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REVIEW ARTICLE

Microplastics crisis in India and Research gaps in their toxicological assessment

Sandeepa Bhan[1] and Binu Bhat[2]
Department of Toxicology, Shriram Institute for Industrial Research,
Delhi – 110007
Corresponding emails: sandeepatickoo@gmail.com[1], binu@shriraminstitute.org[2]

ABSTRACT

In the recent years, microplastics have emerged as an important environmental pollutants as well as potential health threat. In this review, an attempt has been made to summarize some of the recently published research papers under Indian context for presence of microplastics in sediments, water bodies, aquatic life and other samples to provide an overview of the problem. Due to increasing levels of plastic pollution, it is imperative to evaluate the health hazard risks associated with it. Therefore, the factors to consider for in vivo toxicological assessment of microplastics and their potential toxic effects on human health, based on mammalian toxicology studies are discussed. However, more active research is needed in India, on the occurrence of microplastics in water, sediment and marine environments to generate data in order to know the sources and pathways involved in plastic pollution for designing plastic pollution preventive strategies. There is a need to conduct both short term and repeated dose in vivo rodent toxicological studies which can be of more relevance to create data for human health safety and risk assessment. This data may be helpful in ranking of plastic polymers according to health hazard risks to form an effective waste management strategy and for future designs of sustainable plastics polymers.
Keywords: *Microplastics, human health safety, rodent toxicological*

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INTRODUCTION

Plastic is widely distributed throughout aquatic and terrestrial environments. Plastic pollution has become a major ecological and societal concern. Microplastics (MPs) are defined generally, as plastic particles with less than 5 mm in their longest dimension (1) and more specifically as plastic particles with size ranging between 0.1 to 5000 µm in their longest dimension (2). The impacts of large plastic debris also known as macroplastics in marine environments has been well documented, however the potential harm caused by microplastics is not much clear. Microplastics fall into two categories: they are either produced intentionally e.g., microbeads, plastic production pellets and are called as “primary microplastics” or are degraded from larger plastics to produce smaller pieces e.g., fibres and are called as “secondary microplastics” (3). MPs are heterogeneous class of materials that consist of various polymers like polyethylene (PE), polypropylene (PP), polystyrene (PS), nylon (N), polyvinyl chloride (PVC), polyethylene terephthalate (PET), polysester (PL) etc. In addition, they are also found in various sizes and various shapes like beads, fibers, fragments, pellets. In the marine environment, it takes nearly 320 years to disintegrate 1mm sized microplastic to nano-sized plastic particle(4). This indicates that the microplastics already present in the environment will have long term impacts on the aquatic animal health (5).
Since the early 1950s, the production of plastic has been increasing exponentially.It is expected that the demand for plastic products in the market would increase. The projections indicate that the production levels may reach around 600 million tonnes by 2025 and exceed one billion tonnes by 2050(6).As per Plastics Europe, 2019, the global production of plastics in the year 2018reached almost 360million tonnes (Mt)(7). In order to tackle the problem of plastic waste, the first attempt by the Indian government came in 2011 with the notification of Plastic Waste (Management and Handling) Rules, 2011 (8).These rules helped to set up a plastic waste management system and also a regulatory framework for restricting the manufacture and use of plastic carry bags. The rules were then replaced with a Plastic Waste

Management Rules, 2016 which emphasized for a complete ban on plastics below 50 microns(9). Since then several amendments have taken place.As per FICCI, 2017, the average per capita consumption of plastics in India is 11 kg (10).
Microplastics, being very small sized plastic particles are an issue of scientific concern. They are easily assessible to a wide range of aquatic organism which further transfer it to the food web(11). Here, we have reviewed the scientific literature from India, to look for the evidence and abundance of microplastics in different samples like sediments, salts, aquatic animals and other water bodies. TheMP concentrations varied significantly between sampling sites. In addition to that, the toxicological aspects of microplastics were also reviewed. It was observed that a lot of ecotoxicological research has beenconducted globally on microplastics in the marine environment, while there were not enough toxicity studies on mammals, the data of which can be of direct relevance to humans. The objectives of this review are:
(1)to provide an overview of the abundance of microplastics in Indian environment.
(2)to discuss the factors to be considered for the toxicological assessment of microplastics for mammalian toxicity studies.
(3)to evaluate the potential toxicity of microplastics on human health based on mammalian toxicology studies.

