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Magnesium oxide nanoparticles administered orally promote degenerative changes and dysfunctioning in the brain

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Magnesium oxide nanoparticles (MgO NPs) have shown immense potential due to their unique and versatile properties useful for various biological applications. However, concerns about their potential toxicity to living organisms and the environment invite thorough assessment of their safety and long-term effects. Here, we examined the *in vivo* effects of MgO NPs on the brain in order to assess their potential harm. The result revealed that MgO NPs when administered orally, induced degenerative changes in brain regions like the cerebrum, cerebral cortex, medulla oblongata, and olfactory bulb. A reduction in granular, molecular, Purkinje, glial, and pyramidal cells, as well as degeneration, inflammation, and induction of pyknosis of nuclei in mitral cells and vacuolation in the granular and plexiform layers, are among these alterations. ALP, SGOT, SGPT, AChE, GS, Mg^{2+}- ATPases, Ca^{+2}- ATPases, GPx, SOD, and catalase activities declined by MgO NPs, while those of ACP, GD, and Na^{+}-K^{+}- ATPases activities elevated. Antioxidant concentrations, specifically TBARS, increased while reduced glutathione decreased. Neurotransmitters like glutamate levels were elevated, whereas those of dopamine, serotonin, and GABA declined. As a result, the study provides a glimpse into the adverse effects of MgO NPs, demonstrating their potential risk in medicine and various applications, as the alterations caused by these NPs would not only impede regular brain activity, causing neurological disorders but may also disrupt the entire organ system.

Keywords: Antioxidants, Gavaging, Neurotoxicity, Neurotransmitters

Magnesium oxide nanoparticles (MgO NPs) have emerged as the principal entity of clinical, agricultural, and environmental domains due to their unique properties. They are known as a potential candidate for meeting the ends of various problems by contributing to biomedical applications[1]. MgO, despite having a wide range of applications lacks experimental shreds of evidence to showcase their effectiveness. All the NPs used in industries including, MgO find their way into the human body via inhalation, skin, and oral route. Moreover, it is said that most health hazards occur due to its entry into the GI tract[2] via accidental ingestion through various sources, contact with nanostructures, hand-to-mouth contact while eating or along with drinking water, and food contaminated with NPs.

Numerous studies have demonstrated that MgO NPs have a variety of biological applications in cellular studies. MgO NPs effectively bind human serum albumin, mediating apoptosis in cancer cell lines through ROS induction, demonstrating their potential in cancer treatment without affecting proteins or normal cells[1]. Low concentration of MgO NPs can induce antioxidant, antiapoptotic, and antidiabetic effects in pancreatic islets, potentially benefiting islet transplantation procedures[3]. Acute administration shows more effective anticonvulsive effects than its conventional form[4]. MgO has negligible deleterious effects on oxidative stress and gene expression, suggesting that it has a wide range of potential uses in nanomedicine[5]. Conversely, some reports show its cytotoxicity toward human umbilical vein and human cardiac microvascular endothelial cells[6]. Alongside, studies have also provided evidence about the long-term effects of MgO NPs causing allergenicity, mutagenicity, and embryotoxicity in humans[7]. Additionally, the cytotoxicity of MgO NPs in human cancer cell lines caused oxidative stress triggering cancerous growth[5].

The studies have revealed that the lower concentrations of MgO NPs are safe to be used for water purification, encapsulated drugs, and other desired applications[5].On the other hand, these NPs showed dose-dependent pulmonary toxicity in rats

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and a reduction in total antioxidant capacity in the serum after acute intratracheal instillation[2]. Acute exposure to high doses of MgO caused DNA damage, biochemical alterations, oxidative stress, and accumulation in liver and kidney tissues[5]. Complementing the previous study reports also showed the proliferation of bile ductules, congestion in some regions of the liver sinusoids, and apoptotic cells in Wistar rats[8].

