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Plastic pollution and its pathophysiological impacts on mammalian cells

Monika Joon[1]*, Shashi Raparia[2]

[1,2] Assistant Professor, Department of Zoology, Government College Bahadurgarh, Jhajjar, Haryana

(Affiliated to Maharshi Dayanand University, Rohtak, Haryana)

Abstract: The non-natural anthropogenic product, plastic once heralded as a durable, inert, resilient, multipurpose and long-lasting polymer has now become a problem of gigantic dimensions. Plastics are either non-biodegradable or have a very long half-life and hence persist in environment for very long period of time. However, the impacts of physical, biological and chemical forces of nature on plastics break down its bigger pieces into fragments of micro and nano scale thus giving rise to microplastics (MPs) and nanoplastics (NPs). Their persistence in environment has resulted in pollution. MPs and NPs enter zooplankton and microscopic organisms by ingestion and get accumulated in organisms by trophic transfer from prey to predator. Lab simulated studies have demonstrated trophic transfer in food chain. Their presence inside living organisms is worrisome as the organisms cannot digest or even get rid of them by egestion. Detrimental and toxicological effects of MPs and NPs on zooplanktons and plants have been widely studied and documented by many research groups across the world. Studies have shown that the effects may be either direct like accumulation in tissues and obstruction of the gut of organisms or indirect wherein organic pollutants could be adsorbed onto MPs/NPs and then gain entry inside living organisms via ingestion. The present review focuses on the critical question of potential toxicity arising from the uptake or entry of MPs and NPs by mammalian cells. Prevailing research studies data suggest the imminent threat to mammalian tissues. For long-term consequences, the data may be insufficient but speculations hint to a grim situation. This review brings to light the need for more concentrated efforts at the global level to investigate potential cellular and systemic toxicity due to micro- and nanoplastics.

Keywords: microplastics, MPs, trophic transfer, nanoplastics, NPs, mammalian cells, toxicity

1. INTRODUCTION

Plastics are practically indispensable in modern times. Henri Braconnot in 1833 synthetically produced nitrocellulose that was later used as a substitute for ivory, an animal-based product for manufacturing billiard balls [1]. Today, plastics are a part of our clothing, medicines, packaging, sports gears, kitchenware, furniture and practically in every article used on land to space technology equipments. These are synthetic, unnatural (man-made), pliable, flexible, inert and resilient materials that are produced and applied in almost all aspects of life. Plastic is sourced from petrochemical industry and is produced from oil or natural gas. Since their discovery in early twentieth century, plastics manufacturing and production has grown in leaps and bounds, particularly around and after World War I as evidenced by the discovery of synthetic materials such as cellophane (1913), polyvinyl chloride or PVC (1927), polystyrene and nylon (1938), and polyethylene in 1942. While the plastic production from 1950s to 1970s was manageable, today the world produces about 300 million tonnes plastic waste every year. Over the years, there has been a massive shift towards the production and use of single-use plastic products. Approximately 98% of the single use plastic production is based on fossil fuel. Also, the production, use and disposal of the conventional fossil fuel-based plastics contribute to immense amounts of greenhouse gas emissions and is forecasted to grow to 19 per cent of the global carbon budget by 2040 [1, 2]. However, its once celebrated property of having a long half-life has actually made a monster of it today. Plastics have accumulated in the environment to levels that we have plastic pollution of air, water and soil. The Great Pacific Garbage Patch in the North Pacific Ocean is the "visible from space" evidence of the immensity of plastic menace. It is a collection of marine debris of which plastics make up the majority as these are not biodegradable and simply break into smaller pieces. More importantly, oceanographers and ecologists report that a major chunk of surface/floating marine debris eventually sink to the seafloor. This finding implicates the impact of plastic pollution on the seafloor ecology [3]. In sea and on land, plastics are now ubiquitous and are reported now as a geological indicator (as a distinctive stratal component) of the current geological era, the Anthropocene [4]. More interestingly, plastics (particularly microplastics) have been found to serve as substrates for colonization by microbial life in the oceans. A new biotope has been named as the "plastisphere" after the plastic component [5,6]. Considering the magnanimity of the current situation, the world now has urgent issues at hand dealing primarily in regulated production of the necessary plastics, reduction of mismanaged plastic waste disseminated in our environment and to upscale the efforts in recycling the waste plastic. Like any other polluting

