ORIENTAL JOURNAL OF CHEMISTRY
An International Open Access, Peer Reviewed Research Journal
www.orientjchem.org

ISSN: 0970-020 X
CODEN: OJCHEG
2025, Vol. 41, No.(5):
Pg. 1451-1463

Neurotoxicity of Plastics: Mechanistic Insights into the Progression of Neurodegenerative Diseases in Animal Models

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http://dx.doi.org/10.13005/ojc/410502

(Received: April 25, 2025; Accepted: September 21, 2025)

ABSTRACT

The extensive buildup of plastics in the environment has sparked grave worries about how they can affect human health, especially the central nervous system. It has been discovered that a number of substances generated from plastic, including as phthalates, polybrominated diphenyl ethers (PBDEs), styrene, bisphenol A (BPA), and micro- or nanoplastics, either penetrate or impair the blood-brain barrier. Evidence from preclinical animal studies, particularly in rodents and zebrafish, indicates that these substances can trigger a cascade of harmful effects such as oxidative stress, inflammatory responses, mitochondrial dysfunction, endocrine disturbances, and epigenetic modifications. The onset and course of neurodegenerative illnesses, such as Parkinson's disease, Alzheimer's disease, and amyotrophic lateral sclerosis (ALS), are also significantly influenced by these pathogenic mechanisms. Review compiles and critically analyses the existing animal research to explore how plastic-associated neurotoxicity may contribute to neurodegeneration. We also stress the importance of exposure levels and developmental timing, explore the wider implications of these findings to human health, and address present limitations in experimental models. To reduce the neurological dangers associated with plastic pollution, future research, public health initiatives, and regulatory frameworks must be guided by a better knowledge of these molecular processes.

Keywords: Neurotoxicity, Plastic exposure, Neurodegenerative diseases, Animal models, Mechanisms of toxicity.

INTRODUCTION

The extensive usage of plastics in contemporary life has raised serious concerns about the environment and human health. From food containers and packaging materials to electronics and medical equipment, plastics are omnipresent, resulting in continuous and often unavoidable human exposure. As plastic products degrade, they release microplastics, nano plastics, and a variety of chemical additives into the environment. These chemicals, in particular bisphenol A, phthalates, polybrominated diphenyl ethers, styrene, and plasticizers, have been found in human tissues such as blood, urine, placenta, and even the brain. They are also known to leak into food, water, and air.[1]

Concern over the possible neurological effects of these compounds linked to plastic has grown in recent studies. Many of these substances can penetrate the blood-brain barrier (BBB) or compromise its integrity because they are lipophilic, enabling direct contact with neural tissue.[2] This is particularly critical during early development, when the nervous system is still forming and is highly sensitive to environmental disruptions. However, emerging evidence suggests that plastic exposure is not limited to developmental toxicity it may also contribute to the development of neurodegenerative illnesses such amyotrophic lateral sclerosis (ALS), Parkinson's disease (PD), and Alzheimer's disease (AD).[3,4]

Animal studies have been instrumental in uncovering the mechanistic pathways through which plastic-associated chemicals exert their effects on the nervous system. These include the induction of oxidative stress, neuroinflammation, mitochondrial dysfunction, endocrine disruption, epigenetic alterations, and neurotransmitter system dysregulation[5,6]. For instance, BPA and certain phthalates mimic hormones like estrogen and thyroid hormones, disrupting critical neurodevelopmental signalling[7]. PBDEs and styrene are known to produce reactive oxygen species (ROS), impair mitochondrial function, and activate microglia, leading to chronic inflammation pathological features shared with many neurodegenerative conditions[8].

Preclinical models such as rodents and zebrafish have demonstrated behavioural and cognitive impairments following exposure to these compounds, along with structural and molecular changes in brain regions like the hippocampus, prefrontal cortex, and substantia nigra[9,10]. These studies offer important insights into how long-term or developmental exposure to plastics might increase susceptibility to neurological disorders later in life. Despite increasing evidence, many questions remain regarding the dose-response relationships, combined effects of multiple plastic components, and relevance to human pathophysiology. Moreover, regulatory frameworks have yet to fully account for the neurotoxic potential of plastic-derived chemicals, especially in the context of chronic, low-dose exposure[11].