The review of the literature reveals limited research on the toxicity of MgO NPs. With a handful of higher animals, the majority of investigations are restricted to bacterial systems and various cell lines. The understanding that MgO NPs are safe has led to their widespread use in various industrial applications. However, studies on the impact of MgO NPs on brain function are lacking. Hence, in this study, we looked into how MgO NPs affect the brain when they enter the body through different routes.

Materials and Methods

Synthesis and characterization of MgO NPs

The MgO NPs were synthesized using the chemical precipitation approach, with minor modifications, by using water as a suspension medium and sodium carbonate as a precipitation agent[9]. Magnesium nitrate was dissolved in sodium carbonate solution and the obtained precipitate was thoroughly cleaned of any impurities using distilled water before being dried at 100°C. Further, they were calcined at different temperatures (400, 500 and 600°C) in a muffle furnace keeping them for 1 h at each temperature regimen with intermittent grinding.

The prepared NPs were characterized using SEM (Carl-Zeiss), TEM (Philips CM200), XRD (Rigaku), FTIR (Perkin Elmer BX), and Zeta sizer (Zeta sizer Ver. 6.32, serial number -MAL1037088, Malvern Instruments Ltd). The specific surface area was measured using the Saunter formula and density was recorded.

Exposure of mice to MgO NPs

Maintenance of animals

The Swiss albino mice of 20-35 g were housed in polypropylene cages. They were fed a conventional pellet diet (Hindustan Lever, Bangalore, India) and kept in ambient laboratory settings with a 12 h light/dark cycle and free access to water. Ethical approval was obtained for using mice from the Institutional Animal Ethics Committee (Certificate No. 105/C), based on the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines. The animals were maintained at the Animal House facility of the Department of Zoology, Goa University.

Preparation of nanoparticle suspensions

The NPs were suspended in distilled water and dispersed using a sonicator (BRANSON Digital Sniffier) at 30% amplitude for 10 min. Different concentrations (6, 12 and 24 mg/kg) were prepared for chronic exposure based on the LD_{50} values (1315 mg/kg).

Chronic treatment

Animals were divided into four groups, each group comprising 5 animals. The groups were divided into Control, Experimental 1, 2 and 3. Control mice were fed with distilled water and the experimental mice with NPs suspended in distilled water with different concentrations (viz., 6, 12 and 24 mg/kg body wt. of mice), respectively for each experimental set. The animals were orally gavaged with NPs daily once in the morning, continuously for 30 days. After the completion of the time interval, the animals were euthanized by cervical dislocation.

Histological examination

The isolated tissues were processed carefully and gently by washing 3-4 times in mammalian saline to get rid of any impurities and blood clots. Tissues were then fixed with formalin (10%) and were embedded in paraffin blocks, and then sliced into 5 µM thick slices and stained with hematoxylin-eosin using a standard protocol[10]. The bright-field images were taken using an Olympus BX51 microscope, equipped with a ProgRes® Capture Pro 2.8.8 JENOPTIK Camera.

Biochemical estimation

Enzymes

The enzyme activities were assayed for analyzing any alterations using enzyme assay kits viz. Alkaline phosphatase (ALP, Product no-ALP3166, Crest Biosystems), acid phosphatase (ACP, Product no-ACP2125A, Crest Biosystems no), Serum glutamic oxaloacetic transaminase (SGOT, Product no-GOT2160C, Crest Biosystems), serum glutamic-pyruvic transaminase (SGPT, Product no-GPT2178, Crest Biosystems), acetylcholinesterase kit (Molecular probes, Invitrogen detection technologies), ATPases[11], glutamine synthetase (GS) and glutamate dehydrogenase (GDH)[12].

Neurotransmitters

Neurotransmitters like serotonin (Product No-ELA-5061, USA) and dopamine (Product No-ElA-4824, USA), were assayed using an Elisa kit from DRG Diagnostics, with the help of Elisa Plate Reader (Analytical Technologies Ltd). Acetylcholine was

assayed using Acetyl choline kit (Molecular probes, Invitrogen detection technologies), and Glutamate and GABA were assayed spectrophotometrically using standard protocols[13].