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component of the environment, plastics levels are also required to be assessed for their potential risks due to exposure and impacts on living beings as wells as ecology. Plastics are of primary origin if they are intentionally manufactured in industry like beads, fibres, nurdles etc. Subsequently, in use or discarded plastic articles do not degrade but undergo continuous fragmentation over a period of time due to the different forces of nature such as radiation, wave action, wind etc. Such fragments are said to be of secondary origin [7]. These fragments may be found in the ranges of centimetres to micrometres. While larger pieces of plastic pose threat and obstruction to living organisms on land and in water, the smaller pieces are of much greater worry as they have been found to be ingested by organisms. Once inside organisms, plastics pose a bigger threat ranging from gut obstruction to toxicity. Post fragmentation, the plastics are termed as microplastics (MPs) or nanoplastics (NPs) based on their size ranges. Emerging from the various descriptions and properties of plastic fragments as revealed by various research groups around the world, some scientists have defined these terms by consolidating the major conclusions regarding defining MPs and NPs [7,8,9] For MPs, Frias et al. (2018) have defined them as "synthetic solid particles or polymeric matrices, with regular or irregular shape and with size ranging from 1 µm to 5 mm, of either primary or secondary manufacturing origin, which are insoluble in water". Nanoplastics are a sub-category of microplastics. Different research groups have adopted the upper size limit at either 1000 nm or 100 nm, and a formal definition is still under debate [9]. However, Gigault et al. (2018) have provided an apt definition for the same as "particles unintentionally produced (from the degradation and manufacturing of plastic objects) and presenting a colloidal behaviour, within the size range from 1 to 1,000 nm [nanometres]". Several studies have reported the occurrence of trophic transfer of MPs and NPs in food chain. Zooplanktonic organisms ingest/uptake MPs deliberately mistaking these for food particles or accidentally with food. Sufficient data (laboratory based and field studies) have shown that MPs and NPs are harmful to fauna ranging from the zooplanktons up to higher taxa [10]. MPs have been reported not only to enter food chains but also show bioaccumulation in organisms. The exposure to plastics may be detrimental to animal life by several mechanisms like entanglement, ingestion, laceration of tissues, smothering etc. The physiological and toxicological impacts could arise due to leaching of the chemical components or additives; exposure to harmful chemicals or pathogens that are adsorbed on the surface of plastic fragments; and by physical obstruction of the gut post ingestion. [6,10,11,12,13,14]. In recent decades, there has been remarkable spike in research and epidemiological studies to determine the impact of plastics on living beings and their implication on human health. The present study aims at reviewing the recent studies focussing on the pathophysiological impacts of MPs and NPs particularly on mammalian cells. The study aims at providing an insight into the current data available for a better understanding of the problem at hand and the way forward in alleviating the global burden of plastic pollution.

2. EXPERIMENTAL METHODS OR METHODOLOGY

Methods: PUBMED, Google Scholar, Researchgate, various public and private domain databases were searched during October 2021 to March 2022 using a combination of keywords including 'plastic', 'microplastic(s)', 'nanoplastic(s)', 'bio-accumulated', 'mammalian cells', 'trophic transfer', 'toxicity'. The combinations of keywords used as input were such as: "(microplastics) AND mammalian cells [Title]"; (Microplastic) AND (nanoplastics) AND (ingestion); "(microplastics) AND human health"; "(microplastics) AND mammalian cells [Title]) AND trophic transfer [Title]; (Microplastic) AND (nanoplastics) AND (toxicity) etc. Special attention was given to research studies within last few years (2017 till 2022) particularly pertaining to impacts of MP and NP exposure on mammalian cells. During screening for relevant hits, abstracts and full texts were analyzed. Spurious as well as irrelevant hits were ignored.

3. RESULTS AND DISCUSSION

3.1 Pathophysiology of mammalian cells due to exposure to microplastics.

Toxicity due to MPs may arise due to the inherent chemical composition and additives or adsorption of harmful chemicals and/or pathogens by forming biofilms on surface. Hence, MPs can potentially serve as carriers for toxic chemicals such as heavy metals and organic pollutants [15,16]. These factors may have additive toxic effects as studies have confirmed that formation of biofilms on MPs improve their capacity to adsorb and carry heavy metals. If these loaded MPs gain entry in living beings, their toxicity potential is plausible to be increased.

3.2 Routes of entry/exposure to Mammalian cells

Before one can assess the potential hazards on the different tissues of mammalian cells, the knowledge about all the possible routes of exposure is crucial. The route of uptake or exposure will determine the challenges that the MPs and NPs will face being foreign materials and hence will also determine their fate. Therefore, reviewing publications has revealed that diverse routes of exposure and uptake of MPs and NPs in animal cells have been proposed and investigated by several research groups. In our review methodology, on focussing upon the routes of entry or exposure, it was found that there are at least three such possibilities based on the tissue that MPs and NPs first encounter namely, gastrointestinal

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(GI) or via ingestion route, dermal or via contact route and respiratory or inhalation route. Figure 1 provides a diagrammatic representation of the same.

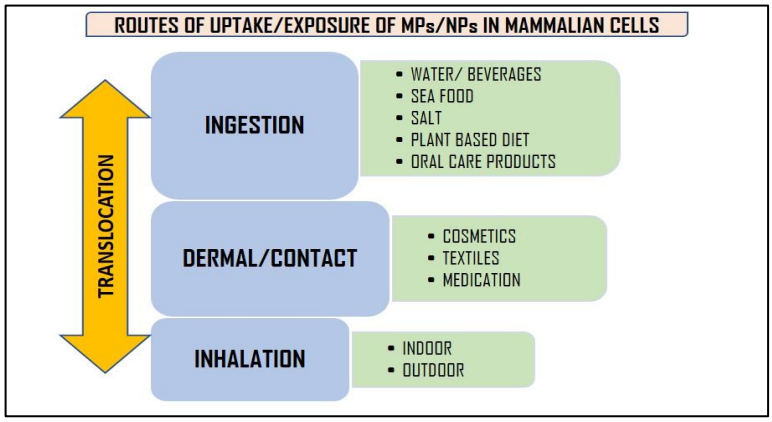

Fig. 1. Various routes of uptake or exposure to MPs or NPs in mammalian cells.