This review aims to consolidate current knowledge on the neurotoxic effects of plastics using evidence from animal models, with a focus on mechanisms that may link plastic exposure to the initiation and progression of neurodegenerative diseases. By highlighting both experimental findings and mechanistic pathways, we hope to inform future research, risk assessment, and policy development to mitigate the potential neurological impact of plastic pollution.

Types of plastics

Epoxy resins and polycarbonate plastics are two common products made with the synthetic organic chemical bisphenol A. These substances are frequently found in the linings of canned products, baby bottles, and containers for food and drink. BPA is a recognized endocrine-disrupting chemical (EDC) that can disrupt hormonal signalling and mimic estrogen. Because BPA is lipophilic, it can penetrate the blood-brain barrier and directly impact neural tissues. Exposure to BPA during important windows of brain development has been linked to altered synaptic formation, anxiety-like behaviours, and decreased learning and memory in animal models[12,13]. These results raise questions regarding its possible involvement in the development or aggravation of neurodegenerative diseases.

Phthalates, such as dibutyl phthalate (DBP) and di(2-ethylhexyl) phthalate (DEHP), are mainly employed as plasticizers to increase the flexibility and durability of polyvinyl chloride (PVC) and other plastics. Consumer goods including toys, flooring materials, medical tubing, and personal care products like lotions and shampoos frequently contain them. Additionally, phthalates are strong endocrine disruptors that can interfere with the signalling of thyroid hormones and androgens[14]. According to research on animals, both short-term and long-term exposure to phthalates causes neurodevelopmental abnormalities, such as impaired cognitive function, altered dopaminergic transmission, and structural abnormalities in the hippocampus[15,16]. These effects are more noticeable during the early stages, which may indicate a connection between exposure to phthalates and a higher risk of developing neurological illnesses.

Polystyrene is a lightweight, rigid plastic used extensively in disposable containers, insulation, and packaging materials. Its monomer, styrene, can leach into food or volatilize into indoor air, leading to potential human exposure. Styrene is classified as a possible human carcinogen and has demonstrated neurotoxic effects in multiple animal studies[17]. Exposure to styrene or polystyrene micro/nanoplastics has been linked to oxidative stress, inflammation, aberrant behaviour, and motor deficits in rats and aquatic models[18,19]. Reactive oxygen species (ROS) buildup, mitochondrial damage, and glial cell activation are hypothesized to be the causes of these consequences; these processes are common to many neurodegenerative disease pathways.

One of the most extensively produced plastics in the world, polyvinyl chloride (PVC) is utilized in consumer items, medical equipment, and building materials. PVC is frequently mixed with plasticizers, mostly phthalates, which are not chemically bonded and can leak into the environment, to increase its flexibility[20]. Despite PVC's apparent inertness, the plasticizers it contains are extremely harmful to human health. In experimental models, these chemicals have been linked to developmental neurotoxicity, neurobehavioral alterations, and hormone disruption[21]. Research has indicated that early-life exposure to PVC-derived plasticizers may contribute to the risk of neurodegenerative diseases by causing cognitive impairments, altered neurotransmitter systems, and alterations in brain morphology[22,23].

A class of flame retardants known as polybrominated diphenyl ethers is added to a wide range of plastic-based goods, such as construction materials, electronics, and upholstered furniture. These are persistent organic pollutants (POPs), which have been found in human blood, breast milk, and even the developing fetal brain[24]. They bioaccumulate in tissues that are high in fat. Because PBDEs can pass through the placenta and the blood-brain barrier, there is worry about how they may affect neurotoxicity in both adults and children. Exposure to PBDEs has been associated in animal studies with neuroinflammation, oxidative damage, impaired thyroid hormone regulation, and learning and memory deficits[25]. These processes are similar to those linked to neurodegenerative illnesses including Parkinson's and Alzheimer's, underscoring PBDEs as environmental risk factors for neurological conditions.