Antioxidants and antioxidant enzymes

Thiobarbituric acid reactive substances, reduced glutathione, glutathione peroxidase, superoxide dismutase, and catalase were also estimated using standard protocols[14].

Statistical analysis

All experimental data are expressed as mean ± SE. Statistical analysis of the data obtained was analysed using Student's t-test (Graph pad Software, San Diego, CA) and one-way analysis of variance (ANOVA) using XLSTAT software. The criteria values $P \leq 0.05$ were considered as significant and $P \leq 0.001$ as highly significant.

Results

MgO NPs characterization

The MgO nanoparticles synthesized by the chemical precipitation method were 95% pure, white in colour with a specific surface area of ≥50 m^2/g and a density of 0.18 g/cm^3. The NP's average size was between 40-90 nm. Under SEM imaging NPs appeared as tiny crystallites of varying sizes having irregular shapes forming aggregations and TEM micrographs showed them as cuboidal and spherical-shaped structures that were homogenous without any observable pores (Fig. 1 A & B). The XRD analysis of the MgO NPs showed peaks at 2θ = 37.08°, 42.90°, 62.38°, 74.56° and 78.5° and FTIR spectra exhibited transmittance peaks at 440 cm^{-1} and 671 cm^{-1}, 883.4 cm^{-1}, 1435 cm^{-1}, 2356 cm^{-1} and 3649 cm^{-1} (Fig. 2A & B). The zeta potential of the NPs was –22.7 mV (Fig 2C).

Histological effects of MgO NPs

The normal architecture of the brain regions was compared with the ones administered with MgO NPs. The normal mice cerebellum showed three distinct layers viz., granular layer, molecular layer, and Purkinje layer. The cerebellum of the mice treated with MgO NPs showed a decline in the number and inflammation of granular cells along with degeneration and a decrease in the number of Purkinje

