerging evidence, MPs are biologically active environmental pollutants that can trigger an inflammatory response through various interconnected molecular pathways. The review's findings indicate that exposure to MPs regularly triggers innate immune signaling,

increases oxidative stress, and alters the expression of proinflammatory cytokines, including IL-6. The existing data collectively support the theory that MPs contribute to persistent low-grade inflammation; however, the strength of these effects varies with factors such as particle size, polymer composition, exposure period and experimental type. [13]

IL-6 as a key mediator of inflammatory responses to microplastic exposure

IL-6 has been identified as one of the inflammatory mediators that is most consistently elevated after exposure to MP. Research has shown that exposure to polystyrene, polypropylene, polyethylene, and other polymeric particles increases the release of IL-6 from macrophages, epithelial cells, hepatocytes and intestinal cells.[14] As a pleiotropic cytokine, IL-6 regulate the production of acute-phase proteins, influences immune cell differentiation, and facilitates communication between innate and adaptive immunity. Consequently, persistent activation of IL-6 may serve as a critical mechanism linking exposure to ambient MP exposure to ambient MP with chronic inflammatory disease [12,14]

Microplastic-induced cytokine dysregulation

Widespread immunological dysregulation is indicated by alterations in several key cytokines, including TNF-α, IL-1β, IL-8, MCP-1, IFN-γ, as well as anti-inflammatory cytokines such as IL-10. The simultaneous activation of multiple cytokines, rather than isolated changes in biomarkers, indicates a coordinated network of inflammatory response. An imbalance in cytokines may affect immunological homeostasis, tissue remodelling, leucocyte recruitment, endothelial activation and macrophage polarisation. [15] However, direct comparisons between studies have been complicated by variations in experimental techniques. Inconsistent results primarly arise from differences in polymer type, particle morphology, ecologically relevant concentration and exposure duration. [16]

Oxidative stress-mediated IL-6 production following microplastic exposure

Oxidative stress appears to be directly linked to IL-6 production. Internalised MPs disrupt the cellular redox equilibrium, impair mitochondrial function, and increase intracellular levels of Reactive oxygen species (ROS). Redox-sensitive transcription factors, particularly NF-κB, are activated by excessive ROS, leading to increased transcription of pro-inflammatory cytokines such as IL-6, IL-1β, TNF-α, and various chemokines. [17] At the same time, oxidative damage triggers the NLRP3 inflammasome, further amplifying inflammatory signals. These findings suggest that oxidative stress and inflammation may contribute to long-term tissue damage from the prolonged exposure to MP through mutually reinforcing positive feedback pathways. [18]

ROLE OF PATTERN RECOGNITION RECEPTORS IN MICROPLASTIC-INDUCED INFLAMMATION

MPs are recognised as foreign particles by innate immune cells. In response, macrophages and dendritic cells initiate an intracellular signalling cascade by activating pattern recognition receptors (PRRs), including Toll-like receptors (TLRs).[18,19] The activation of TLRs leads to increased transcription of proinflammatory mediators such as IL-6, IL-1β, and TNF-α, which subsequently attract adaptor proteins that activate downstream pathways, including NF-κB and MAPK. Chronic activation of the immune system and subsequent tissue damage results in the ongoing stimulation of these receptors. [19]

NF-κB and MAPK signaling in IL- 6 regulation

NF-κB acts as a key regulator of inflammatory gene expression. Proinflammatory cytokines are transcribed, and NF-κB is translocated to the nucleus due to ROS produced during MPs exposure, which activates the inhibitor of κB (IκB) kinase. Simultaneously, the activation of MAPK pathways, including extracellular signal-regulated kinase (ERK), c-Jun N-terminal kinase (JNK) and p38MAPK, enhances cytokine production. When these pathways are combined, they significantly increase IL-6 production, creating a positive feedback loop that sustains inflammation. [18,19,20]

NLRP3 inflammasome signaling in microplastic-induced inflammation

Internalised MPs activate the NLRP3 inflammasome through mechanisms such as lysosomal instability, potassium efflux, mitochondrial damage, and accumulation of ROS. [18] The activation of NLRP3 leads to the maturation of IL-1β and IL-18 by stimulating caspase-1, and indirectly enhances IL-6 expression. Persistent inflammasome activation contributes to tissue fibrosis and chronic inflammation. [19,20]

