Biological Environment and Pollution
Vol. 5(1) 2025 | 20 - 30
ISSN 2798-2378
ISSN 2798-2777

Cellular mechanisms of microplastic and nanoparticle exposure and its relationship with metabolic diseases: Literature review

Ismi Farah Syarifah [a, 1, *], Rizal Maulana Hasby [b, 2], Opik Taupiqurrohman [c, 3], Mokhamad Mahroji [d, 4]

[a] Department of Public Health, Universitas Pembangunan Nasional Veteran Jakarta, Jakarta, Indonesia
[b] Department of Biology Education, Universitas Bina Bangsa, Serang, Indonesia
[c] Department of Health Analyst, Sekolah Tinggi Analis Bakti Asih, Bandung, Indonesia
[d] Department of Pharmacy, Universitas Bina Bangsa, Serang, Indonesia
[1] ismifarah@upnvj.ac.id; [2] rizalmaulanahasby@gmail.com;
[3] opiktaupiqurrohman@staba.ac.id; [4] ojierasyidi11@gmail.com
* Corresponding author

ARTICLE INFO

Article history
Submission
February 5, 2025
Revision
May 13, 2025
Accepted
May 16, 2025

Keywords
Cellular mechanisms
Metabolic diseases
Microplastics
Nanoparticles

ABSTRACT

Microplastics (MP) and nanoparticles (PS-NPs) are emerging environmental contaminants of significant concern due to their adverse effects on human health. This study systematically reviews the impact of these pollutants on cellular mechanisms, with a specific focus on their association with metabolic diseases. Data were collected from various scientific publications relevant to the research topic. Research findings indicate that exposure to microplastics (MP) can result in a reduction in triglyceride and total cholesterol levels, while also disrupting insulin signaling pathways, thereby contributing to insulin resistance. Additional studies have demonstrated that exposure to nanoparticles (PS-NPs) in pregnant mice may increase the risk of metabolic disorders in their offspring. Moreover, PS-NP exposure has been shown to exacerbate type 2 diabetes by inhibiting the AKT/GSK3β pathway. Collectively, exposure to microplastics and nanoparticles has the potential to aggravate metabolic disorders and increase the risk of metabolic diseases, including diabetes, obesity, and cardiovascular conditions. These findings offer valuable insights into the potential health risks associated with environmental exposure to microplastics and nanoparticles and underscore the critical importance of addressing microplastic pollution to human health.

Conflict of interest: The authors declare that they have no conflicts of interest.

Introduction

Microplastics are plastic particles smaller than 5 mm, whilst nanoparticles are defined as 100 nanometers. These polymers are extensively prevalent in diverse aquatic ecosystems, encompassing marine, river, and soil ecosystems[1]. Microplastics and nanoplastics, ubiquitous environmental pollutants, arise from multiple main and secondary sources. Primary microplastics are deliberately produced microscopic particles, such as microbeads in cosmetic items, plastic pellets utilized in manufacturing, and microfibers released from synthetic fabrics after laundering. Secondary microplastics arise from the decomposition of bigger plastic products, including plastic bags, bottles, discarded fishing nets, and tire wear particles, via environmental weathering processes. Moreover, paints and varnishes facilitate the generation of microplastic particles via weathering. Recent concerns emphasize materials such as nylon or polypropylene teabags, which emit microplastics when infused in hot water, and single-use plastic products like lined coffee cups that release microplastics during utilization[2]. The proliferation of microplastics and nanoparticles is escalating in accordance with the expansion of human activities. Both pollutants degrade the ecosystem and adversely affect human health through the ingestion of tained food and beverages or the inhalation of air containing these pollutant particles[3,4].

From a biological standpoint, the presence of microplastics and nanoparticles in the human body might induce various pathophysiological responses at the cellular level[5], thereby posing a substantial risk to human health. A significant result is the emergence of metabolic disorders, such as diabetes, obesity, and other metabolic syndromes. These pollutants exhibit significant toxicity, inducing oxidative stress and inflammation, hence impairing cellular metabolic activities and promoting the advancement of metabolic disorders[6].

Nonetheless, a comprehensive investigation into the cellular and molecular mechanisms that govern the impact of microplastics and nanoparticles on metabolic disorders is still insufficient. This review is to critically evaluate the current literature about the biological processes of microplastics and nanoparticles, along with their correlation to metabolic diseases. The insights provided herein aim to elucidate the impact of these pollutants on human health. The insights provided herein aim to elucidate the impact of these pollutants on human health, thereby guiding future research efforts to devise effective measures for their prevention and mitigation.