Animal Models Utilized Mice and rats were frequently used to assess behavioral changes, cognitive functions, and biochemical markers associated with neurodegeneration. Fish Models: Zebrafish (Danio rerio) were utilized due to their transparent embryos and rapid development, allowing for real-time observation of neurodevelopmental effects. Invertebrates: Species like Caenorhabditis elegans provided insights into fundamental neurotoxic mechanisms due to their well-mapped neural circuits.[26]

Predominantly polystyrene microplastics and nanoplastics, with some studies examining polyethylene and polypropylene particles.Particle Sizes: Ranged from nanometers (<100nm) to micrometers (>1µm), affecting their ability to cross biological barriers. Exposure Routes: Included oral ingestion, injection, and environmental exposure through contaminated water or food sources. Varied across studies, with some employing acute high-dose exposures and others chronic low-dose exposures to mimic environmental condition[27]. Tests such as the Morris water maze and open field tests in rodents Novel Tank Diving Test Light/Dark Preference Test and T-Maze Test in zebrafish assessed cognitive and motor functions. Measurement of oxidative stress markers, neurotransmitter levels, and enzyme activities provided insights into molecular disruptions. Histological Examinations: Brain tissues were examined for structural changes, inflammation, and neuronal loss. Molecular techniques: Gene expression analyses and protein assays identified alterations in pathways related to neurodegeneration.[28]

Routes of Exposure to Plastic-Associated Chemicals

The most frequent and important way to be exposed to toxins linked to plastic is by oral ingestion. When plastics are heated or damaged, they can release microplastics and additives including bisphenol A (BPA), phthalates, and PBDEs into food and drink[29,30]. Cans lined with epoxy resins, plastic containers, food packaging materials, and even drinking water contain these chemicals[31]. Given the great absorption capacity of the gastrointestinal tract, dietary consumption is particularly problematic. After being consumed, these substances have the potential to enter the bloodstream and either penetrate or disrupt the blood-brain barrier (BBB), which could result in neurotoxic effects on the central nervous system[32].

Inhalation of airborne plastic particles and volatile organic compounds (VOCs) is another important route, particularly in indoor environments where synthetic materials, furnishings, and electronic devices are common. Styrene, a monomer of polystyrene, is a known inhalation hazard and can volatilize into air from consumer products. Inhaled microplastics and PBDE-laden dust particles can deposit in the lungs, translocate into the bloodstream, and potentially reach the brain[33]. Animal studies have shown that inhalation of nano plastics may trigger neuroinflammation and oxidative stress, similar to ingestion-based exposure[34].

Even though it's usually regarded as a less significant route than eating or inhalation, dermal absorption can nonetheless add to the body's exposure to plastic additives. This is especially true when using lotions, cosmetics, and personal care items that include BPA derivatives and phthalates[35]. The skin, especially when damaged or exposed for prolonged periods, can absorb lipophilic substances. While dermal absorption is less efficient for reaching the brain, it can contribute to systemic endocrine disruption, which indirectly affects neurodevelopment and brain function[36].

Because of the growing brain's increased susceptibility, placental and breast milk transfer poses a serious risk. According to research, toxins linked to plastic can penetrate the placental barrier and expose the fetus at crucial stages of neurodevelopment[37]. Cord blood, amniotic fluid, and placental tissue have all been found to contain BPA, phthalates, and PBDEs[38]. In animal models, these exposures are linked to long-lasting neurodevelopmental alterations, such as disrupted neural connections and learning impairment. As lipophilic pollutants build up in breast milk, postnatal exposure can increase for infants[39].

In some groups, occupational and medical exposure can be substantial. PVC-made IV bags, tubing, and catheters are examples of medical equipment that frequently include phthalates like DEHP, which can seep into intravenous fluids, particularly in neonatal intensive care units[40]. Bypassing natural barriers, this method delivers plastic compounds straight into the circulation, potentially resulting in high systemic dosages. Workers in the electronics, recycling, and plastics manufacturing sectors may also be exposed to high concentrations of PVC fumes, PBDEs, and styrene, which increases the risk of neurological and endocrine consequences[41,42].

Animal Models in Plastic Neurotoxicity Research

Understanding the neurotoxic consequences of chemicals associated with plastic, such as phthalates, bisphenol A (BPA), polybrominated diphenyl ethers (PBDEs), and styrene, requires the use of animal models. Because of their neurological resemblance to humans and the availability of disease-relevant transgenic strains, rodents-particularly mice and rats-are frequently used[43,44]. The Morris water maze and rotarod are two behavioural tests used to evaluate cognitive and motor deficits after chemical exposure. Furthermore, transgenic models such as APP/PS1 (Alzheimer's disease) and SOD1-G93A (ALS) shed light on how plastics worsen the course of the disease by causing neuroinflammation, mitochondrial dysfunction, and oxidative stress[45,46]. Histological and molecular analyses further reveal alterations in neuronal integrity and inflammation, supporting the mechanistic links between plastic exposure and neurodegeneration. These models are indispensable for identifying environmental risks and testing preventive or therapeutic strategies in neurodegenerative disease research.