There is a possibility of translocation of MPs and NPs from the primary site of uptake to other tissues in an animal. the In the GI route, the entry of MPs and NPs in human may occur via plastics contaminated food, water, salt, medicines and/or oral care products [17,18,19]. Drinking water samples (packaged as well as sourced from ground water directly) have been reported to carry microplastics [20,21,22]. Even beverages like beer that are consumed in large quantities have been found to be contaminated with synthetic fibres [17]. MPs have been detected in salt samples and find their way into humans via salt consumption [18]. Lee et al. (2019) examined 11 salt samples in Taiwan that are widely consumed by the Taiwanese population. Their study concluded that all these salt samples contained microplastics. They also conclude MP contamination in 94% of salt products tested worldwide [23]. Studies have for now concluded that the MP contaminated salt consumption pose negligible or no health risk. However, salt being an important daily diet component, the long term exposure is plausible to cause bioaccumulation and may cause detrimental health issues. Oral care products like toothpaste, scrubs, oral or face washing solutions are another source by which MPs come in close contact with gut mucosa and may be ingested indirectly [20, 24]. Many of these products have microbeads intentionally added to them. In addition to the risk of epithelial damage or abrasions, potential translocation and bioaccumulation of MPs may also result over a long period of exposure to these products. Humans get exposed to MPs vis food chain pathway which involves consuming animals and plants that have already been exposed to and carry MPs in their tissues. Sufficient convincing data is available that shows the presence and accumulation of MPs in organisms from zooplanktonic organisms to the higher invertebrates and vertebrates. The fact that aquatic organisms and sea food are a major source of food to huge populations all over the world makes one think critically of the long term effects of MP contamination of our animals. Thiele et al. (2021) in their study provide a suitable MP extraction technique from fishmeal samples and have proposed fishmeal as an important pathway for microplastics into the environment because fishmeal is introduced in the sea as aquaculture feed. Fishmeal is also used as food in animal husbandry of poultry, pigs and aquaculture amongst others [25]. Smith et al. (2018) in their review have described evidence pertaining to human exposure to MPs via consumption of seafood [26]. As another evidence, Güven et al. (2017) in their study in the Mediterranean coast of Turkey have reported the extraction of significant number of MP particles from stomachs and intestines of fishes [14]. Li et al. (2019) have reported the uptake of microplastics by lettuce, an edible plant from contaminated soil. Their findings bring forth the concerns pertaining to human exposure to MPs via the consumption of contaminated plant-based food crops [27]. It also necessitates the need to investigate newer control and management strategies to combat MP pollution and its impacts. Contact with skin may result in penetration of nanoplastics through the dermal pores by the use of personal care and biomedical use products containing MPs and NPs [28]. Airborne MPs and NPs can potentially be taken in via inhalation. It can happen indoors or outdoors. For the MPs and NPs to be inhalable, size plays a crucial role as it will determine if the particle will reach the interiors and smallest spaces of the respiratory tract [29]. One of the major sources of inhalable MPs are synthetic textiles, wind transfer from landfills, debris etc. Due to textiles, the concentration of indoor MPs has been found to be higher than that in outdoor air. Xie et al. (2022) have demonstrated suspended atmospheric MPs qualitatively and quantitively using Raman microscopy. Also, in their case study comprising of eight sites in Shanghai, China it was found that inhalable MPs existed in all samples with higher concentrations indoors as compared to outdoors. However, it was found that sufficiently ventilated indoors showed similar MPs distribution as outdoors [30]. Vianello et al. (2019) in their simulated study in three apartments showed the human exposure to indoor airborne MPs using a Breathing Thermal Manikin [31]. The study attests that MPs exist as indoor airborne particulates that are potentially inhaled and ingested. Facciolà et al. (2021) have reviewed the existing research pertaining to human

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exposure to airborne MPs and NPs [32]. Their study highlights that there is an urgent need to develop standardized method for the analysis of MPs and NPs in environmental matrices as the existing studies have majorly focussed on the toxicity of MPs.

3.3 Fate of MPs and NPs after uptake by animal cells: Translocation, bioaccumulation and/or egestion

Size of plastic fragment plays a significant role in its fate post uptake by an organism. While the larger pieces are easy to egest, the ones sufficiently smaller may interact with the plasma membrane of cells to potentially enter them and may further be systemically translocated to other tissues. Figure 2 summarises the fate of MPs and NPs after uptake by an organism.

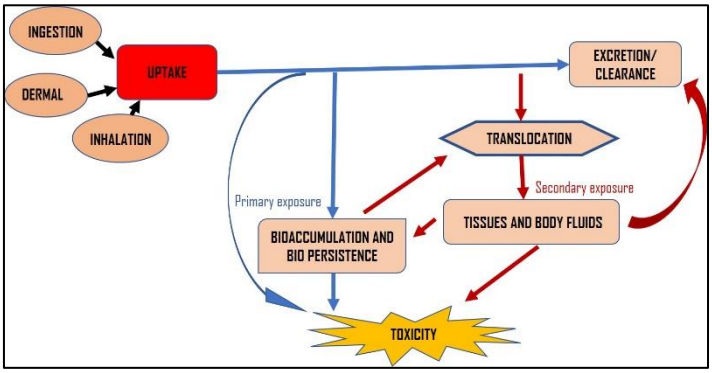

Fig. 2. The possible fate of MPs and NPs after uptake.

Walczak et al. (2014) demonstrated in their in vitro study that after oral intake of NPs, intestinal translocation is crucial for determining their bioavailability. They used NPs varying in size and surface charge properties. Intestinal translocation is a key factor for determining bioavailability of nanoparticles (NPs) after oral uptake. Their study showed that smaller sized (50 nm) particles translocated much more efficiently as compared to larger ones (100nm) [33]. Several research studies have indicated and shown that the MPs and NPs after being uptaken by cells translocate from the primary site of exposure to other organs (the secondary site) and even body fluids of organisms [33,34,35,36]. Revel et al. (2018) have shown MPs to translocate to the livers of fish that were fed plastic particles. Messinetti et al. (2019) in their study on ascidian Ciona intestinalis have shown that in just 8 days post ingestion, 1 µm particles translocated from the GIT to internal extracellular compartment. In a very recent study, Clark et al. (2022) for the first time have demonstrated NPs to pass through the intestinal barrier comprising of mucosa and muscularis in fish. This study is the first quantitative account of NPs uptake by the fish gut and highlights the potential of NPs to systemic spread thus having grave toxicological effects on the animal and the increased potential for trophic transfer.