Method

Research design

This study employs a systematic review as its research design. The study was conducted from November 2024 to December 2024, employing the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Flow methodology.

Searching Method

The data set comprises study findings on scientific articles published nationally and internationally over the past decade, from 2014 to 2024. This information was sourced from scientific resources such as PubMed, Scopus, and Google Scholar. Search criteria employed for data retrieval encompass "microplastics", "nanoparticles", "cellular mechanisms", "metabolic diseases", and other pertinent terminology.

Inclusion and exclusion criteria

The inclusion criteria for the research are: 1) The publications must be experimental studies, 2) The findings must address the biological mechanisms of microplastic and nanoparticle exposure in relation to metabolic disorders, 3) Employing keywords such as "microplastics", "nanoparticles", "metabolic diseases", and additional terms pertinent to the primary subject, 4) The publishing year criteria are restricted to 2014 - 2024. 5) The article must be written in either Bahasa Indonesia or English. The research exclusion criterion includes: 1) Duplicate article. 2) Article presented as a literature review. 3) Investigate scholarly articles employing qualitative methodologies.

Article update

The selected publications were obtained from a review of the latest literature accessible in academic sources, including PubMed, Scopus, and Google Scholar. This decision is based on an evaluation of article titles and abstracts to ascertain the relevance of each article to the research topic. Articles meeting the inclusion criteria were thereafter examined meticulously to ascertain the relevance and validity of their content prior to further research.

Data extraction

The data extraction process follows the PRISMA flow as in Fig. 1, by selecting the data obtained based on the established criteria so that 10 articles were reviewed.

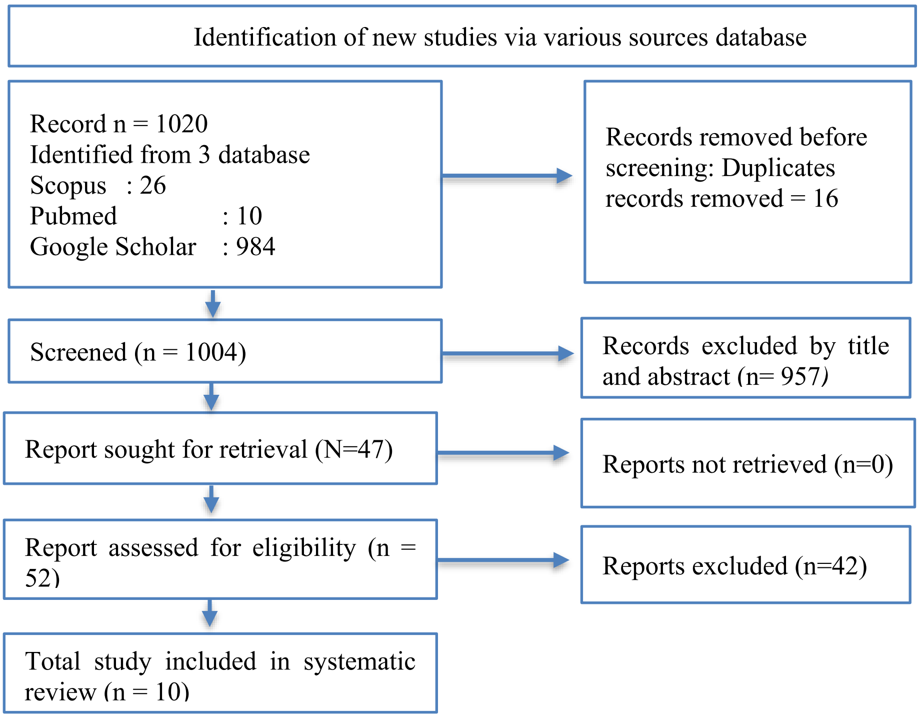

Fig. 1 | Data extraction using PRISMA

Quality research

The quality of articles selected from various scientific sources is established by evaluating article titles and abstracts to identify their relevance to the research topic. Relevant articles are assessed according to methodological rigor, data integrity, and argumentative analysis.

Data analysis

A descriptive data analysis was performed by screening publications to identify and elucidate essential parameters associated with the cellular mechanisms of metabolic diseases induced by exposure to microplastic and nanoparticle. Each article was meticulously examined, and pertinent information was recorded. This investigation was presented elucidate the biological pathways associated with microplastic and nanoparticle exposure and their correlation with metabolic diseases.