Plastic-Associated Chemicals and Their Role in Alzheimer's Disease: Mechanisms and Evidence

The most common neurodegenerative disease, Alzheimer's disease (AD), is becoming more and more linked to environmental exposures, especially to endocrine-disrupting chemicals generated from plastic, like polybrominated diphenyl ethers, bisphenol A and phthalates. Commonly present in epoxy resins and polycarbonate plastics, bisphenol A functions as a xenoestrogen and interferes with the brain's natural estrogen receptor signalling. Hippocampal function has been demonstrated to be hampered by BPA's disruption of estrogenic pathways, which are essential for synaptic plasticity and memory. Additionally, BPA causes mitochondrial malfunction and oxidative stress, both of which lead to neuronal death. The two neuropathological characteristics of AD, tau hyperphosphorylation and increased amyloid-beta (Aβ) formation, have also been linked to BPA exposure, most likely through increased β-secretase activity and neuroinflammatory reactions.[47] Peroxisome proliferator-activated receptors (PPARs), which are important in lipid metabolism and neuronal maintenance, have also been demonstrated to be disrupted by phthalates, such as di-(2-ethylhexyl) phthalate (DEHP) and dibutyl phthalate (DBP), which are employed as plasticizers in PVC and other polymers. These substances contribute to persistent neuroinflammation and neuronal injury by encouraging microglial activation and the release of pro-inflammatory cytokines (such as TNF-α and IL-6)[48]. In rat models, prolonged exposure to phthalates has been linked to elevated expression of genes related to Aβand deficiencies in spatial memory[49]. Furthermore, PBDEs, which replace thyroid hormones as flame retardants in consumer electronics and plastics, mimic thyroid hormones and competitively block their signalling. This interferes with adult neurogenesis and brain growth[50]. In addition, PBDEs cause oxidative stress, change intracellular calcium levels, and worsen tau and Aβpathogenesis[51,52]. The need for more research into plastic-related neurotoxicity is highlighted by the fact that these chemicals collectively contribute to AD pathogenesis through interrelated processes involving oxidative stress, hormone disturbance, neuroinflammation, and interference with protein aggregation.

Plastic-Associated Chemicals and Their Role in Parkinsonism: Mechanisms and Evidence

Progressive degradation of dopaminergic neurons in the substantia nigra is a hallmark of Parkinsonism, especially Parkinson's disease (PD), which results in motor dysfunctions such bradykinesia, tremor, and rigidity. Styrene, polybrominated diphenyl ethers, phthalates, and bisphenol A are among the plastic-associated chemicals that have been linked in recent research to the development and progression of Parkinsonism through mechanisms involving oxidative stress, mitochondrial dysfunction, neuroinflammation, and disrupted neurotransmission. Styrene oxide, a reactive intermediate that can pass across the blood-brain barrier and build up in brain tissues, is produced during the metabolism of styrene, a volatile chemical molecule used to make polystyrene plastics[53]. According to studies, long-term exposure to styrene causes mitochondrial dysfunction and oxidative damage, especially in dopaminergic neurons, which results in neuronal death and motor impairment resembling Parkinson's disease[54]. Further supporting its function in dopaminergic neurodegeneration, styrene exposure has also been connected to elevated dopamine turnover and depletion of dopamine reserves in the striatum[55].

PBDEs, widely used as flame retardants in plastics and electronics, are lipophilic and bioaccumulate in neural tissues. They induce oxidative stress, disrupt calcium homeostasis, and impair mitochondrial function, all of which are mechanisms implicated in PD. PBDEs can also alter the expression of genes involved in dopamine synthesis and metabolism, including tyrosine hydroxylase and dopamine transporter, potentially leading to dopamine dysregulation and nigrostriatal damage.