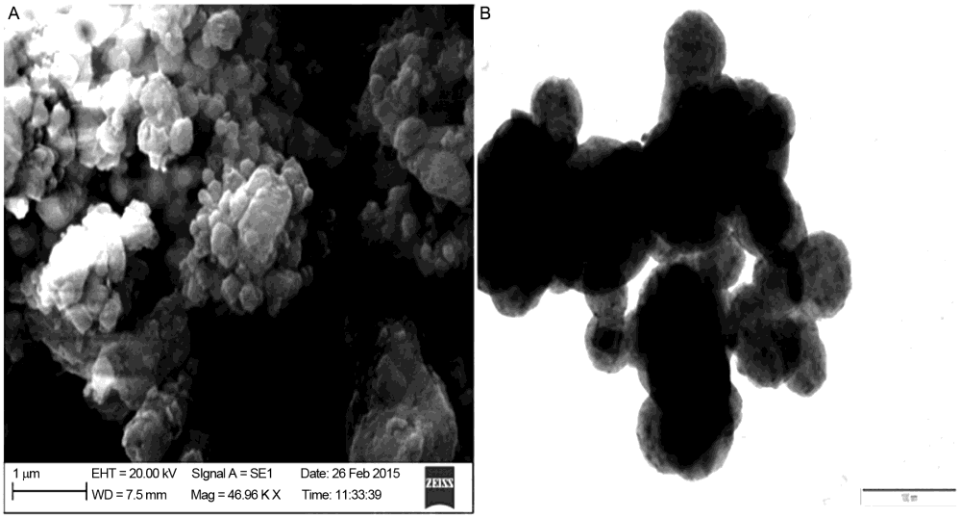

Fig. 1 — Electron microscopy of MgO NPs (A) SEM image (B) TEM image

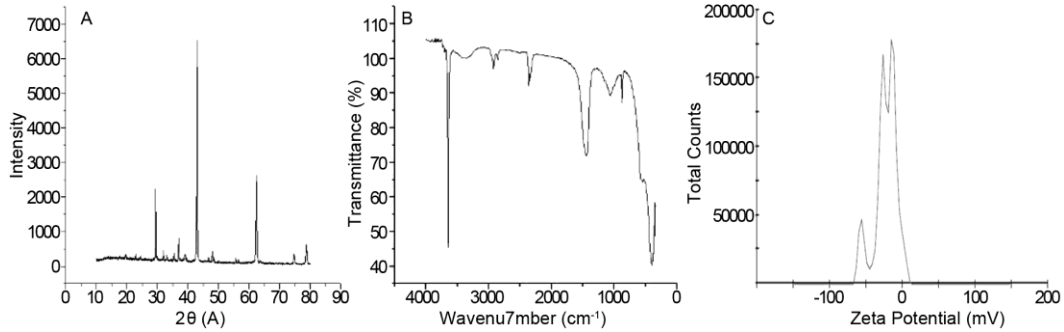

Fig. 2 — Spectral analysis of MgO NPs (A) XRD (B) FTIR; and (C) Zeta Potential

and molecular cells with Ca^{+2} deposits within them (Fig. 3A). The normal histological structure of the cerebral cortex (CC) shows a good number of glial cells and pyramidal cells with distinct and intact blood vessels and capillaries. The experimental CC of the mice showed a drop in the number of glial cells and pyramidal cells with degeneration. Some of the pyramidal cells also showed elongation of shape with inflammation and deposition of MgO NPs in neurons (Fig. 3B).

The medulla oblongata (MO) of the control mice showed well-defined nerve rootlets and nerve cells. Whereas the treated mice depicted inflammation in the nerve rootlets and fibres along with degeneration of nerve cells (Fig 3C). The normal architecture of the olfactory bulb (OB) exhibited an external granular layer containing granular cells, an internal plexiform layer, a mitral layer containing mitral cells, an internal plexiform layer, and an internal granular layer containing granular and mitral cells in a specific pattern. The mice gavaged with the MgO NPs also showed mitral cells but with dark pycnotic nuclei, and vacuolation in the granular and plexiform layer (Fig. 3D).

Enzymes

After 30 days of exposure to MgO NPs, the mice displayed a notable and dose-dependent rise in ACP (F=4-14.6, $P \leq 0.05$) and a decline in ALP (F=6-19.9, $P \leq 0.05$-0.001) activities in C, CC, MO and OB (Fig. 4A). The SGOT (F=15.4-51.8, $P \leq 0.001$) and SGPT (F=6.47-38.2, $P \leq 0.05$-0.001) activities diminished significantly and dose-dependently in these brain regions (Fig. 4B). Further, the AChE activity exhibited a significant and dose-dependent decrease (F=56.7-313.44, $P \leq 0.001$) and the GDH activity elevated significantly in C, CC, MO and OB (F=4.97-20.81, $P \leq 0.05$-0.001) (Fig. 4C). The GS activity dropped significantly in these brain regions (F= 43.06-94.57, $P \leq 0.001$) (Fig. 4D). The Mg^{2+}-ATPases activity decreased significantly and dose-dependently in C, CC, MO and OB (F=9.82-45.36, $P \leq 0.05$- 0.001) (Fig. 4E). The Ca^{+2}- ATPases activity also declined in CC, MO, and OB (F=10.69-37.99, $P \leq 0.05$-0.001), but did not show many variations in C (Fig. 4E). Further, the Na^{+}-K^{+}- ATPases activity showed significant elevation in these discrete brain regions (F=21-84, $P \leq 0.001$) (Fig. 4E).