Results and Discussion

Cellular Mechanisms of Microplastics and Nanoparticles

The subsequent graphic depicts the principal cellular pathways activated by exposure to microplastics and nanoparticles within the human body. These pathways encompass oxidative damage, inflammation, and disruption of cellular metabolic systems. The exposure triggers the release of cytokines such as TNF-α and IL-6, which lead to metabolic dysfunction and damage to critical cellular constituents, including lipids, proteins, and DNA. This graphic representation seeks to elucidate the biological impacts of microplastic and nanoparticle contamination, particularly at the cellular level.

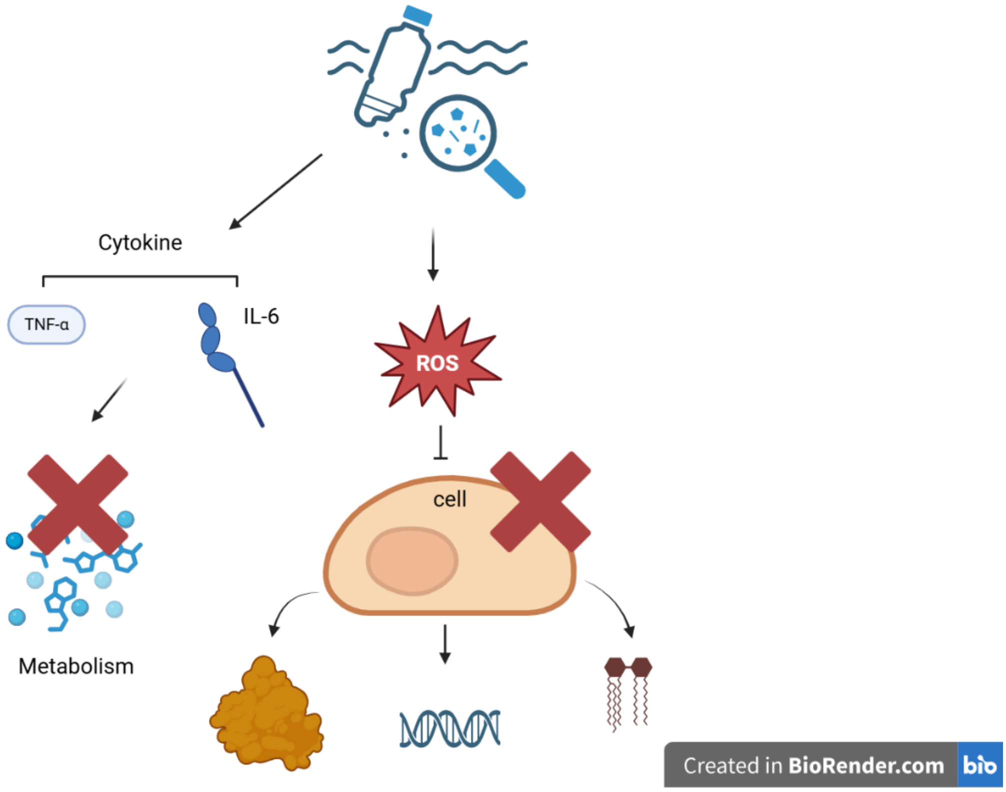

Fig. 2 | The effect of microplastics and nanoparticles on cells and metabolism

Microplastics affect cellular functions via multiple essential pathways. Their exposure causes oxidative stress, resulting in the production of reactive oxygen species (ROS) that can harm cellular components. These free radicals adversely affect lipids, proteins, and DNA, resulting in oxidative damage that disrupts cell and tissue function[7]. Moreover, microplastics stimulate the synthesis of inflammatory cytokines, including TNF-α and IL-6, resulting in chronic inflammation that undermines tissue integrity and elevates the susceptibility to metabolic disorders (Fig. 2). They also alter endocytosis and exocytosis, which are critical cellular processes for molecular uptake and release, hence impairing cellular metabolism and general functionality[8].

Nanoparticles, owing to their diminutive size, can infiltrate cell membranes and engage directly with organelles, including mitochondria and the nucleus. This interaction may lead to structural damage and organelle dysfunction, negatively impacting energy production and genetic regulation[9]. Moreover, nanoparticles stimulate inflammatory and oxidative signaling pathways, undermining cellular homeostasis, hindering cell proliferation, and elevating the risk of metabolic disorders, including diabetes and obesity[10]. These pathways underscore the capacity of nanoparticles to aggravate metabolic disorders and adversely affect overall health.