ABUNDANCE OF MICROPLASTICS IN INDIAN ENVIRONMENT

Some of the studies highlighting the presence of microplastics in different samples at different locations in India were studied. The presence of microplastics was found in aquatic animals, sediments, salts and many water bodies.

Aquatic animals:

In India, plastic ingestion among marine fishes has been reported along the south-west and south-east coasts from almost all the states. The different marine fishes caught from such coastal areas include sardine, mackerel, anchovy, ribbon fishes, dolphin-fish, tunas and several other fishes (5).The microplastics have been found in the intestine of fishes from fish landing sites at Tuticorin (12). The gut content analysis of commercially important fishes, collected from the coastal waters along the beaches of southeast coast of India, revealed microplastics ingestion in 10.1% of fishes (13). The epipelagic fishes were found to have higher levels of MP contamination than the mesopelagic ones(14).Microplastics were also found in the benthic invertebrates *Sternaspisscutata, Magelonacinta* (deposit feeders) and *Tellina sp.* (suspension feeder) from the coastal waters of Kochi, Southeastern Arabian Sea(15).The soft tissues of the commercially important green mussel, *Pernaviridis* at the fishing harbour of Chennai, southeast coast of India also had evidence of microplastics (16). The samples from oysters of different sizes from three sites along Tuticorin coast in Gulf of Mannar in Southeast India revealed that largest oysters (14-16 cm) contained highest abundance and concentrations of MPs(17).

Beaches/ sediments:

Researchers have found abundance of microplastics on the beaches from different coastal areas in India. The microplastics have been found in the beach sediments of Chennai (east coast of India) and remote Island Tinnakkara (west coast of India) (18), Rameswaram Coral Island, Gulf of Mannar (Southeast coast of India) (19), Kerala (southwest coast of India) (20) Girgaon coast (the Arabian sea coast) and Dhanshkodi (Bay of Bengal coast) (21). Numerous factors are considered to be responsible for the distribution of MPs in beaches from different coastal regions. During pre-Chennai flood in March 2015 and during post-Chennai flood in November 2015, themicroplastic pellets in the surface sedimentsalong the Chennai coast were checked for sources, surface features, distribution,polymer composition and age.The wind and the surface currents were considered to be the driving force for the transportation and deposition of microplastic pellets from the sea to beaches(22). The similar observations were found for the Goa beaches also, where winds and surface currents during southwest monsoon were found to be the driving forces for the transportation and deposition of microplastic pellets (23). The aeolian process and the nature of the coast were considered to dominantly control the distribution of the plastics. Besides this, the tourist activities and fishing practices werealso considered to be the possible sources of the microplastic debris. (19). Thesamples collected from the beaches from high tide areas of Tamil Nadu coast, the south east coast of India, contained higher abundance of microplastics than lower tide. Moreover, the beaches adjacent to the rivers had higher abundance of microplastics than those influenced by tourism and fishing activities(13).The recreation, religious and fishing activities were the major contributors to plastic pollution and occurrence of microplastics in the high and low-tide sediments of five coastal areas in Tamil Nadu beaches (24). The studies on analyses of the prevalence of microplastics in the beaches of Puducherry coast found that a strong positive correlation existed between fishing activity and microplastic abundance while a weak correlation existed between microplastic abundance and recreational activities (25). The study on the beaches of Tuticorin district, Southeast coast of India found a correlation between intensity of fishing activity and the degree of recreational activity with the concentration of macro, meso and microplastics (26).