Neurotransmitters

The mice given MgO NPs orally for 30 days demonstrated a dose-dependent and significant decrease in dopamine levels (F=3.3-60.2, $P \leq 0.05$-0.001) and serotonin levels in C, CC, MO, and OB (F=11-49.98, $P \leq 0.05$-0.001) (Fig. 4F). The glutamate levels increased significantly and dose-dependently (F=30.59-78.4, $P \leq 0.05$-0.001), but the GABA levels

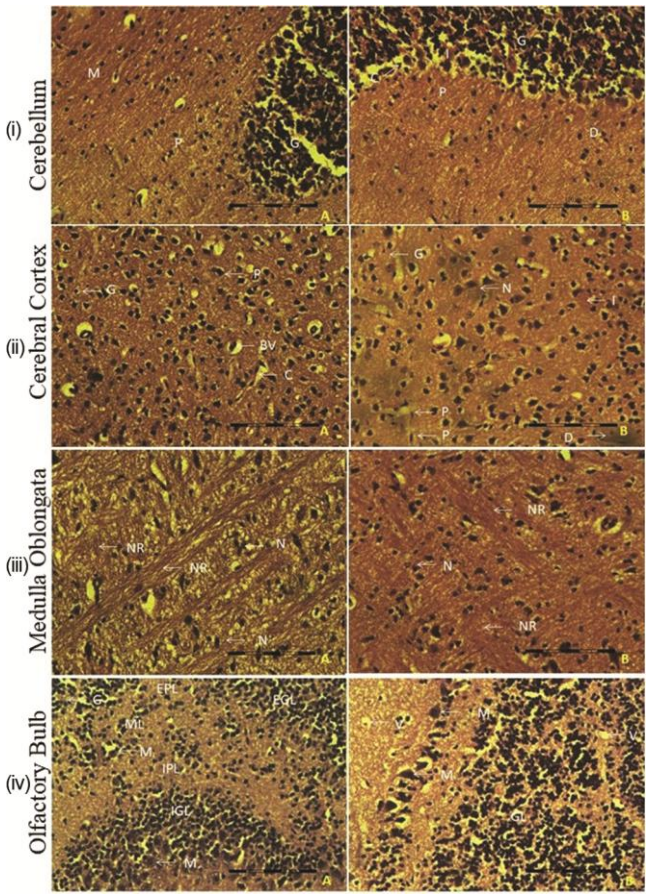

Fig. 3 — Chronic effects of MgO NPs on cerebellum A- Control showing granular layer (G), molecular layer (M) and Purkinje cell layer (P), B- Exposed to MgO NPs showed a decrease in the number of granular cells (G) and Inflammation (I) in the granular layer, degeneration (D) and decrease in the number of Purkinje (P) and molecular cells (M). Calcium deposition in the cells (C); Cerebral cortex A- Control showing glial cells (G), blood vessel (BV), capillaries (C) and Pyramidal cells (P),B- Exposed to MgO NPs showed a decrease in the number and degeneration of glial cells (G), a decrease in the number, elongation, and degeneration of pyramidal cells (P), inflammation of the tissue (I), deposition of NPs, inflammation of neurons (N); Medulla oblongata A- Control showing nerve rootlets (NR) and nerve cells (N), B- Exposed to MgO NPs showed inflammation in the nerve rootlets (NR) due to inflammation in fibers and degeneration of nerve cells (N); and Olfactory bulb A- Control external granular layer (EGL) containing granular cells (G), internal plexiform layer (IPL), mitral layer (ML) containing mitral cells (M), internal plexiform layer (IPL) and internal granular layer (IGL) containing granular (G) and mitral cells (M),B- Exposed to MgO NPs mitral cells with dark pyknotic nuclei (M), vacuoles in the granular and plexiform layer (v)