The correlation between Microplastics,Nanoparticles, and Metabolic Disorders

Table 1 indicates that exposure to polystyrene microplastics (MP) and nanoparticles (PS-NPs) might adversely affect health, including the induction of metabolic disorders. Numerous studies indicate that exposure to MP can lead to numerous lipid metabolism disorders, including reduced levels of triglycerides and total cholesterol, along with alterations in the expression of genes associated with lipogenesis[11]. This transpires as a result of alterations in the lipid metabolic pathway inside the liver and adipose tissue, alongside modifications in the composition of the gut microbiota[12]. These outcomes indicate that MP may induce metabolic disorders linked to conditions such as dyslipidemia and insulin resistance[13].

Table 1 | Literature review result

Author(s)	Cases	Methods	Results
Lu et al.[11]	Microplastics and Lipid Metabolism Disorders	Male rats were subjected to polystyrene microplastics (MP) measuring 0.5 μm and 50 μm at a concentration of 1000 μg/L via drinking water for a duration of 5 weeks. The investigation encompassed gut microbiota (16S rRNA sequencing), lipid metabolism, and the expression of genes associated with lipogenesis.	Exposure to polystyrene microplastics (MP) in mice led in reduced levels of triglyceride and total cholesterol. This phenomenon is ascribed to MP-induced modifications in the expression of mRNA genes related to lipogenesis and triglyceride synthesis, resulting in lipid metabolic abnormalities in the liver and epididymal adipose tissue, together with alterations in gut microbiota composition. These findings highlight the significant health hazards associated with molecular alterations induced by MP exposure.
Wang et al.[13]	Nanoparticles and Diabetes Mellitus	120 C57BL/6 mice were allocated into 12 groups and administered polystyrene nanoparticles (PS-NPs), a high-fat diet streptozotocin STZ for type 2 diabetes model, and the SC79 activator. Subsequently, blood glucose levels, glucose tolerance, insulin, and indicators of oxidative stress were assessed. Staining was employed to examine the histological features of liver and pancreatic tissues.	Exposure to polystyrene nanoparticles (PS-NPs) has been shown to elevate fasting blood glucose (FBG) levels, provoke glucose intolerance, and facilitate to insulin resistance in rat models Type 2 diabetes mellitus (T2DM). The study findings indicate that exposure to PS-NP can result in glycogen accumulation, hepatocyte edema, and injury pancreatic tissue.
Ceballos-Gutiérrez et al.[14]	Nanoparticles and Dyslipidemia	Healthy mice were categorized into two groups: control group and treatment group. The treatment group received an oral administration of ZnO nanoparticles (ZnONPs) at a dosage of 10 mg/kg/day for one, two, or three months. This study assessed	The oral treatment of zinc oxide nanoparticles (ZnONPs) at low dosages (10 mg/kg/day) in healthy mice over a duration of one to three months may elevate the risk of atherosclerosis and affect aortic contractility, along with the expression of cannabinoid receptors (CB1 and CB2) in the aortic wall. Moreover, exposure to ZnONP has been shown to

Author(s)	Cases	Methods	Results
		indicators of dyslipidemia, blood pressure, aortic wall structure, vascular contractility, and the expresson of cannabinoid receptor (CB1 and CB2) within the aortic wall. Histologic examination of the aorta was conducted to identiy atherosclerotic alterations, while in vitro assays were utilized to assess modifications in aortic contractility and cannabinoid receptor expression.	elevate blood pressure, indicating a potentially substantial cardiovascular health risk.
Huang et al.[15]	Nanoparticles and Hypertension	Mice were administered a conventional diet (NCD) or high-fat diet (HFD) and subjected to polystyrene (PS) exposure. Subsequently, assessment of insulin resistance, investigation of gut microbiota, and measurements of inflammatory cytokines were conducted. The 5 µm PS was examined for accumulation in the liver, kidney, and blood vessels. Concurrently, the expression analysis of IRS1 and PI3K in the liver was conducted to assess the insulin signaling pathway.	Exposure to polystyrene (PS) microplastics has been shown to provoke insulin resistance (IR) in rats, irrespective of their diet being conventional or high-fat diet. PS exposure may incite inflammation, disrupt gut microbiota, and result in microbial accumulation in organs, including the liver and kidneys. The mechanism by which PSinduces IR may entail the suppression of the insulin signaling pathway in the liver, indicating that PS could function as an environmental contaminant leading to metabolic disorders, including insulin resistance.
Luo et al.[16]	Microplastics and Metabolic Syndrome	Polystyrene (PS) particles measuring 0.5 and 5 µm polystyrene (PS) were administered to pregnant rats at concentrations of 100 and 1000 µg/L. The impact of this exposure during gestation on the progeny of PND42 rats was assessed by quantifying triglycerides, total cholesterol, HDL-C, LDL-C, and TC and TG levels in the liver.	The data indicates that exposure to PS of different sizes in pregnant rats may elevate the risk of metabolic disorders in their progeny, with bigger microplastics (5 µm) exhibiting the most significant impact.
Wang et al.[17]	Nanoparticles and Diabetes	Male rats were administered polystyrene nanoplastics (PS-NPs) orally at doses of 1, 10, and 30 mg/kg/day for a duration of 8 weeks.	Administration of PS-NPs at a dosage of 30 mg/kg/day markedly elevated blood glucose levels, induced glucose intolerance, and enhanced insulin resistance. When administered