3.4 Detection of MPs and NPs in Human samples

While there is significant data on the translocation of MPs and NPs in lower fauna, studies specifically targeting the mammalian cells are still insufficient. However, recent human specific studies have provided immense impetus and encouragement to deeper and more systematic research on mammalian systems with implications on human health. Pauly et al. (1998) reported inhaled plastic fibres in 83% of nonneoplastic human lung specimens (n = 67/81) and in 97% of malignant human lung specimens (n = 32/33) in the histopathology slides of human lung tissue observed with polarized light. The authors suggest that these plastic fibres can potentially cause risk of lung cancer [37]. Schwabl et al. (2019) in their study used Fourier-transform infrared microspectroscopy to investigate the presence of MPs in human stool samples. All of the 8 human stool samples tested were found positive for the presence of MPs with sizes ranging from 50 to 500 µm in size. The study indicates that MPs do find their way inside human bodies inadvertently thus exposing them to health risks [38]. In yet another study, Gopinath et al. investigated the possible toxicological potential of NPs on human blood cells. The study revealed that some plasma proteins (like HSA) interact with NPs and form multi-layered corona (size range 13 nm to 600 nm size) which subsequently result in protein-induced coalescence in NPs. These coronated NPs caused genotoxic and cytotoxic effect in human blood cells [39]. Similarly, Ragusa et al. (2021) have reported the presence of MPs in Human placenta samples for the first time using Raman Microspectroscopy. The group has called it "Plasticenta" [40]. Further studies are needed to assess the potential toxicological and transgenerational outcomes of plastics on developing foetus in such cases. Nor et al. (2021) in their study provide a human exposure assessment toolkit (HEASI) that probabilistically simulates MPs lifetime exposure model for children and adults accounting for intake via food, inhalation, intestinal absorption, biliary excretion, and plastic-associated chemical exposure [41]. All these studies are not only significant in their findings but also have used technology in a pathbreaking fashion. These studies will account for some of the most important pillars while shaping the future of risk assessment, control and management of MP and NP impacts on human health.

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3.5 Impacts of MPs/NPs exposure on mammalian cells: Experimental data

Since past few years, there has been a surge in research studies based on the impact of MPs and NPs on mammalian systems. Table 1 documents some such representative studies of last few years (2017 till 2022) to highlight the diverse pathophysiological impacts on MPs/NPs.

Table 1. Representative studies of last few years (2017 till 2022) to highlight the diverse pathophysiological impacts on MPs/NPs.

Reference	Mammalian cell type	Experimental design	Observations	Pathophysiological impacts/ implications
Schirinzi et al. 2017 [42]	Human	Cerebral and epithelial human cells, T98G and HeLa respectively were exposed to commonly used nanomaterials and microplastics in vitro	Cytotoxicity at cellular level via oxidative stress pathway for both cell lines.	Cytotoxic effects may lead to several anomalies at cellular level due to continued or incidental exposure to commonly used nanomaterials.
An et al. 2021 [43]	Rat	in vivo female Wistar rats were exposed to 0.5 μm polystyrene microplastics (PS-MPs) at different concentrations for 90 days.	PS-MPs induced oxidative stress, apoptosis of granulosa cells and ovary fibrosis; PS-MPs could enter into GCs and result in the reducing of growing follicles number.	Decrease of ovarian reserve capacity, granulosa cells apoptosis of ovary through oxidative stress in rats.
Li et al. 2020 [44]	Mice	C57BL/6 mice exposed to different amounts of polyethylene (PE) microplastics for 5 consecutive weeks.	Exposure to MPs affect the gut microflora in terms of abundance and diversity. In addition, serum levels of inflammation markers show marked increase.	PE microplastics can induce intestinal dysbacteriosis and inflammation.
Wu et al. 2020 [45]	Human	Illumina RNA seq. technique is used to identify the genes and associated pathways involved in polystyrene microplastics (PS-MPs) induced toxicity to Caco-2 cells. Subsequently, transcriptional levels of some proliferation and inflammation related genes related genes were investigated by qPCR.	Exposure to PS-MPs result in dose-dependent decreased in cell viability. Also, inflammation modulating and proliferation pathways, were strongly influenced.	Decreased in cell viability, cell inflammatory and proliferation pathways affected.
Wang et al. 2021 [46]	Human and Mice	Impacts of exposure of PS-MPs in human kidney PCT epithelial cells (HK-2 cells) and male C57BL/6 mice were evaluated. Following parameters were analysed in kidney cells: Mitochondrial ROS, endoplasmic reticulum (ER)stress, inflammation, and autophagy. Additionally, biomarkers of kidney function and ultrastructure, musclemass, urine	Exposure to PS-MPs resulted in higher levels of mitochondrial ROS and ER stress; elevated markers of inflammation. In vivo study shows bioaccumulation of PS-MPs, histopathological lesions in the kidneys.	PS-MPs can cause mitochondrial dysfunction, ER stress, inflammation, and autophagy in kidney cells. Results suggest the detrimental impacts of MPs on kidney structure and function.