Phthalates such as di-(2-ethylhexyl) phthalate are plasticizers that leach from consumer products and are known to disrupt endocrine and neurological functions. DEHP and its metabolites have been shown to activate microglia and increase neuroinflammatory cytokines (e.g., TNF-α, IL-1β), which are central to dopaminergic neurotoxicity[56]. Moreover, phthalate exposure can impair mitochondrial membrane potential and promote apoptosis of dopaminergic neurons, exacerbating PD-like pathology in animal models.

Bisphenol A while more commonly associated with Alzheimer's-type neurotoxicity, has also shown effects relevant to Parkinsonism. BPA alters dopaminergic signalling, increases oxidative stress, and reduces dopamine levels in the midbrain. Prenatal or chronic exposure to BPA may sensitize neurons to further environmental stressors, thereby increasing susceptibility to PD later in life.

In sum, plastic-associated chemicals such as styrene, PBDEs, phthalates, and BPA contribute to Parkinsonism through shared pathways of oxidative stress, dopamine depletion, inflammation, and mitochondrial dysfunction, underscoring the environmental risk these compounds pose to dopaminergic systems and neurodegenerative disease progression.

Plastic-Associated Chemicals and Their Role in Amyotrophic Lateral Sclerosis (ALS): Mechanisms and Evidence

Muscle atrophy, paralysis, and eventually death are the outcomes of amyotrophic lateral sclerosis (ALS), a progressive neurodegenerative disease marked by the selective loss of upper and lower motor neurons. Environmental risk factors, such as plastic-associated chemicals like bisphenol A, phthalates, polybrominated diphenyl ethers, polychlorinated biphenyls (PCBs) (sometimes found in materials containing plastic), and vinyl chloride monomer (VCM) used in the production of PVC, have drawn more attention even though the majority of ALS cases are sporadic. Through processes like oxidative stress, glutamate excitotoxicity, neuroinflammation, and mitochondrial dysfunction, these substances are believed to play a role in the pathophysiology of ALS.

Widely used in plastics and food containers, bisphenol A is an endocrine disruptor that has been demonstrated to change glutamate signal ling and raise oxidative stress, two factors linked to the pathophysiology of ALS. By interfering with astrocytic glutamate uptake and raising synaptic glutamate levels, BPA can cause excitotoxic damage. This overstimulation of NMDA receptors causes calcium influx and neuronal death. Additionally, BPA increases the production of reactive oxygen species (ROS) and modifies mitochondrial function, both of which increase neuronal sensitivity, especially in motor neurons.

Numerous consumer products contain phthalates as plasticizers, such as diethyl hexyl phthalate (DEHP). Chronic exposure to phthalates has been associated with two important characteristics seen in tissues affected by ALS: mitochondrial malfunction and decreased autophagy in neuronal cells. Phthalates also contribute to non-cell-autonomous mechanisms of motor neuron degeneration by inducing microglial activation and neuroinflammatory cascades.

PBDEs, flame retardants used in plastic-containing electronics and furniture, have demonstrated neurotoxic effects that include oxidative stress, disruption of calcium homeostasis, and altered expression of genes involved in synaptic integrity and neuronal survival. In animal models, PBDE exposure has led to motor coordination deficits and motor neuron loss, mimicking ALS-like symptoms.

Furthermore, vinyl chloride, a precursor to PVC plastic, has long been associated with neurological symptoms in industrial workers. Long-term exposure to vinyl chloride may be linked to an increased prevalence of ALS, according to epidemiological research. This could be because vinyl chloride's neurotoxic metabolites disrupt mitochondrial dynamics and axonal transport[57]. Similarly, PCBs, though now banned, persist in the environment and are often found in older plastic components; they disrupt motor neuron function by interfering with calcium signalling, increasing ROS, and impairing axonal integrity.

Collectively, these chemicals share a convergence of toxicological mechanisms oxidative damage, glutamate excitotoxicity, and neuroinflammation that are central to ALS pathophysiology. While direct causality in humans remains under investigation, both in vivo and in vitro evidence strongly suggests that plastic-associated compounds are capable of initiating or exacerbating motor neuron degeneration characteristic of ALS.