Author(s)	Cases	Methods	Results
		Experiments were performed under two conditions: exposure to PS-NPs only and a combination of PS-NPs with a high-fat diet and streptozocin (STZ) injection to induce diabetes. The assessed parameters encompassed blood glucose levels, glucose and insulin tolerance, insulin resistance, oxidative stress (ROS) levels in the liver and pancreas, and phosphorylation levels of AKT and GSK3β proteins. Mice were administered SC79, a selective AKT activator, to assess if enhanced phosphorylation of AKT and GSK3β may mitigate the detrimental effects of PS-NPs.	alongside a high-fat diet and STZ, PS-NPs intensified oxidative stress, diminished glucose and insulin tolerance, and inflicted damage to the liver and pancreas. Molecularly, PS-NPs decreased the phosphorylation of AKT and GSK3β, which are pivotal in the regulation of glucose metabolism. Treatment with SC79 effectively enhanced the phosphorylation of AKT and GSK3β, decreased ROS levels in the liver and pancreas, and marginally reduced blood glucose levels and insulin resistance. These findings indicate that exposure to PS-NPs may aggravate type 2 diabetes by inhibiting the AKT/GSK3β pathway, the principal mechanism of underlying the diabetogenic effects of nanoplastics.
Chen et al.[18]	Nanoparticles and Metabolic Disorder	This research employed rats as a model to assess the imoact of polystyrene nanoplastics (PS-NPs) exposure on the placenta and fetus. Pregnant rats were administered 100 nm PS-NPs at doses of 1 and 10 mg/L via drinking water during gestation during gestation. The investigations encompassed fetal weight, placental and fetal cell morphology, and multi-omics approaches, including transcriptomic and metabolomic analyses, to discern molecular disruptions in the placenta and fetal skeletal muscle.	Exposure to elevated doses of PS-NPs (10 mg/L) markedly reduced fetal weight and induced morphological abnormalities in placental and fetal cells. Analysis of the placental transcriptome revealed substantial disruptions in cholesterol metabolism, the complement pathway, and the coagulation cascade. Metabolomics identified metabolic abnormalities, particularly concerning sucrose and daidzein levels. Transcriptomics in embryonic skeletal muscle revealed substantial gene regulation associated with muscle tissue development, lipid metabolism, and skin formation. Transcriptome investigation of the placenta and fetal skeletal muscle at elevated doses of PS-NPs indicated considerable regulation of the APOA4 gene and its transcription factors, which are essential for cholesterol transport. This work revealed that exposure to PS-NPs can result in fetal growth limitation and disrupted cholesterol metabolism in both the placenta and fetus, providing new understanding of the mechanisms underlying nanoplastic impacts on pregnancy and fetal development.