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		protein levels and accumulation of PS-MPs in the kidney tissue were also analyzed.		
Visalli et al. 2021 [47]	Human	An In vitro study on human intestinal cell line HT29 to assess the impact of sub-chronic exposure extending the treatment up to 48 days, simulating the in vivo situation.	Moderate cytotoxicity after 24 h exposure. Microscopic observation revealed pronounced lysosomal membrane permeabilization in HT29 exposed to PS of size 3µm. ROS production was higher in cells exposed to PS 10 µm. Comet-assay confirmed PS-induced temporary oxidative damage.	On prolonged exposure, PS-MPs in size range 3 and 10 µm could trigger intestinal disorders.
Dong et al. 2020 [48]	Human	To study the impacts of and the association between pulmonary toxicity and PS-MPs exposure on normal human lung epithelial BEAS-2B cells.	PS-MPs exposure causes cytotoxic and inflammatory effects in BEAS-2B cells via ROS pathway. Decrease in transepithelial electrical resistance due to depletion of zonula occludens proteins.	Increased risk of chronic obstructive pulmonary disease and potentially harm the lung function in humans.
Liu et al. 2022 [49]	Mice	To explore the effect of PS-MPs on the female reproductive system of mice.	Results show inflammation and oxidative stress of ovaries, reduced the number of ovarian antral follicles in mice and impacted the maturation and development of oocytes in mice.	Impacts on female reproductive health.
Sun et al. 2021 [50]	mice	Exposure to PE MPs via oral route in female mice for 30 days. Quantification of colon mucin, gut flora from faeces, inflammatory factors (IL-1β, IL-6, IL-8 and IL-10), short-chain fatty acid receptors (GPR41 and GPR43), LPS receptors (TLR4 and MyD88) and LPS pathway downstream genes (ERK1 and NF-κB) in colon.	Decreased colon mucin. Microflora data altered microflora levels. Enhanced amino acids metabolism in microflora and a slight immune response.	Effects on mucin secretion in colon, gut microflora and inflammation.
Lee et al. 2022 [51]	mice	single- and 28-day repeated oral administration of different doses of MPs in ICR mice was carried out. Post exposure, histological and clinical pathology evaluations were performed to evaluate toxicity. Raman spectroscopy was used to	Histopathological studies revealed inflammation in the lung tissue from the 28-day repeated oral dose toxicity group. Presence of MPs was detected in the lung, stomach, duodenum, ileum, and serum by Raman spectroscopy.	Lung inflammation and toxicity. Translocation of MPs to different body tissues and fluids.

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		confirm the presence of MPs.		
Fan et al. 2022 [52]	Mouse	Oral administration of monodisperse (PS-NPs) (prepared by emulsion polymerization) and accumulation of fluorescent PS-NPs in various organs was examined.	Oral administration of PS-NPs resulted in visceral organ injury. Main toxicity effects were damage to hepatic function and abnormal lipid metabolism. Significantly increased ROS, hepatic triglycerides, and cholesterol accumulation and increased plasma glucose levels in the mouse liver.	Hepatic toxicity and altered glucose metabolism.
Sun et al. 2021 [53]	Mouse	Impact of two doses of PS-MPs on the hematological system of mice and to study the impacts by applying traditional toxicology e xperiments and transcriptome sequencing analysis.	the 0.5 mg dose significantly decreased WBC count, and inhibition of formation of colony-forming unit CFU-G, CFU-M and CFU-GM. Gene ontology analysis revealed differentially expressed genes (DEGs) and alteration in the transcription of mainly of those involved in T cell homeostasis, osmotic stress, extracellular matrix, structure organization, NADP and nucleotides metabolic pathways.	Hematotoxicity, altered gene expression in mouse bone marrow cells.
Lu et al. 2018 [54]		Male mice were exposed to differently sized PS-MPs for 5 weeks.	Oral exposure to 1000 µg/L of 0.5 and 50 µm PS- MPs decreased the body, liver and lipid weights in mice, decreased mucus secretion in the gut, altered gut microbiota. Also, decrease in the hepatic triglyceride (TG) and total cholesterol (TCH) levels.	Gut microbiota dysbiosis in mice. Polystyrene microplastic induced hepatic lipid metabolism disorder in mice
Poma et al. 2019 [56]	Human	To study the effects of polystyrene nanoparticles (PNPs) in the Hs27 cell line. cytokinesis-block micronucleus (CBMN) assay was employed to assess the genotoxic effects after exposure to PNPs.	CBMN test results show DNA damage, increased formation of micronuclei and nuclear buds, production of ROS.	Genotoxic effects.
Çobanoğlu et al. 2021 [57]	Human	To study the genotoxic and cytotoxic effects of 10-45 µm PE-MPs on human peripheral lymphocytes via CBMN assay.	The first study to identify MPs' genotoxic potential in human peripheral blood lymphocytes. Even lower concentrations of MPs resulted in elevated genomic instability.	Genotoxic potential in human peripheral blood lymphocytes.

Studies on animal models have shown aberrations and malfunctioning of various organs like liver, kidney, bone marrow, lungs and reproductive organs (Refer Figure no. 3). On a closer look at the data these studies bring to light the fact that at the cellular level there are cytotoxic effects, inflammation, oxidative stress, apoptosis decreased cell viability, ER stress, elevated ROS levels, in human as well as model system (rat and mouse) cells via oxidative stress pathway in the various cell lines used for experimentation [42,43,44,45,46,47,48,49,51,52]. Another interesting observation in a few

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research studies show that exposure to MPs/NPs alter the gut microflora in terms of abundance and diversity by inducing intestinal dysbacteriosis, inflammation and decreased colon mucin secretion [44,50,54]. Fan et al. (2022) and Kannan et al. (2021) have both indicated MPs as obesogens as the blood glucose levels have been found to be elevated on exposure to MPs [52,55]. As a more sinister finding, genotoxic effects have also been reported in Hs27 cell line and human peripheral blood lymphocytes on exposure to MPs and NPs in different studies [56,57]. Finally, analysis of Table no. 1 hints that the cellular mechanisms of the observed detrimental effects of MPs are closely interconnected and hence, often a slight alteration of one pathway may lead to a cascade effect to trigger disruption in others.