Plastic-Associated Chemicals and Their Neurotoxic Effects in Animal Models

Chemical	Animal model	Neurological Outcomes	Mechanistic Pathways	Related Neurodegenerative Disease
Bisphenol A (BPA)	APP/PS1 mice, C57BL/6 mice	Memory impairment, Aβaccumulation	Oxidative stress, A aggregation, synaptic loss	Alzheimer's Disease[58]
DEHP (Phthalate)	Sprague-Dawley rats	Motor dysfunction, cognitive deficits	Mitochondrial dysfunction, apoptosis, inflammation	Parkinsonism, Alzheimer's Disease[59]
PBDEs	Wistar rats, mice	Motor deficits, learning impairment	ROS generation, calcium dysregulation, neuroinflammation	ALS, Parkinsonism[60]
Vinyl chloride	Rat models	Motor neuron loss, neuromuscular deficits	Mitochondrial dysfunction, axonal transport disruption	Amyotrophic Lateral Sclerosis (ALS)[61]
Styrene	Mice, rats	Impaired memory and coordination	Lipid peroxidation, oxidative damage to neurons	General neurodegeneration[62]

Summary of Plastic-Related Chemicals and Associated Neurotoxicity in Animal Models

Sr. No	Plastic Chemical	Animal Model	Exposure Dose & Duration	Observed Neurotoxic Outcomes
1	Bisphenol A (BPA)	C57BL/6 mice	1 mg/kg/day orally throughout life	Impaired memory, hippocampal apoptosis[63]
2	BPA	Zebrafish embryos	0.1–10 mg/L during embryonic development	Axon pathfinding defects[64]
3	BPA	Rats	0.1-1 mg/kg/day orally during gestation and lactation	Altered locomotor activity, learning deficits[65]
4	Di(2-ethylhexyl) phthalate (DEHP)	Mice	0.2-200 mg/kg/day orally for 28 days	Elevated anxiety behaviour, impaired recognition memory[66]
5	Polystyrene Nanoparticles (PS-NPs)	Zebrafish embryos	0.1-10 mg/L during embryonic development	Developmental toxicity, neuronal loss, behavioural abnormalities[67]
6	Dibutyl Phthalate (DBP)	Rats	10 μg/kg/day orally during gestation	Decreased grooming behaviour in male offspring[68]
7	Diisononyl Phthalate (DINP)	Mice	0.2-200 mg/kg/day for 28 days	Cognitive deficits, anxiety-like behavior[69]
8	Polyethylene Terephthalate (PET) Microplastics	Mice	25 mg/kg/day orally for 180 days	Neuroinflammation, oxidative stress, behavioural changes[70]
9	Bisphenol S (BPS)	Zebrafish larvae	0.3 and 3 mg/L during early life stages	Altered catalase activity, behavioural changes[71]
7	Butyl Benzyl Phthalate (BBP)	Rats	270-2100 mg/kg/day orally from gestation day 5 to 20	Increased liver and kidney weights, liver enzyme alterations[72]
11	Bisphenol F (BPF)	Mice	0.1–10 mg/kg/day orally during perinatal period	Neurodevelopmental impairments in male offspring[73]
12	Tetrabromo bisphenol A (TBBPA)	Wister Rats	0–3000 mg/kg/day orally throughout life	Neurobehavioral effects, nephrotoxicity at higher doses[74]
13	Dimethyl Phthalate (DMP)	Zebrafish larvae	0.1–10 mg/L during embryonic development	Decreased survival and hatching rates, neurodevelopmental toxicity[75]
14	Diisodecyl Phthalate (DIDP)	Mice	0.1–100 mg/kg/day orally during gestation	Learning and memory impairments, depressive-like behavior[76]
15	Polyvinyl Chloride (PVC) Particulates	Rats	25 mg/kg/day orally for 28 days	Neuroinflammation, oxidative stress, behavioural changes[77]
16	Nanoplastics (unspecified)	Zebrafish larvae	0.1–10 mg/L during early development	Disrupted expression of neurodevelopmental genes, impaired swimming ability[78]
17	Phthalic Acid	Rats	500 mg/kg orally	Oxidative DNA damage, increased 8-OHdG levels in brain tissue[79]
18	PVC Fumes	Rats	Inhalation exposure (concentration and duration not specified)	Dopaminergic neurodegeneration, decreased dopamine levels in striatum[80]
19	Polybrominated Diphenyl Ethers (PBDEs)	Mice	0.1–10 mg/kg/day orally during gestation and lactation	Memory loss, neuroinflammation, altered NMDA receptor expression[81]
20	Nonylphenol	Rats	50mg/kg/day orally for 30 days	Hormonal imbalance, increased anxiety-like behavior[82]
21	polystyrene	Mice	4 weeks	obstruct cerebral blood vessels, leading to impaired motor skills and memory in mice[83]
22	Polystyrene nanoplastics	Zebrafish embryos	100–400 mg/L96 hours	Exposure aggravated ammonia-induced neurotoxic effects, leading to developmental defects and impaired motor neuron development[84]
23	Polystyrene microplastics	Zebrafish	25 and 250 μg/L 40 days	Exposure induced depression-like behavior via neuroinflammation and circadian rhythm disruption[85]
24	Polystyrene microplastics	BALB/c mice	0.01,0.1,1 mg/day 4 weeks	Chronic exposure led to neurobehavioral changes, including decreased locomotor activity and memory impairment[86]
25	Photoaged polystyrene microplastics	Caenorhabditis elegans	0.1–100 μg/L Not specified	Induced neurotoxicity associated with damage to serotonergic, glutamatergic, dopaminergic, and GABAergic neuronal systems[87]

