Toxic Components of Plastic Pose Carcinogenic Threat to Public Health

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Abstract

The toxicity of plastics and its components is increasing day by day for human needs. In modern days, plastics are widely used in every product in our daily life. In 2021, it was predicted that the world would produce 390.7 million metric tons of plastic. A year’s worth of plastic waste is produced in India at 3.4 million tons. Many products are manufactured with plastic due to its impressive characteristics such as inert, flexibility, durability, versatility, lightweight, and less costly. They encourage dangers to the planet and human health. Numerous chemical and toxic contaminants, including Bisphenol A (BPA), phthalates, antimonitroxide, brominated flame retardants, poly-fluorinated chemicals, nonylphenol, polychlorinated biphenylethers, dichlorodiphényldichloroéthylene, phenanthrene, among others, are found in plastics and pose a major risk to human health and the environment. These chemical and hazardous compounds are used in the manufacturing of plastic bottles, containers, pharmaceuticals, food packaging, baby toys, etc. The impact of plastics on the environment gets more dangerous day by day. Not only the environment but also exposure to plastics leads to various human health risks. Toxic components of plastics lead to several serious cancers even; they are also possessing their genotoxic effects on human health. This review contains the toxicity of plastic components on human health and the environment by low-level exposure and gives a proper awareness about the health problems and focuses on degrading ways to reduce its effects.

Keywords: Toxicity of plastics, hazardous compounds, human health risks, cancer, genotoxic effects

1. Introduction

Plastics are a need for modern life. It is important for people since it has acceptable qualities including stretchability, inertness, durability, affordability, lightweight, ease of carrying, and many others. Long polymer chains like plastic are essential components of daily life. The craziness around plastic use is on the rise like a freight train every day. Plastic has certain unique qualities, including the capacity to burn at high temperatures, having a water content that is significantly lower than that of biomass, not absorbing a lot of moisture, and growing availability in the community. To maintain its feature, it is made up of some chemical and hazardous compounds. Bisphenol A (BPA), phthalates, antimonitroxide, brominated flame retardants, poly-fluorinated chemicals, nonylphenol, polychlorinated biphenylethers, dichlorodiphényldichloroéthylene, phenanthrene, among others, are harmful chemical substances that are utilized in the production of plastics (Proshad et al. 2018). In 2018, it was predicted that 380 million tons of plastic will be produced globally. In the period from 1950 to 2018, around 6.3 billion tons of plastics were created globally, of which 9% and 12%, respectively, were recycled and burned. Global production of plastics, which was at 311 million tons in 2014, is anticipated to more than double in the next 20 years and maybe quadruple by the year 2050. Human health is affected by exposure to these substances. The synthetic organic polymers that make up plastics are widely utilized in a variety of products, including water bottles, clothes, food packaging, medical supplies, electronics, building materials, etc. (Alabi et al. 2019). Mainly, those are composed of many chemical components, which act as a factor causing serious health issue, such as breathing difficulties, lung problems, liver dysfunction, respiratory problems etc. and more importantly it may cause various cancers and genotoxic effects also, which present in plastic bottles, and containers. Several times reusing plastic bottles and
containers may increase the possibility of contamination risks. Because of the flammability, phthalates, and BPA can be found in dust, water, and aquatic habitats (Proshad et al. 2018). BPA is mainly present in food-related plastic containers, and that transfer is magnified by heat, excessive use, contact with acidic and alkaline compounds, exposure to microwaves, etc. leads to exuding BPA in foods (Bertoli et al. 2015). Compared to bottled water, phthalates leach more quickly into lower pH items like soda and vinegar. The leaching of phthalates and antimony from PET also appears to be affected by temperature, with higher temperatures causing more leaching (Rustagi et al. 2011). Recent studies have also looked into the role of BPA in the development of cancer, and they have found evidence that it may be partially to blame for the rise in the incidence of several cancers, including liver cancer, prostate cancer, testicular cancer, ovarian cancer, breast cancer, and uterine cancer (Wang et al. 2017). Also, microplastics are introduced in humans in various ways such as bottled water, tap water, food chain, fish, milk, beverage, etc. microplastics frequently include polystyrene (PS) and polyvinyl chloride (PC), which can lead to carcinogenesis when ingested, inhaled, or exposed topically to human implants (Kumar et al. 2022).