Salt:

India is considered a leading producer and exporter of sea salts.Most people consume food products containing commercial salt throughout their lives. There are numerous studies revealing the presence of microplastics in salts. As per the World Health Organisation (2012) guidelines, salt intake of up to 5gm salt per day for adults is recommended (27). An IIT-B study, on different brands of Indian sea salts, found the presence of the microplastic particles in all the studied eight brands and the types of MPs present were found to be independent of the salt brand and packaging type.As per this study, the concentration of these particles ranged from 56 ± 49 to 103 ± 39 particleskg^{-1} of salt. The maximum microplastic ingestion for Indians from these salts was estimated to be approximately 117 micrograms every year(28). A study on 14 different brands of sea salt and bore well salts collected from salt manufacturing units in the Tuticorin, Tamil Nadu, Southeast coast of India found microplastics in the food-grade salts produced from seawater as well as bore-well water. The sea water was found to have the highest quantities of different microplastic particles. Based on an average daily salt intake of 5 g, the study revealed that people consume approximately 216 particles of MPs per year via sea salt and 48 items per year via bore-well salt (29).Another study conducted on 25 types of sea salt samples in the Tuticorin coastal salt pan stations, found that the sea salts produced from the sea water columns of salt pans possessed MPs. The MPs that measured less than 100 μm, formed the major part of the salts, accounting to 60% of the MPs among the total pollutants (30).The salt consumption can be considered to have a long-term exposure to the human population and therefore their degree of contamination with microplastics and effects on human population needs thorough research.

Fresh water , surface water, ground water, drinking water, ballast water:

Vast data exists in the literature on marine microplastics while there are very scarce reports on other water sources. The presence of microplastics was found in the sediments of Vembanad Lake, Kerala (31) and in the sediments of river Ganga (32).Another study found the microplastics in surface water, groundwater and branded drinking water bottles in and around Chennai, Tamil Nadu, India (33). The microplastics have also been found in the ballast waters where theywere considered as a source and vector for chemicals and pathogens (34).

The data collected by different scientists discussed above is very useful to understand the possible risks by microplastics. Their presence in the soft tissues of the commercially important green mussel, *Pernaviridis* concluded that the filter feeding bivalves were at the highest risk in the coastal zones(16).The samples collected from different size oysters in three sites along Tuticorin coast, provedthat a greater proportion of microplastics in the water column was ingested with increasing size of oysters. Based on this evidence, it was suggested that the bioavailability of microplastics increased with increasing size of oysters. The distribution patterns of microplastic abundance, shape and size in oysters also resembled closely with microplasticsin water than in the sediment(17).Therefore, it is evident that the research on distribution and abundance of microplastics in different samples helps to identify the potential risks on different aquatic animals.

The information on polymer types from the collected samples can help us to identify the potential origin of the detected microplastics. The microplastics found in the sediments of river Ganga revealed a strong correlation between microplastics abundance and the pollution traits (32).The sediment samples from different sea beaches revealed different possible reasons like wind, surface current, fishing, religious activities, recreational activities etc. In India, active research is needed in this field, to gather more data on the abundance and distribution of microplastics so as to identify the potential origins and make strategies for plastic waste management accordingly.

Based on our literature search, the distribution of microplastics and the different types of polymersextracted and identifiedin different samples at different locations in India have been summarized (Table 1).