Author(s)	Cases	Methods	Results
Zhang et al.[19]	Nanoparticles and Metabolic Disorder	C57BL/6J male mice were administered a high-fat diet (HFD) with or without exposure to polystyrene nanoparticles (PS-NPs) for 12 weeks to assess their metabolic impacts. The analysis of inguinal white adipose tissue (iWAT) focused on the accumulation of PS-NPs and alternations in thermogenic gene expression, particularly UCP1. Primary beige adipocytes derived from mice were subjected to PS-NPs to evaluate their direct impact on mitochondrial function, oxidative stress, and inflammation. The antioxidant properties were assessed to determine their potential to alleviate the impact of PS-NPs.	Oral administration to PS-NPs intensified metabolic disorders in mice on a high-fat diet, resulting in diminished energy expenditure, augmented fat mass and hepatic steatosis, impaired insulin sensitivity, disrupted glucose homeostasis, and lower cold tolerance relative to the control group. PS-NPs accumulated in inguinal white adipose tissue (iWAT) and inhibited thermogenic gene programs, particularly the production of UCP1 protein, a crucial regulator in the browning of beige adipocytes. PS-NPs impair mitochondrial activity, induce oxidative damage, and elevate inflammation in beige adipocytes, hence obstructing their thermogenic capacity. Antioxidant supplements can alleviate these harmful effects. This study is the inaugural demonstration that exposure to PS-NPs aggravates metabolic abnormalities in mice on a high-fat diet by generating malfunction in beige adipocytes.
Fan et al.[20]	Nanoparticles and Glycolipid Metabolic Disorders	This research assessed the impact of polystyrene nanoparticles (PS-NPs) exposure on glycolipid metabolism in mice. Mice received oral administration of PS-NPs, and investigations were conducted to ascertain molecular alterations, encompassing the generation of reactive oxygen species (ROS), inflammatory signaling pathways, and metabolic mechanisms. The NFκB and MAPK signaling pathways were examined to assess their function in glycolipid metabolism. Mice were administered resveratrol to evaluate the effect of evaluate the effect of antioxidants while exposure to PS-NP.	Exposure to PS-NPs impairs glycolipid metabolism by producing excessive ROS, which initiates an inflammatory response and activates the antioxidant pathway via the transcription factor Nrf2. The activation of NFκB and MAPK signaling pathways enhances the phosphorylation of MAPK proteins, such as ERK and p38, leading to sustained phosphorylation of insulin receptor substrate-1, a reduction in protein kinase B (Akt) activity, and the onset of insulin resistance. The phosphorylation of Akt activates gluconeogenesis genes, including G6PC and PEPCK via the PGC1α-FoXO1 pathway. Moreover, ERK activation promotes lipid accumulation via the ERK-PPARγ pathway, resulting in the production of lipogenic enzymes such as ACC-1. Resveratrol treatment mitigated the disrupted glucose and lipid metabolism caused by PS-NPs by decreasing ROS activation in the NFκB and MAPK pathways. These findings indicate that ROS is a pivotal molecule in glycolipid metabolic disorders resulting from PS-NPs exposure.

Author(s)	Cases	Methods	Results
Qiao et al.[12]	Microplactic and Metabolic Disorder	Zebrafish were subjected to experimental exposure to polystyrene microplastics (MPs) in the form of 5 µm beads at doses of 50 µg/L and 500 µg/L during a duration of 21 days. Changes in tissue histology, enzymatic indicators, gut microbiome, and metabolomic responses were identified during the investigation to assess the effects of MP exposure on the gut.	Exposure to MPs induced inflammation and oxidative stress in the zebrafish gut. Moreover, substantial alterations were noted in the gut microbiome and tissue metabolic profiles, predominantly linked to oxidative stress, inflammation, and lipid metabolism. This work indicates that exposure to MPs not only harms intestinal tissues but also alters in the gut metabolome and microbiome.

Another study shown that administration to PS-NPs in type 2 diabetic rats elevated blood glucose levels, induced glucose intolerance, and heightened insulin resistance[17]. This result is ascribed to the reduced phosphorylation of AKT and GSK3β proteins, which play a role in the regulation of glucose metabolism. PS-NPs are known to disrupt the insulin signaling system, ultimately exacerbating metabolic disorders. Furthermore, administration to PS-NPs in rats on a high-fat diet results in augmented fat mass, hepatic steatosis, and diminished insulin sensitivity, consequently intensifying metabolic disorders in the organism[19]. Exposure to PS-NPs in pregnant rats resulted in placental disturbances and fetal developmental, including reduced fetal weight and morphological abnormalities in placental and fetal cells[16,18]. Moreover, disruptions in cholesterol metabolism were noted in the placenta and fetal skeletal muscles, suggesting that PS-NPs exposure may inhibit fetal growth and influence metabolism at the molecular level.

At the molecular level, reactive oxygen species (ROS) are pivotal in the metabolic disturbances caused by PS-NPs[21,22]. The activation of inflammatory signaling pathways, including NFκB and MAPK, results in enhanced phosphorylation of proteins associated with glucose and lipid metabolism, leading to glycolipid metabolic abnormalities and heightened lipid accumulation[20]. Research indicates that the injection of antioxidants, including resveratrol, can alleviate the effects of PS-NPs exposure by decreasing ROS activation and inflammatory pathways[19].