2. Materials And Methods
The relevant data for this review study was discovered by searching Google Scholar, PubMed, PubMed Central, and published research papers and review articles from throughout the world on the toxicity of plastics that causes cancer in the human population. Only publicly available data were used, and speculative assertions concerning exposure were disregarded. Utilizing information from reputable sources of information on the issue is one of these inclusion criteria. The study excluded all other languages than English.

3. Results and Discussion

The routes of exposing plastic:
According to their sizes, plastics are exposed to humans and wildlife. Humans are partially and fully exposed to plastic in their lifestyles. Various products used in the daily routine are made up of plastic. Moreover, some have short lifespans that affect aquatic and terrestrial organisms. Exposure to microplastics leads to bioaccumulation in the food chain (Shown in Fig. 1).

Processed food (such as sugar, salt, and honey), alcoholic drinks (such as beer), drinking water, and heated/stored food might indirectly expose people. The quality of food gets reduced because of leaching out of macroplastics, while processing and storage of food and water (Rodrigues et al. 2019). Although, MP can be ingested by human through bottled drinking water (Winkler et al. 2019). When it comes to humans, endocytic pathways in the gastrointestinal tract (GIT) and perception in the GIT can both play a role in the absorption and translocation of tiny particles if they are breathed or swallowed. The fluid in the lung lining or the mucus in the stomach is prone to trap particles (Rodrigues et al. 2019).

Effects on environment:
In modern days, the environment becomes more worsen due to humankind's work. The population of humans has increased the demand for plastic production, which may release huge amounts of debris into the environment. Huge amounts of production cause various types of pollution (air pollution, water pollution, and soil pollution) causing its form with chemical substances. Large quantities of plastics are unlocked in the open air, and can easily leach out various heavy metals, and toxic compounds. It reduced soil fertility and damages terrestrial animals. Uncontrolled disposal of waste from plastics and plastic products can result in environmental pollution, which can be seen in several ways, such as the degradation of the environment's natural beauty, the entanglement, and death of aquatic organisms, the obstruction of sewage systems in cities, especially in developing nations, which leads to the breeding of mosquitoes and other disease-carrying vectors, the production of foul odors, and a decrease in water percolation (Alabi et al. 2019). Numerous freshwater and marine creatures, including vertebrates like chordata and invertebrates like Protozoa, Crustaceans, Cnidarians, Mollusks, and Annelids, have been shown in experiments to be capable of ingesting MPs (Rodrigues et
That disrupted aquatic organisms’ life. Chlorinated plastics can release poisonous chemicals into the soil, which can then seep into nearby water sources or the subterranean water itself, damaging the environment. Combustion of plastics leads to release CO2 and methane and this CO2 may absorb radiant heat and prevent it from exiting the planet, which would otherwise lead to global warming. Biodegradation released greenhouse gas (methane) into the air which contributes to global warming (Alabi et al. 2019), which increases the sea level. Inhaling these particles from air pollution has an impact on public health. Because of that, the following generation might perish (Proshad et al. 2018).

**Types of plastics and their effects on human health:** The production of plastic depends on its composition, which divides into different types of plastic. Most of them are hazardous to the environment, animal, and human health such as PVC, PC, PS, PE, and PET (shown in Table 1). High-density polyethylene and polypropylene are safer than those because they don’t contain any toxic substances (BPA, Phthalates). Benzene ring compounds (PS) are introduced as carcinogenic to the human body (Alabi et al. 2019). PET release antimony in drinking water which may be performed as a carcinogen (Proshad et al. 2018).