Table 1: Indian data of the distribution of microplastics

Sample	Location	Polymers identified	Reference
Aquatic life	Thirespuram and Punnakayal fish landing sites in Tuticorin: (Fishes namely Rastrillegerkanagurta and Epinephalusmerra)	PE, PP	(12)
	Kochi, Southeastern Arabian Sea :Benthic invertebrates Sternaspisscutata, Magelonacinta (deposit feeders) and Tellina sp. (suspension feeder)	PS	(15)
	Tuticorin coast, Gulf of Mannar, Southeastern India (Indian edible oyster – Magallanabilineata)	PE, PP	(17)
	Chennai southeast fishing harbor (Green mussel – Pernaviridis)	PS	(16)
	Kerala, southwest coast of India.: Marine fishes	PE , CE, RY, PL, PP	(20)
	Tuticorin, Southeast coast of India: GI tract of fishes	PE, PL, PA	(14)
Sea sediments	Chennai coast	PE, PP	(22)
	Goa coast	PE, PP	(23)
	Chennai coast andTinnakkara Island	Not identified	(18)
	Tamil Nadu coasts, Southeast coast of India	PE, PP, PS	(13)
	Rameswaram Coral Island, Gulf of Mannar, Southeast coast of India	PP, PE, PS, PVC, NY	(19)
	Tamil Nadu coasts	PE, PP, N, PS, PL	(24)
	Puducherry coast	PP, LDPE, HDPE, PS, PVC	(28)
	Tuticorin, Tamil Nadu	PE, PP, PET, NY, PS, PVC	(26)
	Kerala, southwest coast of India.	PE, PP	(20)
	Girgaon Mumbai (Arabian sea coast), Tuticorin, and Dhanushkodi (Bay of Bengal coast).	PE , PET, PS, PP, PVC	(21)
Sea salt	Various locations (8 brands of Indian Sea salts)	PL, PET, PA, PE, PS	(28)
	Tuticorin Coastal salt pan stations, gulf of Mannar, South India (Marine sea salts)	NY,CE,PE, PP	(30)
	Tuticorin, Southeast Coast of India (Fourteen different brands of sea salts and bore-well salts)	PE, PP,PL, PA	(29)
Different water sources	Vembanad lake	HDPE, LDPE, PP, PS	(31)
	Chennai, Tamil Nadu, India (Surface water, groundwater and branded drinking water bottles)	PET , PA	(33)
	River Ganga	PET , PE	(32)

Abbrevations used:PA (polyamide), **PS** (polystyrene), **PE** (polyethylene), **PET** (polyethylene terephthalate), **PP** (polypropylene), **PVC** (polyvinyl chloride), **PL**(polyester), **CE**(cellulose),**NY** (Nylon), **HDPE**(High-density polyethylene),**LDPE**(low density polyethylene)

TOXICOLOGICAL ASSESSMENT OF MICROPLASTICS

Microplastics constitute a diverse range of material types, shapes,sizes and colours (35). The toxicological aspects of microplastics have been illustrated by various reseracher s. Their physical effects include blocking the digestive organs and preventing the animals from feeding (36) while their chemical effects includes affecting theimmune systemby way of the substances that the microplastics contain, absorb or release, which can in turn be toxic (37). The nine critical determining factors for plastic particle toxicity on aquatic and shoreline data as suggested by Kögel et al. 2020 areconcentration, particle size, exposure time, particle condition, environmental condition, polymer type, species, developmental stage, and sex(38).Broadly, the major toxic effects of MPs on living beings has been categorized into four categories: physical toxicity, chemical toxicity, cellular toxicity, and toxicity due to pathogenic microbes(39). Based on different scientific views and literature search, the different factors to be considered for toxicological assessmentof microplasticsin mammalian toxicity studies are beingdiscussed below:

1. Source2. Concentrations 3. Particle size4. Shape 5. Surface characteristics
6. Routes of administration 7. Exposure duration8. Polymer types 9. Species and strain10. Coexposure of microplastics and other contaminants

Source of microplastics

Microplastics are ubiquitous in the environment. The most common type of studies by researchers include counting the number of microplastic particles in different water bodies (stream, river, estuary, ocean, lake), food types, drinking water, soils,aquatic animals etc.Among aquatic animals, the majority of the studies concerns fishes and sea mammals. The second most studied group includes bivalves such as mussels, oysters and scallops(40).For the toxicological assessments, the microplastic sources can be grouped as primary or secondary depending on the sample of scientific interest. Primary microplastics are manufactured in a micro-size range, such as pellets, powder plastics and microbeads in cosmetics (3,41). Such particlescan be procured easily as they are commercially available and extensively being used in industrial processes. Secondary sources of microplastics result from the fragmentation and degradation of macroplastics exposed to UV or physical abrasion in the environment (41). These can be derived from the environmental samples via different techniques.However, the challenge is to retrieve these microplastics from environmental samples and food matrices as well as to collect the representative fields of samples(40).The extraction methods commonly in use for MPs in environmental samples include flotation (separation by density), chemical digestion (separation by biogenic material removal), sieving or filtration (separation by size), and visual identification (separation by manual sorting). However,these analytical method and protocols for extraction of MPs need better standardization and optimization (42).