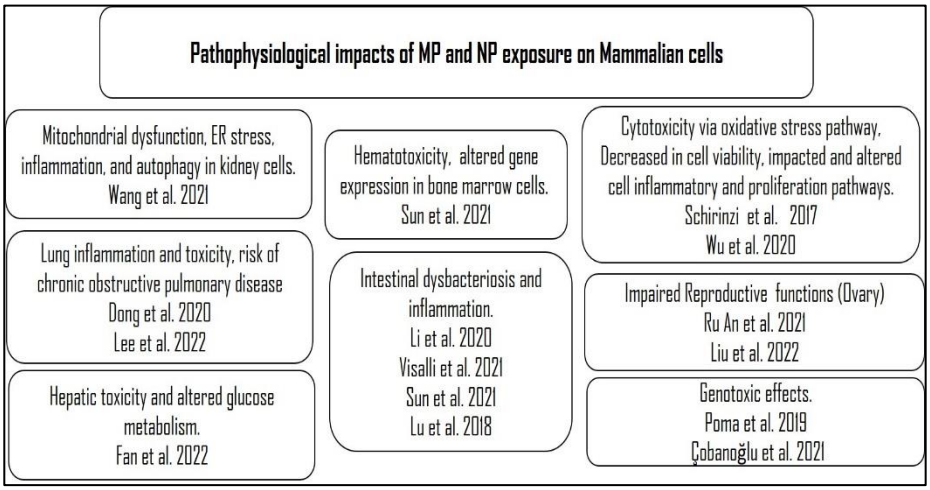

Fig. 3. Major pathophysiological impacts of MPs and NPs exposure on mammalian cells corroborated with recent significant references as evidences.

CONCLUSION

There is significant convincing data that exposure of mammalian cells to MPs and NPs result in pathophysiological impacts that range from altered inflammatory markers to genotoxicity to dysbacteriosis (Figure 3). The present study highlights that most research groups have found that NPs show greater detrimental impact. Owing to their smaller size and hence a greater probability to interact with subcellular components, these particles may bring about alterations in physical properties of small molecules in mammalian systems and bring about catastrophic chronic results. The discovery of translocation across placental barrier is worrisome. Although today there is not enough experimental data and standardized methodologies as well as techniques to assess the environmental levels of MPs and NPs and their exposure assessment in animals, tomorrow is not far away as shown by some of the recent trends. Our study highlights the need of consolidated efforts at global level to urgently develop standardized protocols for MP and NP monitoring, assessment and control measures by engaging all the concerned stakeholders. Research in the direction of mitigation of impacts of MPs and NPs must be encouraged and incentivized for the sake of all life forms on earth.

REFERENCES

1. Chalmin P. (2019) The history of plastics: from the Capitol to the Tarpeian Rock. Field Actions Science Reports [Online], Special Issue 19.
2. UNEP https://www.unep.org/interactives/beat-plastic-pollution/ (Accessed on January 29, 2022).
3. https://www.nationalgeographic.org/encyclopedia ((Accessed on February 19, 2022).
4. Zalasiewicz, J., Waters, C.N., Do Sul I.J.A., Corcoran, P.L., Barnosky, A.D., Cearreta, A., Edgeworth, M., Gałuszka, A., Jeandel, C., Leinfelder, R., et al. (2016). The geological cycle of plastics and their use as a stratigraphic indicator of the Anthropocene. Anthropocene,13, 4–17.
5. Amaral-Zettler et al., 2020, Amaral-Zettler, L.A., Zettler, E.R., and Mincer, T.J. (2020). Ecology of the plastisphere. Nature Reviews in Microbiology,18, 139-151.
6. United Nations Environment Programme (2021). From Pollution to Solution: A global assessment of marine litter and plastic pollution. Nairobi. (Accessed on February 25, 2022)
7. Cole, M., Lindeque, P., Halsband, C. and Galloway, T. S. (2011). Microplastics as contaminants in the marine environment: A review. Marine Pollution Bulletin, 62, 2588−2597.
8. Frias, J., Nash, R. (2018). Microplastics: Finding a consensus on the definition. Mar. Pollut. Bull., 138, 145–147