<table>
<thead>
<tr>
<th>Types of plastic</th>
<th>Commercial uses</th>
<th>Characteristic</th>
<th>Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyethylene Terephthalates (PET)</td>
<td>Water bottles, soft drinks bottles, containers, salad dressing.</td>
<td>Transparent, thin, smooth, anti-inflammatory, anti-air (to prevent entry of oxygen).</td>
<td>Release of antimony cause cancer.</td>
</tr>
<tr>
<td>High density polyethylene (HDPE)</td>
<td>Shopping bags, milk bottles, ice cream containers, juice bottles, detergent bottles.</td>
<td>Excellent moisture barrier properties and chemical resistance</td>
<td>Irritation on skin, eye damage, inhalation cause lung problems.</td>
</tr>
<tr>
<td>Polyvinyl Chloride (PVC)</td>
<td>Cosmetic container, plumbing pipes, blister packs, roof sheeting, bottles, Shoe soles, cable sheathing etc.</td>
<td>Transparent, hard, long-term stability, rigid.</td>
<td>Carcinogenic, birth defect, liver dysfunction, respiratory disorders, skin disease, type II diabetes, hormonal disbalance.</td>
</tr>
<tr>
<td>Low density polyethylene (LDPE)</td>
<td>Sandwich bags, grocery bags, squeezable bottles, thick-plastic bags.</td>
<td>Durable, flexible, transparent, good stability and moisture barrier.</td>
<td>Byincineration respiratory disorders, swelling causes chocking, skin and eye irritation.</td>
</tr>
<tr>
<td>Polypropylene (PP)</td>
<td>Packaging of medicine, yogurt, beverage, microwave dishes, straw.</td>
<td>Hydrophobic, semi-transparent, strong, heat-resistant.</td>
<td>Asthma, neurotoxic raised the cellular toxicity of liver cell.</td>
</tr>
<tr>
<td>Polystyrene (PS)</td>
<td>Disposable cups, plastic cutlery, food boxes and packing foam.</td>
<td>Opaque, transparent, rigid.</td>
<td>Neurotoxic, hematological, carcinogenic, cytogenetic effects and stored in body fat via food, anxiety and social impairment.</td>
</tr>
<tr>
<td>Polycarbonate (PC)</td>
<td>Automotive components, computers, cooler bottles, electronics.</td>
<td>Transparent, rigid, flexible.</td>
<td>Carcinogenic effect, birth defect, liver dysfunction.</td>
</tr>
</tbody>
</table>

Table 1: Different types of plastic and their effects on human health (Alabi et al. 2019) (Proshad et al. 2018) (Jeyavani et al. 2021).

**Carcinogenic constituents of plastic components:**

**Bisphenol A:** Due to its extensive usage and biological build-up, the synthetic molecule with a carbon basis known as bisphenol A (BPA) has hormone-like qualities and is found in abundance in both the environment and human tissues (Gao et al., 2015). BPA is an industrial chemical that is widely used in the production of reusable water bottle, baby bottle, food container, food can, epoxy resin, etc. BPA molecules may contaminate beverages and food if plastic containers are used repeatedly and for an extended length of time. By exposing the plastic container to high temperatures, storing acidic or basic substances that can break down the plastic polymers, and repeatedly cleaning the plastic container, the process of BPA leaching from plastics is sped up (Alabi et al. 2019). The absorption of BPA occurs in the human body via the digestive tract even through the skin. It is metabolized in the GI tract (liver, intestine), where some micro flora induces its metabolism in the body (Zwierelio et al. 2020). As an endocrine disruptor, it can mimic oestrogen in females which is interact with oestrogen receptors α and β. BPA causes a decrease in thyroid hormone receptor function by activating transcriptional
corepressors of the thyroid hormone receptor. This modification to the thyroid axis results in hypothyroidism (Mathieu-Denoncourt et al. 2015). Prenatal exposure to BPA leads to alter cell proliferation, development of mammary glands & apoptosis which may predispose mammary glands to carcinogenesis. However, it interacts with steroid receptors which play a major role in the development of prostate cancer (Gao et al. 2015). ERRs (oestrogen-related receptors) are another receptor that BPA may bind to. Breast cancer cells proliferate more quickly after being exposed to modest concentrations of BPA thanks to activated ERK1/2/ERR (Song et al. 2015). BPA binds to ER and GPR30 membrane receptors like oestradiol by accelerating cellular responses via non-genomic signalling pathways (shown in Fig. 2) (Almeida et al. 2018). Low-dose exposure to BPA binds with the orphan oestrogen-related receptor gamma (ERR) which increase breast cancer in human. As an illustration, BPA exposure causes calcium flux and the release of prolactin in pituitary cells via mER pathways (Wang et al. 2017).