Concentrations of microplastics:

Microplastics with varied concentrations are found in different field samples and their concentration in the samples are an indicator of their contamination in the environment. There is ample evidence to prove that the acute as well as chronic effects of microplastics are concentration-dependent. In general, extremely high concentration of microplastics are considered cytotoxic. At high concentrations, microplasticscan lead to cell death by disrupting the lipid bilayer of the plasma membrane (43). In an vivo study on male mice, where the exposure to very high concentrations of PS particles 1.5 x 10^{10} particles/L of 0.5 μm at 100 or 1000 μg/L or 1.5 x 10^{4} particles/L of 50 μm at 100 or 1000 μg/L was used in drinking-water for 5 weeks, there was an alteration of lipid metabolism and gut microbiota as compared to the controls(44).Another study found that the high-concentration of MPs induced inflammation of the small intestine(45).Similar theory has been proved by way of in -vitro assays in human cell lines by PS microplastics where the highest concentration of 10 mg/L resulted in oxidative stress (46). However, it is to be noted, that the adverse effects of microplastic exposure have mostly been investigated by administering single doses of unrealistically high concentrations of microplastics to the test organisms (47). While comparing the concentrations used in the laboratory studies to the concentrations of microplastics found in the environment, it was concluded that only 17% of doses used in experimental studies were concentrations of microplastics that have been found in nature (48).Thus, in order to have realistic results, it is very important to conduct experiments with environmentally relevant concentrations of microplastics.

Particle Size

Size plays acrucial factor in determining uptake, retention and effects of microplastics. It also determines the range of organisms it can effect. There is ample evidence to point out that the smaller plastic particles have a tendency to have a larger negative impact as compared to the larger particles. As far as implications on human health is concerned, it is speculated that microplastics particles > 150 μm are not absorbed while those that are smaller <150 μm are able to translocate from the gut cavity to the lymph and circulatory system causing systemic exposure. Only microplastics with size ≤ 20 μm are able to penetrate into organs while the smallest fraction ranging 0.1 > 10 μm are able to access all organs,cross cell membranes and translocate to the blood-brain as well as placental barriers (49). In many in vivo studies, 5μm microplasticwas used, considering it to be the smallest diameter of plastic debris found in marine habitats and also therepresentative of the smaller size range of particles known to be ingested by many aquatic organisms. In an in vivo study on mice, it was concluded that the tissue accumulationkinetics and distribution pattern was related to MP particle size(50).The size of the microplastic also determines the rate of uptake and release ofpersistent organic pollutants(POPs) from plastics. With increase in the size of plastics, sorption and desorptionbecomes slower (1). Thus selection of appropriate size is a very important factor before performing any toxicological assessment.

Shape of microplastic:

Microplastics are known to have a variety of shapes such as microbeads or spheres, fragments, fibers, and granules (51). The shapes of nanoplastics in the environment are relatively unknown, due to the unavailabilityof themethods to detect these nano-sized polymers in the environment(4).Most of the experimental studies have used microspheres of uniform size. These microspheres are available commercially but are in actual,rare in the environment. It is predicted that thespheres may pass more easilythrough the gutwhile the fragments having sharp edges might damage the gut, whereas the long fibers might clog up the gut.It is estimated thatthe sea and beach samples globally have 5 times more fibers than particles(40).Asmicrofibers are being considered as the most abundant form of MPs in the environment, it is suggested thatthe focus of exposure and effects studies should mostly be on them rather than on convenient microspheres (52). Therefore, the choice of the shape of microplastics for the toxicological assessment will definitely decide the outcome of the study.