DOI: 10.17148/IARJSET.2022.9294

9. Gigault, J., Halle, A.T., Baudrimont, M., Pascal, P-Y., Gauffre, F., Phi, T-L., Hadri, H.E., Grassl, B., Reynaud, S. (2018). Current opinion: What is a nanoplastic? Environ. Pollut., 235:1030-1034.
10. Joon M. (2019). Trophic transfer of microplastics in zooplanktons towards its speculations on human health A review. J. Biomed.Ther. Sci., 6(1), 8-14.
11. Smith, M., Love, D.C., Rochman, C.M., Neff, R.A. (2018). Microplastics in Seafood and the Implications for Human Health. Curr. Environ. Health Rep, 5(3):375– 86.
12. Campanale, C., Massarelli, C., Savino, I., Locaputo, V., Uricchio, V.F. (2020). A Detailed Review Study on Potential Effects of Microplastics and Additives of Concern on Human Health. Int J Environ Res Public Health 17(4):1212.
13. Toussaint., B., Raffael., B., Angers-Loustau, A., Gilliland, D., Kestens, V., Petrillo, M., et al. (2019). Review of Micro-and Nanoplastic Contamination in the Food Chain. Food Addit Contam Part A, 36(5):639–73.
14. Güven, O., Gökdağ, K., Jovanović, B. and Kideys, A.E. (2017). Microplastic litter composition of the Turkish territorial waters of the Mediterranean Sea, and its occurrence in the gastrointestinal tract of fish. Environmental Pollution 223, 286-294.
15. Wu, S., Wu, M., Tian, D., Qiu, L., Li, T. (2020). Effects of polystyrene microbeads on cytotoxicity and transcriptomic profiles in human Caco-2 cells. Environ Toxicol. 35(4):495-506.
16. Wang, Y-L., Lee, Y-H., Hsu, Y-H., Chiu, I-J., Huang, C. C-Y., Huang, C-C., Chia, Z-C., Lee C-P., , Lin Y-F. and Chiu, H-W. (2021). The Kidney-Related Effects of Polystyrene Microplastics on Human Kidney Proximal Tubular Epithelial Cells HK-2 and Male C57BL/6 Mice. Environmental Health Perspectives, 129:5
17. Liebezeit, G. and Liebezeit, E. (2014). Synthetic particles as contaminants in German beers. Food Addit Contam Part A Chem Anal Control Expo Risk Assess, 31(9):1574–8.
18. Karami, A., Golieskardi, A., Ho, Y.B., Larat, V., Salamatinia, B. (2017) Microplastics in eviscerated flesh and excised organs of dried fish. Sci Rep., 7(1):5473.
19. Iñiguez, M.E., Conesa, Juan A. & Fullana, Andrés. (2017). Microplastics in Spanish Table Salt. Scientific Reports. 7. 10.1038/s41598-017-09128-x.
20. World Health Organization. (2019). Microplastics in drinking-water. Geneva. Licence: CC BY-NC-SA 3.0 IGO.
21. S.M. Mintenig, M.G.J. Löder, S. Primpke, G. Gerdts. (2019). Low numbers of microplastics detected in drinking water from ground water sources. Science of The Total Environment, Volume 648, 631-635.
22. Koelmans, A.A., Mohamed Nor, N.H., Hermsen, E., Kooi, M., Mintenig, S.M., De France, J. (2019). Microplastics in freshwaters and drinking water: Critical review and assessment of data quality. Water Research 155, 410-422.
23. Lee, H., Kunz, A., Shim, W. J. & Walther, B.A. (2019). Microplastic contamination of table salts from Taiwan, including a global review. Nature Scientific Reports, 9:10145.
24. Praveena, S.M., Shaifuddin, S.N.M., Akizuki, S. (2018). Exploration of microplastics from personal care and cosmetic products and its estimated emissions to marine environment: An evidence from Malaysia. Mar Pollut Bull,136:135-140.
25. Thiele, C.J., Hudson, M.D., Russell, A.E., Saluveer, M. & Sidaoui-Haddad, G. (2021). Microplastics in fish and fishmeal: an emerging environmental challenge? Nature Scientific Reports. 11:2045
26. Smith, M., Love, D. C., Rochman, C. M., & Neff, R. A. (2018). Microplastics in Seafood and the Implications for Human Health. Current environmental health reports, 5(3), 375–386.
27. Li, L., Zhou, Q., Yin, N., Tu, C., & Luo, Y. (2019). Uptake and accumulation of microplastics in an edible plant. Chinese Science Bulletin.
28. Hwang, J., Choi, D., Han, S., Choi, J., Hong, J. (2019). An assessment of the toxicity of polypropylene microplastics in human derived cells. Sci Total Environ. 684:657-669.
29. Stapleton, P.A. (2021). Microplastic and nanoplastic transfer, accumulation, and toxicity in humans. Current Opinion in Toxicology, 28, 62-69
30. Xie,Y., Li, Y., Feng, Y., Cheng, W. & Wang, Y. (2022). Inhalable microplastics prevails in air: Exploring the size detection limit. Environment International, 162, 107151.
31. Vianello, A., Jensen, R.L., Liu, L. et al. (2019). Simulating human exposure to indoor airborne microplastics using a Breathing Thermal Manikin. Sci Rep 9, 8670.
32. Facciolà, A., Visalli, G., Pruiti Ciarello, M., Di Pietro, A. (2021) Newly Emerging Airborne Pollutants: Current Knowledge of Health Impact of Micro and Nanoplastics. Int J Environ Res Public Health. 18(6):2997
33. Walczak, A. P., Kramer, E., Hendriksen, P. J., Tromp, P., Helsper, J. P., van der Zande, M., Rietjens, I. M., & Bouwmeester, H. (2015). Translocation of differently sized and charged polystyrene nanoparticles in in vitro intestinal cell models of increasing complexity. Nanotoxicology, 9(4), 453–461.
34. Revel, M., Châtel, A. & Mouneyrac, C. (2018). Micro(nano)plastics: A threat to human health? Current Opinion in Environmental Science & Health, Volume 1, Pages 17-23
35. Messinetti, S., Mercurio, S., Scarì, G., Pennati, A. & Pennati, R. (2019). Ingested microscopic plastics translocate from the gut cavity of juveniles of the ascidian Ciona intestinalis. The European Zoological Journal, 86:1, 189-195,