ANIMAL STUDIES ON MICROPLASTIC-INDUCED INFLAMMATION

According to strong evidence from animal studies, MPs induce inflammatory reactions in various systems, including cardiovascular tissues, the gastrointestinal system, liver, lungs, kidneys, and reproductive organs. A molecular connection between the accumulation of these particles and tissue inflammation is indicated by the observation that histopathological changes frequently coincide with increased production of IL-6 and other cytokines.[18] Many experimental studies use exposure concentrations that exceed expected environmental human exposure levels, raising concerns about the relevance of those findings. As a result, future toxicological research must prioritise consistent particle characterisation and realistic exposure scenarios that reflect real-world conditions. [21]

HUMAN EVIDENCE OF MICROPLASTIC-INDUCED INFLAMMATION

Although the human evidence is still limited, it is rapidly increasing. It has been confirmed that human exposure is systemic rather than confined to the gastrointestinal tract, as MPs have been detected in blood, placenta, breast milk, lung tissue, liver and reproductive system. Due to methodological issues, small sample sizes, and insufficient exposure assessment, definite causal correlation between MP exposure and inflammatory biomarkers cannot currently be established, even though several observational studies indicate potential associations. [22] To enhance epidemiological research, it remains essential to develop a standardised analytical method for measuring MPs in biological materials. [23]

CONTRIBUTION OF CO-CONTAMINANTS AND PLASTISPHERE TO MICROPLASTIC-INDUCED INFLAMMATION

A new concept suggests that the biological effects of MPs may not be entirely dependent on the particles themselves. MPs are often associated with heavy metals, persistent organic pollutants, antibiotics, endocrine-disrupting chemicals and harmful microorganisms- collectively known as the plastisphere. These additional pollutants can influence the overall impact of MPs.[24] The impact of MPs alone is not the only concern; related pollutants may also contribute to increased oxidative stress and cytokine production. Therefore, future studies need to evaluate these cumulative ambient exposures instead of treating MPs as isolated toxicants.[25]

CURRENT RESEARCH GAP

Despite significant advancements, several knowledge gaps remain. While chronic low-dose exposure more accurately reflects real-world scenarios, most mechanistic research focuses on short-term exposures. [23] To clarify temporal correlations and assess disease risk, longitudinal human cohort studies with repeated exposure measurements and inflammatory biomarker testing are essential.[26]

ADVANCED TECHNOLOGY TO UNDERSTAND MICROPLASTIC-INDUCED INFLAMMATION

Additionally, single-cell sequencing, transcriptomics, proteomics, metabolomics, and other multi-omics technologies may provide a deeper understanding of the molecular mechanisms that drive immune dysregulation induced by MP. [27]

BIOLOGICAL SIGNIFICANCE OF IL-6 IN MICROPLASTIC-INDUCED INFLAMMATION

The available data indicate that IL-6 plays a key role in the inflammatory cascade triggered by exposure to MP. However, it is important to view IL-6 not as an isolated biomarker, but within the broader context of the larger cytokine network. [28,29] To determine whether long-term exposure significantly contributes to inflammation-related human disorders, it is essential to integrate mechanistic toxicology, epidemiology, clinical studies, and advanced analytical technologies [23]

CONCLUSION

MPs have emerged as significant environmental pollutants, with increasing research linking exposure to immunological activation and chronic inflammation. The reviewed literature indicates that MPs induce oxidative stress, mitochondrial dysfunction, and activation of NLRP3 and NF-κB signaling pathways, resulting in dysregulation of various inflammatory cytokines. IL-6 consistently appears to be a key biomarker among these mediators, indicating both acute and chronic inflammatory responses following MP Exposure.

The experimental results strongly support the proinflammatory potential of MPs. However, translating these findings to human health remains challenging due to variation in exposure settings, particle properties, analytical techniques, and biological models. There are still a few human studies, which underscore the need for standardised procedures for MP

identification, exposure assessments and measurement of inflammatory biomarkers

Large-scale prospective cohort studies, mechanistic studies that integrate toxicology, immunology, and molecular biology, and ecologically relevant exposure models should be prioritised for future research. To gain a deeper understanding of MP- induced immune responses and to identify appropriate biomarkers for clinical monitoring, we will utilise multi-omics approaches and advanced imaging technologies.

From a public health perspective, minimising human exposure to MPs and reducing environmental plastic pollution are vital preventive measures. To address the growing health issues associated with MPs, it will be important to foster interdisciplinary collaboration, implement standardised monitoring techniques, and enhance regulatory frameworks. The development of targeted therapies aimed at mitigating the harmful biological effects of prolonged exposure to MPs may be facilitated by a comprehensive understanding of the IL-6-centered inflammatory pathway.

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