Surface characteristics of the particle:

On exposure to the marine environmental conditions, it is expected that the plastics undergomechanical alterationon their surface. Thesurface properties likepoint of zero charge, surface area, pore volume, surface topography, functional groups and acid-base behavior affect sorption. While floating at the sea surface, the microplastics get exposed to sunlight and saltwater that can cause the surface to be oxidized. This erosion process may cause the surface to be uneven and formation of functional groupscontaining oxygen on the surface.This is assumed to be the possible reason for interaction of eroded plastics with microbes and metals (53).In addition to this, it has been observed that the circulation time is highly dependant on the surface characteristics of the particle. The hydrophilic and positively charged particles show enhanced circulation times(54).Therefore, theexperiments should aim to mimic the surface characteristics of microplasticssimilar to the ones found naturally.

Routes of administration of microplastics:

The four major routes of exposure to microplastics are entanglement, contact, ingestion and inhalation(55). Ingestion is considered the most likely interaction between aquatic organisms and microplastics. The small size of microplastics make them indistinguishable from the natural prey items which can result in accidental ingestion while filter feeding (56).

Human beings being at the peak of food chain may be considered to be the most exposed organism (55). Human population can be affected by various routes. Besides aquatic sources i.e seafood, the otherdietary routes for human populations for being exposed to MPs are a number of non-aquatic consumables such as bottled water, sugar, salt, beer, and honey (2). Microplastic uptake through seafood(mussel) consumption was found to be minimal when compared to other routes of human exposure, like, fibers settling on consumables, or dust in the household (57). Another exposure pathway of microplastics to the human body is via skin contact by way of water while washing or while using scrubs and cosmetics that contain micro and nanoplastics. The probability of penetration of particles lower than 100 nm via the corneous layer was found to be more via this route(58). Thus in order to find the toxic effects of microplastics, there is need to explore all possible routes of exposure.

Exposure duration:

In a natural environment, the organisms are exposed to microplastics throughout their lifetime as compared to the short experimental periods in the laboratories. Different researchers have used different exposure durations for the experiments. In some toxicology studies in mice, the exposure durations of microplastics and routes varied from 28 days via oral gavage (50, 59) to 35 days and 42 days via drinking water (44, 60). Keeping in view, the exposure risks of microplastics to humans, the exposure durations in experimental settings don't look realisticand are often short. Different exposure durations will give different results and conclusion vary from one study to another. Therefore, in addition to short term studies, repeated dose long term studies are also important to come to more relevant conclusions.

Polymer types:

Plastics are formed by the reaction of small organic molecules known asmonomers which in turn result inthe formation of long polymer chains.Though these polymers themselves may not be considered hazardous, however they can release theirconstituent monomers during the product lifecycle which are in turn consideredhazardous. These monomers are released during degradation during the stage ofproduction till the use of the product and finallyits eventual discard. The behavior of these polymers in the environment depends upon their chemical nature and physical properties. On the basis of chemical composition, the researchers have developed a model for comprehensive hazard ranking of plastic polymers (61). In this model, the ranking of the constituent monomer chemicals has been done according tothe internationally agreed criteria for identifying physical, environmental and health risks. As per the literature, it was evident that most of the exposure studies have used polystyrene (PS) micro/nanoplastics. However, PS particles cannot be the representative particles for whole microplastics. Therefore, development of different reference materials for different polymers in different matrices is needed(40).Once it happens, the toxicity studies can be designed with different polymer types.