DOI: 10.17148/IARJSET.2022.9294

36. Clark, N. J., Khan, F. R., Mitrano, D. M., Boyle, D., & Thompson, R. C. (2022). Demonstrating the translocation of nanoplastics across the fish intestine using palladium-doped polystyrene in a salmon gut-sac. Environment international, 159, 106994.
37. Pauly, J. L., Stegmeier, S. J., Allaart, H. A., Cheney, R. T., Zhang, P. J., Mayer, A. G., & Streck, R. J. (1998). Inhaled cellulosic and plastic fibers found in human lung tissue. Cancer epidemiology, biomarkers & prevention: a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology, 7(5), 419–428.
38. Schwabl, P., Köppel, S., Königshofer, P., Bucsics, T., Trauner, M., Reiberger, T., & Liebmann, B. (2019). Detection of Various Microplastics in Human Stool: A Prospective Case Series. Annals of internal medicine, 171(7), 453–457.
39. Gopinath, P. M., Saranya, V., Vijayakumar, S., Mythili Meera, M., Ruprekha, S., Kunal, R., Pranay, A., Thomas, J., Mukherjee, A., & Chandrasekaran, N. (2019). Assessment on interactive prospectives of nanoplastics with plasma proteins and the toxicological impacts of virgin, coronated and environmentally released-nanoplastics. Scientific reports, 9(1), 8860.
40. Ragusa, A., Svelato, A., Santacroce, C., Catalano, P., Notarstefano, V., Carnevali, O., et al. (2021). Plasticenta: First evidence of microplastics in human placenta, Environment International, 146, 106274
41. Nor, N. H. M., Kooi, M., Diepens, N.J., Koelmans, A.A. (2021) Lifetime Accumulation of Microplastic in Children and Adults. Environ. Sci. Technol., 55, 8, 5084–5096
42. Schirinzi, G. F.; Pérez-Pomeda, I.; Sanchís, J.; Rossini, C.; Farré, M.; Barceló, D. (2017). Cytotoxic Effects of Commonly Used Nanomaterials and Microplastics on Cerebral and Epithelial Human Cells. Environ. Res., 579
43. An, R., Wang, X., Yang, L., Zhang, J., Wang, N., Xu, F., Hou, Y., Zhang, H., & Zhang, L. (2021). Polystyrene microplastics cause granulosa cells apoptosis and fibrosis in ovary through oxidative stress in rats. Toxicology, 449, 152665.
44. Li, B., Ding, Y., Cheng, X., Sheng, D., Xu, Z., Rong, Q., Wu, Y., Zhao, H., Ji, X., & Zhang, Y. (2020). Polyethylene microplastics affect the distribution of gut microbiota and inflammation development in mice. Chemosphere, 244, 125492.
45. Wu, S., Wu, M., Tian, D., Qiu, L., & Li, T. (2020). Effects of polystyrene microbeads on cytotoxicity and transcriptomic profiles in human Caco-2 cells. Environmental toxicology, 35(4), 495–506.
46. Wang, Y. L., Lee, Y. H., Hsu, Y. H., Chiu, I. J., Huang, C. C., Huang, C. C., Chia, Z. C., Lee, C. P., Lin, Y. F., & Chiu, H. W. (2021). The Kidney-Related Effects of Polystyrene Microplastics on Human Kidney Proximal Tubular Epithelial Cells HK-2 and Male C57BL/6 Mice. Environmental health perspectives, 129(5), 57003.
47. Visalli, G., Facciolà, A., Pruiti Ciarello, M., De Marco, G., Maisano, M., & Di Pietro, A. (2021). Acute and Sub-Chronic Effects of Microplastics (3 and 10 µm) on the Human Intestinal Cells HT-29. International journal of environmental research and public health, 18(11), 5833.
48. Dong, C. D., Chen, C. W., Chen, Y. C., Chen, H. H., Lee, J. S., & Lin, C. H. (2020). Polystyrene microplastic particles: In vitro pulmonary toxicity assessment. Journal of hazardous materials, 385, 121575.
49. Liu, Z., Zhuan, Q., Zhang, L., Meng, L., Fu, X., & Hou, Y. (2022). Polystyrene microplastics induced female reproductive toxicity in mice. Journal of hazardous materials, 424(Pt C), 127629.
50. Sun, H., Chen, N., Yang, X., Xia, Y., & Wu, D. (2021). Effects induced by polyethylene microplastics oral exposure on colon mucin release, inflammation, gut microflora composition and metabolism in mice. Ecotoxicology and environmental safety, 220, 112340.
51. Lee, S., Kang, K. K., Sung, S. E., Choi, J. H., Sung, M., Seong, K. Y., Lee, S., Yang, S. Y., Seo, M. S., & Kim, K. (2022). Toxicity Study and Quantitative Evaluation of Polyethylene Microplastics in ICR Mice. Polymers, 14(3), 402.
52. Fan, X., Wei, X., Hu, H., Zhang, B., Yang, D., Du, H., Zhu, R., Sun, X., Oh, Y., & Gu, N. (2022). Effects of oral administration of polystyrene nanoplastics on plasma glucose metabolism in mice. Chemosphere, 288(Pt 3), 132607.
53. Sun, R., Xu, K., Yu, L., Pu, Y., Xiong, F., He, Y., Huang, Q., Tang, M., Chen, M., Yin, L., Zhang, J., & Pu, Y. (2021). Preliminary study on impacts of polystyrene microplastics on the hematological system and gene expression in bone marrow cells of mice. Ecotoxicology and environmental safety, 218, 112296. Advance online publication.
54. Lu, L., Wan, Z., Luo, T., Fu, Z., & Jin, Y. (2018). Polystyrene microplastics induce gut microbiota dysbiosis and hepatic lipid metabolism disorder in mice. The Science of the total environment, 631-632, 449–458.
55. Kannan, K., & Vimalkumar, K. (2021). A Review of Human Exposure to Microplastics and Insights Into Microplastics as Obesogens. Frontiers in endocrinology, 12, 724989.
56. Poma, A., Vecchiotti, G., Colafarina, S., Zarivi, O., Aloisi, M., Arrizza, L., Chichiriccò, G., & Di Carlo, P. (2019). In Vitro Genotoxicity of Polystyrene Nanoparticles on the Human Fibroblast Hs27 Cell Line. Nanomaterials (Basel, Switzerland), 9(9), 1299.
57. Çobanoğlu, H., Belivermiş, M., Sıkdokur, E., Kılıç, Ö. & Çayır, A. (2021). Genotoxic and cytotoxic effects of polyethylene microplastics on human peripheral blood lymphocytes, Chemosphere, 272, 129805.