Research Gaps and Future Directions

There are still a number of study gaps despite mounting evidence that plastic-associated compounds cause neurodegeneration[88]. The majority of research used high-dose or acute exposures, which might not be representative of low-dose human exposure in the actual world. Furthermore, little is known about combination toxicity, the combined effects of several plasticizers. There is limited exploration into sex-specific responses, developmental timing, and transgenerational effects. Moreover, current animal models often lack the complexity of human neurodegenerative diseases, calling for more translational models, including humanized or stem cell-based systems[89]. Mechanistic studies should also focus on linking plastic exposure to early biomarkers of disease, such as synaptic proteins or neuroinflammatory markers. Future research should integrate multi-omics approaches and advanced imaging techniques to unravel subtle but progressive changes induced by plastics, ultimately aiding in early diagnosis and preventive interventions.

Implications for Human Health and Policy

Animal studies provide crucial insights into how plastic-associated chemicals like BPA, phthalates, and PBDEs may contribute to neurodegenerative diseases in humans. These models draw attention to processes that are also seen in human neuropathology, such as oxidative stress, inflammation, and synaptic dysfunction. However, careful evaluation of exposure routes, dosages, and chronicity is necessary when extrapolating results to humans. Regulatory bodies, including the EU and US EPA, have begun restricting hazardous plasticizers and promoting safer alternatives, such as bio-based or non-toxic plasticizers[90]. Yet, regulation lags behind emerging evidence. Enhancing public health awareness is essential, particularly around minimizing exposure through food packaging, personal care products, and household plastics. Behavioural shifts such as avoiding microwaving plastics, using glass containers, and reducing plastic waste can reduce cumulative risk. Public education, coupled with stronger regulation and investment in safer alternatives, is vital for protecting neurological health.

CONCLUSION

The increasing amount of data from animal models highlights how important plastic-associated compounds like BPA, phthalates, PBDEs, and styrene are in the development of neurodegenerative diseases. These chemicals cause mitochondrial malfunction, oxidative stress, neuroinflammation, and synaptic impairments all of which are frequently linked to ALS, Parkinson's disease, and Alzheimer's disease. Even while studies on animals offer important mechanistic insights, further research is necessary to apply these findings to human health, particularly in situations when exposure occurs in the real world. To reduce the neurotoxic effects of plastics and protect long-term neurological health, it is imperative to strengthen regulatory measures, advance research using human-relevant models, and increase public awareness.

ACKNOWLEDGMENT

The authors sincerely acknowledge the contributions of researchers whose work has been cited in this review and gratefully acknowledge the invaluable guidance and continuous support of Dr. Praveen Kumar. We extend our gratitude to Raghavendra Institute of Pharmaceutical Education and Research (RIPER)-Autonomous for providing the necessary support and resources to conduct this study. Special thanks to colleagues and peers who offered valuable feedback during the preparation of this manuscript.

Conflict of Interest

The authors declare no conflict of interest.

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