Collectively, exposure to MPs and PS-NPs may induce a range of metabolic changes, encompassing insulin resistance, lipid metabolism disorders, and dysfunction of the liver, pancreas, and adipose tissue. This exposure also influences the gut microbiome, leading to significant metabolic changes. This research provides novel insights into the effects of MP and PS-NPs pollution on metabolic health, emphasizing the underlying molecular mechanisms such as oxidative stress, inflammation, and disturbances in energy metabolism..

Conclusion

The results indicate that microplastics and nanoplastics affect cellular mechanisms via multiple critical pathways. Their exposure causes oxidative stress, leading to the production of reactive oxygen species (ROS) that can harm cellular components. Free radicals adversely affect lipids, proteins, and DNA, resulting in oxidative damage that disrupts cellular and tissue function. Furthemore, microplastics stimulate the synthesis of inflammatory cytokines, including TNF-α and IL-6, resulting in chronic inflammation that undermines tissue integrity and increases the likelihood of metabolic disorders.

References

1. Galloway, T. S., Cole, M. & Lewis, C. Micro- and nanoplastics and human health. In Bergmann, M., Gutow, L. & Klages, M. (Eds.), *Marine Anthropogenic Litter*, 347-370 (Springer, 2017).
2. Morreale, M. & La Mantia, F. P. Current concerns about microplastics and nanoplastics: A brief overview. *Polymers 16*, 1525 (2024). https://doi.org/10.3390/polym16111525
3. Browne, M. A., Niven, S. J., Galloway, T. S., Rowland, S. J. & Thompson, R. C. Microplastic moves pollutants and additives to worms, reducing functions linked to health and biodiversity. *Current Biology* **23**, 2388-2392 (2013). https://doi.org/10.1016/j.cub.2013.10.012
4. Oberdörster, G., Oberdörster, E. & Oberdörster, J. Nanotoxicology: An emerging discipline evolving from studies of ultrafine particles. *Environ Health Perspect* 113, 823-839 (2005). https://doi.org/10.1289/ehp.7339
5. Shvedova, A. A., Kagan, V. E. & Fadeel, B. Unusual inflammatory and fibrogenic pulmonary responses to single-walled carbon nanotubes in mice. *American Journal of Physiology Lung Cellular and Molecular Physiology* 295 (2008). https://doi.org/10.1152/ajplung.00084.2005
6. Mahjoub, S. & Masrour-Roudsari, J. Role of oxidative stress in pathogenesis of metabolic syndrome. *Caspian Journal of Internal Medicine* **3**, 386 (2012).
7. Das, A. The emerging role of microplastics in systemic toxicity: Involvement of reactive oxygen species (ROS). *Scicience of the Total Environment* 165076 (2023). https://doi.org/10.1016/j.scitotenv.2023.165076
8. Liu, S., Wang, Z., Xiang, Q., Wu, B., Lv, W. & Xu, S. A comparative study in healthy and diabetic mice followed the exposure of polystyrene microplastics: Differential lipid metabolism and inflammation reaction. *Ecotoxicology and Environmental Safety* **244**, 114031 (2022). https://doi.org/10.1016/j.ecoenv.2022.114031
9. Liu, N. & Tang, M. Toxic effects and involved molecular pathways of nanoparticles on cells and subcellular organelles. *Journal of Applied Toxicology* **40**, 16-36 (2020). https://doi.org/10.1002/jat.3817
10. Xu, M. X., Wang, M. & Yang, W. W. Gold-quercetin nanoparticles prevent metabolic endotoxemia-induced kidney injury by regulating TLR4/NF-κB signaling and Nrf2 pathway in high fat diet fed mice. *International Journal of Nanomedicine* 327-345 (2017). https://doi.org/10.2147/IJN.S116010
11. Lu, L., Wan, Z., Luo, T., Fu, Z. & Jin, Y. Polystyrene microplastics induce gut microbiota dysbiosis and hepatic lipid metabolism disorder in mice. *Science of The Total Environment* **631**, 449-458 (2018). https://doi.org/10.1016/j.scitotenv.2018.03.051
12. Qiao, R., Sheng, C., Lu, Y., Zhang, Y., Ren, H. & Lemos, B. Microplastics induce intestinal inflammation, oxidative stress, and disorders of metabolome and microbiome in zebrafish. *Science of The Total Environment* **662**, 246-253 (2019). https://doi.org/10.1016/j.scitotenv.2019.01.245
13. Wang, Y., Xu, K., Gao, X., Wei, Z., Han, Q., Wang, S. et al. Polystyrene nanoplastics with different functional groups and charges have different impacts on type 2 diabetes. *Particle and Fibre Toxicology* **21**, 21 (2024). https://doi.org/10.1186/s12989-024-00582-w
14. Ceballos-Gutiérrez, A., Rodríguez-Hernández, A., Álvarez-Valadez, M. D. R., Limón-Miranda, S., Andrade, F., Figueroa-Gutiérrez, A., Díaz-Reval, I., Apolinar-Iribe, A., Castro-Sánchez, L., Alamilla, J., Sánchez-Pastor, E. & Virgen-Ortiz, A. ZnO nanoparticles induce dyslipidemia and atherosclerotic lesions leading to changes in vascular contractility and cannabinoid receptors expression as well as increased blood pressure. *Nanomaterials* **11**, 2319 (2021). https://doi.org/10.3390/nano11092319