The development and spread of prostate cancer are significantly influenced by two steroid receptors (ERs and ARs). BPA can control prostate cancer cells' migratory and proliferative behaviour as well as their ability to form DNA adducts (Derouiche et al. 2013). BPA therapy can increase Cdk4, cyclin D1, ER-a, IGF-1R, and Bcl2 while decreasing p21 and the Aryl-hydrocarbon receptor nuclear translocator 2 (ARNT2), which promotes cell growth and prevents apoptosis, develops cancer. Furthermore, it has been demonstrated that BPA controls the caspase-3 expression and activity via interacting with leptin, as well as the (TGF-b) transforming growth factor beta, MAPK/ERK, JAK/STAT3, and PI3K/Akt signalling pathways. Additionally, MMP-9, an extracellular matrix protein linked to the evolution of ovarian cancer, is expressed by granulosa-lutein cells as a result of BPA stimulation (Gao et al. 2015).

**Fig. 2:** Diagram shows that signalling pathways induced mammary cell proliferation (Wang et al. 2017).

**Phthalates:** A compound consisting of a diester of phthalic acid which is exposed in the human body via ingestion of contaminated goods is called phthalates (1,2-benzene dicarboxylic acid) (Proshad et al. 2018). Bio-metabolism of phthalates in the human body via hydrolyzation, then it undergoes catalysation to form hydrophilic glucuronide conjugate by the enzyme of uridine 5′-diphosphoglucuronyl transferase into the cell. The toxicological fate of phthalates in the body determines by two methods such as hydrolyzation of short-branch phthalates turns into monoester phthalates that excrete via urine and several bio-transformations (hydroxylation &oxidation) of long-branch phthalates to transform into phase 2 conjugated compound that excreted via urine and faeces (Shown in figure 3). MBzP and MiBP, which are metabolites of phthalates, were adversely correlated with female breast cancer (Wang et al., 2021).

**Figure 3:** The mechanical pathway of phthalate (Kim et al. 2014).

Phthalates are also a carcinogenic agent, it leads to protooncogene activation, DNA mutation, DNA reorganization, amplification, or loss of function are a few examples of genetic modifications. Amplifying the oncogenes such as BCL2, and C-Myc both are a common occurrence. C-Myc oncogene is induced via the AhR-cAMP-PKA-CREB1 cascade pathway, where a ligand-activated transcription factor aryl hydrocarbon receptor (AhR) binds with heat shock protein 90 (HSP 90). It leads to increase cell migration, cell proliferation, and develop tumour growth (Shown in Fig. 4). The excess methylation of the tumour suppressor gene BRCA1 is a common factor in breast cancer, and mutations in the BRCA1 and BRCA2 genes are a leading cause of breast cancer in women. Apoptotic pathways in cells
have been discovered to be affected by phthalates. When MCF-7 breast cancer cells are treated with TAM there two apoptosis genes Bax and Bcl2 are expressed as Bax increased and Bcl2 decreased. Otherwise MCF-7 treated with phthalates changes the ratio between two apoptosis genes Bax and Bcl2, where Bcl2 is higher than Bax. It leads to medication resistance in breast cancer cells (Mughees et al. 2022). Tumorogenesis is caused by the interplay of environmental variables and genetic inheritance (Zhang et al. 2022). DEHP and BPA may make people more susceptible to thyroid conditions including thyroid cancer and benign thyroid nodules (Liu et al. 2020).