Species and strain

The species and strain of animals play a major role in the response of microplastics in the body. In one early study, performed on dogs, to study the persorbability and the hematogenous dissemination of PVCmicroplastics with a size ranging from 5 to 110 µm, the PVC particles were detected in the portal veins of dogs (62).A study on rats with ultrafine PS particles resulted in lung inflammation and effect on enzyme activity in a dose-dependent way (63). A 90-day dietary study done as per Organisation for Economic Cooperation and Development (OECD) in Sprague-Dawley rats with PE and PET, did not show any treatment-related adverse effectson blood parameters, organ weights, or histopathology (64). Based on the absence of observed toxicity in this study, the highest test dose was considered to be the no observed effect level (NOEL), equivalent to approximately 2500 mg/kg body weight (bw)/day (66).A study of oral toxicity of PS nanoplastics (mixture of 25 and 50 nm) in adult male Wistar rats, did not show any effect on body weight or on a battery of neurobehavioral tests (65).In most of the recent studies,mouse models have been used. In some studies, ICR mice strain has been used (44,50,60,67) whilewe found one studywithC57BL/6NTac strain of mice (59).It has been observed that the degree of microplastic toxicity observed in mice is less severe than that observed in fishes. The possible reason being given was that the feeding experiments of mice limit the uptake only through the GI route whereas thefishes have multiple routes like gut and gills for plastic uptake and accumulation (43). Using different species and strains for similar research would definitely yield different results and would not allow us to come to common conclusions. Therefore, for toxicological studies, the selection of species and strains with different genetic backgrounds needs to be properly justified.

Coexposure of microplastics and other contaminants:

Microplastics not only contain a mixture of chemicals added during manufacture, but also adsorb or absorb contaminants from the surrounding environment (68). The organic pollutants are adsorbed in significant amounts from the surrounding environment (69). The possible reason for this is the weathering processes as well as mechanical fragmentation of MPs. This leads to formation of smaller particles thus increasing the specific reactive surface area and facilitate the sorption of pollutants (70). The high surface area to volume ratio of small particles also gives them a high potential for leaching and uptaking the chemicals (71). First these toxic chemicals by adsorption processes attach to microplastics in the environment and then by desorption processes get released post-ingestion with potential for toxicity and / or accumulation in the food chain. Studies have reported organic pollutant levels on marine plastic resin pellets apparently being adsorbed from ambient seawater (72). These microplastics on interacting with toxic chemicals like heavy metals such as iron,manganese, aluminium, lead, copper, silver, zinc and hydrophobic organic contaminants can create a problem for the environment. These hydrophobic organic contaminants (HOCs) are also known as persistent organic pollutants (POP) include polyaromatic hydrocarbons (PAHs), organochlorine pesticides (OCPs) and polychlorinated biphenyls (PCBs).These chemicals are found everywhere specially in the areas of high anthropogenic activitiesand are known to beassociated with teratogenic,mutagenic and carcinogenic effects(73,74). MPs can also act as vector for pathogenic microbes. The microbes present in the environment attach to the surface of microplastics via biofilm formation (39).There are substantial data gaps in the understanding of the role of microplastics in the food-chain transfer of HOCs as compared to the other routes of exposure (75). A study on ballast water found that microplastics can act as a source and vector for metals, antibiotics, toxic chemicals, pathogenic bacteria (Vibrio cholerae), and Harmful AlgalBloom (HAB)-forming dinoflagellates across the continents and thus may pose a serious threat to human health due to higher incidences of bacterial disease outbreaks and HABs (34).Therefore, more studies are needed, not just with ‘pristine’ particles, but also with the adsorption properties of microplastics .

As discussed above, it is evident that a single factor cannot be sufficient tounderstand the toxicology of microplastics.In order to gain an in depth knowledge of microplastic toxicity, large scale properly designed multifactorial studies are needed by keeping several factors stable and varying a few (38). Moreover, harmonized protocols are needed as perOECD(Organization for Economic Co-operation and Development) guidelines with specific elements related to MP exposure, for both in vivo and in vitro studies (76).