15. Huang, D., Zhang, Y., Long, J., Yang, X., Bao, L., Yang, Z., Wu, B., Si, R., Zhao, W., Peng, C., Wang, A. & Yan, D. Polystyrene microplastic exposure induces insulin resistance in mice via dysbacteriosis and pro-inflammation. *Science of The Total Environment* **838**, 155937 (2022). https://doi.org/10.1016/j.scitotenv.2022.155937
16. Luo, T., Zhang, Y., Wang, C., Wang, X., Zhou, J., Shen, M., Zaho, Y., Fu, Z. & Jin, Y. Maternal exposure to different sizes of polystyrene microplastics during gestation causes metabolic disorders in their offspring. *Environmental Pollution* **255**, 113122 (2019). https://doi.org/10.1016/j.envpol.2019.113122
17. Wang, Y., Wei, Z., Xu, K., Wang, X., Gao, X., Han, Q., Wang, S. & Chen, M. The effect and a mechanistic evaluation of polystyrene nanoplastics on a mouse model of type 2 diabetes. *Food and Chemical Toxicology* **173**, 113642 (2023). https://doi.org/10.1016/j.fct.2023.113642
18. Chen, G., Xiong, S., Jing, Q., van Gestel, C. A., van Straalen, N. M., Roelofs, D., Sun, L. & Qiu, H. Maternal exposure to polystyrene nanoparticles retarded fetal growth and triggered metabolic disorders of placenta and fetus in mice. *Science of The Total Environment* **854**, 158666 (2023). https://doi.org/10.1016/j.scitotenv.2022.158666
19. Zhang, L., Wan, B., Zheng, J., Chen, L., Xuan, Y., Zhang, R., Chen, L., Hu, C., Zhang, Y. & Yan, C. Polystyrene nanoplastics inhibit beige fat function and exacerbate metabolic disorder in high-fat diet-fed mice. *Science of The Total Environment* **918**, 170700 (2024). https://doi.org/10.1016/j.scitotenv.2024.170700
20. Fan, X., Li, X., Li, J., Zhang, Y., Wei, X., Hu, H., Zhang, B., Du, H., Zhao, M., Zhu, R., Yang, D., Oh, Y. & Gu, N. Polystyrene nanoplastics induce glycolipid metabolism disorder via NF-κB and MAPK signaling pathway in mice. *Journal of Environmental Sciences* **137**, 553-566 (2024). https://doi.org/10.1016/j.jes.2023.02.040
21. Li, Y., Guo, M., Niu, S., Shang, M., Chang, X., Sun, Z., Zhang, R. & Xue, Y. ROS and DRP1 interactions accelerate the mitochondrial injury induced by polystyrene nanoplastics in human liver HepG2 cells. *Chemico-Biological Interactions* **379**, 110502 (2023). https://doi.org/10.1016/j.cbi.2023.110502
22. Pei, J., Chen, S., Li, L., Wang, K., Pang, A., Niu, M., Peng, X., Li, N., Wu, H. & Nie, P. (2024). Impact of polystyrene nanoplastics on apoptosis and inflammation in zebrafish larvae: Insights from reactive oxygen species perspective. *Science of The Total Environment* **948**, 174737 (2024). https://doi.org/10.1016/j.scitotenv.2024.174737

Author contributions

All authors contributed to the study's conception and design. The first draft of the manuscript was written by **[Ismi Farah Syarifah]**, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.