Management of plastic wastes: To resolve the toxic effect of plastic on both environment and humans, waste management and recycling are the favorable way. Globally, the reduction of plastic debris and pollutants need proper treatment via three methods such as reuse, reclamation, and recycling. Alternative options for plastic bags are jute bags, paper bags, clothes bags, etc. These can reduce the effect of plastics on the environment and humans. However, to minimize the effect of plastics there is another alternative way is bioplastic, a type of plastic created from cellulose, a byproduct of the production of wood pulp. In comparison to other forms of plastic, the manufacture of bioplastics uses fewer fossil fuels, making them more ecologically friendly (Alabi et al. 2019). Studies show that bioplastic evolves to use food waste such as banana peels. With the help of glycerol, hydrochloric acid, and sodium hydroxide work together to form the bioplastic from banana peel (Azizeyanti et al. 2020).

Another way to reduce plastic is biodegradation using microbes. Here, plastic fragments are utilized as a source of carbon by microbes for their growth and development. Microbes perform four processes such as biodeterioration, bio-fragmentation, biosynthesis, and mineralization. Several microbes are released extracellular enzymes that can convert complex molecules of plastics into monomers (Zhou et al. 2022).

<table>
<thead>
<tr>
<th>Type of plastic polymer</th>
<th>Microbes involves in degradation</th>
<th>Secreting enzymes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polystyrene (PS)</td>
<td>Pseudomonas, Corynebacterium, Aspergillus</td>
<td>Hydrolase, Oxygenase, Styrene oxide isomerase</td>
</tr>
<tr>
<td>Polyethylene terephthalates (PET)</td>
<td>Ideonella, Thermobifida, Humicola</td>
<td>Lipase, Hydrolase, Depolymerase</td>
</tr>
<tr>
<td>Polyvinyl chloride (PVC)</td>
<td>Candida, Pseudomonas, Aspergillus</td>
<td>Lipase, Esterase, Tannase</td>
</tr>
<tr>
<td>Polyurethane</td>
<td>Pseudomonas, Fusarium, Aspergillus</td>
<td>Lipase, Cutinase, Esterase</td>
</tr>
<tr>
<td>Polypropylene (PP)</td>
<td>Fusarium, Caulobacter, Aspergillus</td>
<td>Lipase, Hydrolase, Esterase</td>
</tr>
<tr>
<td>Polyamide (PA)</td>
<td>Bacillus, Vibrio, Anoxybacillus</td>
<td>Hydrolase, Aminotransferase, Dehydrogenase</td>
</tr>
</tbody>
</table>

Table 2: Types of microorganisms degrade different types of plastic polymer (Zhou et al. 2022).

4. Conclusion
A wide analysis shows that plastics get involved in the ecosystem day by day which effects the environment as well as human health. Due to its flexibility, durability, and cost-effectiveness, the use of plastics increased. The toxic components possess several diseases as well as cause cancer, which increases the mortality rate. Research shows that several types of cancer are appearing like gynecological cancer, thyroid cancer, and liver cancer. Long-term exposure leads to a genotoxic effect on human health, which gives a threat to the next generation. The toxic compounds such as Bisphenol A (BPA) and Phthalates both metabolized inside the body and get involved in various pathways such as MAPK/ERK, PI3K/Akt, AhR-cAMP-PKA-CREB1 cascade pathway and increase the cell growth, cell proliferation which leads to cancer. As these components prevent the apoptosis process, therefore it developed cancer much more drug-resistant. To resolve this problem, reduce the uses level of plastic
which will also decrease the cancer rate. At that end, this study serves as a societal message to raise the population's goodwill and action taken to limit plastic consumption for a brighter future.

**Future Scope:** In the manufacture of water bottles, containers and children's toys, phthalates and bisphenol A should be outlawed; instead, paper bags and jute bags should be used to lessen the impact of plastics. As a solution to this problem, further research should concentrate on creating bioplastics from natural resources. By learning diverse bioremediation strategies, we were able to control the impact of plastic.

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**Author Contributions:** Acquisition and interpretation of data is done by Priti Nandi. Conception, design and revising of the article are done by Rupesh Dutta Banik.

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**References:**