POTENTIAL TOXICITY OF MICROPLATICS ON HUMAN HEALTH:

The mammals are known to be the common model in toxicology research. However, still there islack of evidence of microplastic toxicological studies on them.Therefore, the potential health risks of microplastics to humans indicated by mice models should be considered(77). Here, we have focused our discussion based on potential toxicities demonstrated in recent studies, mostly inmice/rat models:

Gastrointestinal toxicity:

There are sufficient studies depicting the translocation of microplastics across the gut of marine organisms.The few studies carried out in mice show the evidence of gastrointestinal effects due to microplastics. The effects are reduction in mucus secretion (44),gut barrier dysfunction (60,67), intestinal inflammation (45)gut microbiotadysbiosis (44, 45,60, 67).

Liver toxicity:

Microplastics have a large surface area. After their oral administration, microplastics could be distributed in the blood and lymphatic system for their intestinal absorption and consequently into liver. On the basis of mice models, it was found that administration of microplastics resulted indecrease of some key gene expressions related to lipogenesis and triglyceride synthesis and thus the decline of hepatic triglyceride & total cholesterol levels(44). The other changes includeinflammation and lipid accumulation or lipid profile changes (44, 50, 67), changes in the markers of lipid metabolism (44,67,78), disorders in energy metabolism (50,78) and disorders in bile acid metabolism (60).

Neurotoxicity and reproductive toxicity:

Microplastics have shown to cause potential changes in neurotransmitter levels in mice (50). However, a study on male rats reflected that exposure of microplastics did not result in behavioral alterations (65).The studies on theexposure of the mice during gestation, resulted in metabolic disorders in offsprings (67).

Toxicity of microplastics due to associated chemicals:

The toxicity of microplastics can be associated with residual monomers in the plastics, the vector effect and the additives intentionally added to the plastic during manufacture or processing.Additives include stabilizers, plasticizers and flame-retardants which are added intentionally during manufacture. Many of the additives are known toxicants and, upon release from plastic materials, may potentially cause adverse health effects (79). Plastic additives which are of concern to human health include phthalates, bisphenol A, brominated flame retardants, triclosan, bisphenone and organotins (80).The co exposure of MPs and OPFRs (organophosphorus flame retardants) induced neurotoxicity, greater oxidative stress and enhanced disruption of amino acid and energy metabolism in a study on mice model(81).After ingestion, thehydrophobic organic chemicals (HOCs) at relative high concentrations may potentially become bioavailable (82).The contribution of microplastics to the transfer of these organic pollutants to higher order organisms as well as their role as vectors in microbial transfer has been a controversial subject andneedsthorough research.

CONCLUSIONS

Microplastics are heterogeneous class of materials consisting of multitude of polymers, shapes, sizes, conditions, exposure times, routes and concentration ranges. The effects of one polymer will not tell us the effects of microplastics in general. To resolve this, different reference materials for each polymer with different shapes, sizes and surface charges that are more environmentally relevant, need to be created. Also the adsorption of chemicals or microorganisms or the leaching properties of reference materials must accurately mimic the properties of microplastics in the natural environment. In addition to the reference materials, standardized analytical methods need to be developed, so that the data produced is representative and significant.

The toxicological evaluation of microplastics is dependant on different factors. There is a lot of literature regarding the toxicity of microplastics in the marine environment, while there is limited data that can be said to be of direct relevance to humans. The data generated via marine organisms is more important from an ecotoxicological point of view. Therefore, the need is to design standardized protocols with carefully selected species, strain, routes of administration and definite exposure times. The researchers need to focus on both short term and repeated dose in vivo toxicological studies on lab animal mammalian models. Though microplastics are not categorized as chemicals, it is presumed that they may eventually have similar health outcomes. Therefore, once there is good amount of data in relation to hazardous parameters of microplastics, it will help to make a hazard ranking of plastic polymers.The toxicological data generated would further create a more realistic data bank for human health risk and hazard assessments.

In India, there is need for comprehensive studies on abundance and distribution of microplastics in order to know the sources and pathways of plastic pollutions. This will helptoknow potential origins of plastic waste and hencedevelop effective waste management strategies. Moreover considering the threat of microplastics, work needs to be done towards designing of sustainable plastics polymers in the near future.

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