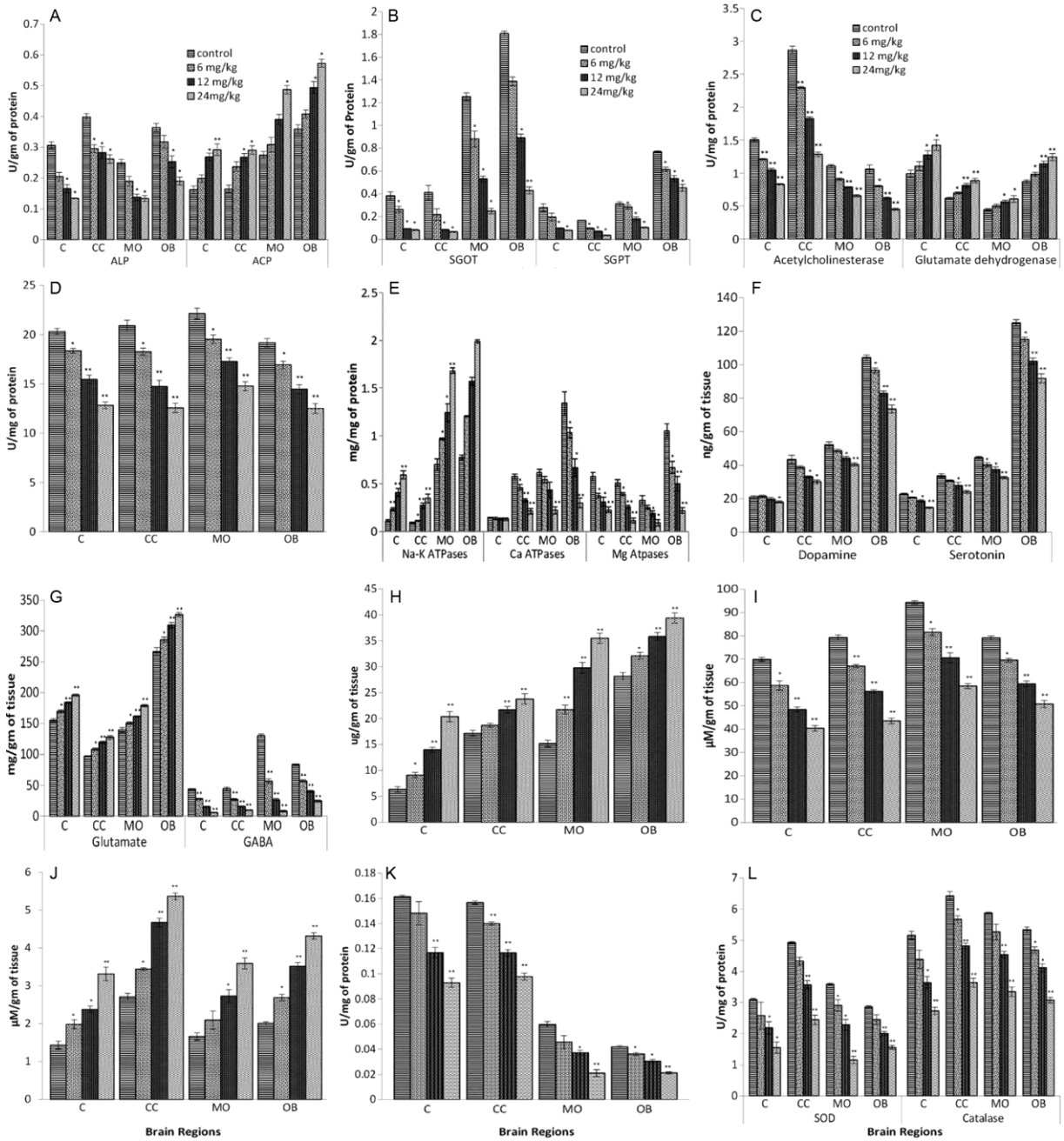

Fig. 4 — Chronic effects of MgO NPs on (A) ACP and ALP; (B) SGOT and SGPT; (C) Acetylcholinesterase and Glutamate dehydrogenase; (D) Glutamine synthetase; (E) Na+-K+, Ca+2- and Mg+2- ATPases activity; (F) Dopamine and serotonin; (G) Glutamate and GABA; (H) Acetylcholine; (I) Reduced Glutathione; (J) TBARS levels; (K) Glutathione peroxidase; (L) SOD and catalase activity in the discrete brain regions of mice. C- Cerebellum, CC- Cerebral cortex, MO- Medulla oblongata and OB-Olfactory bulb. [**P* ≤0.05, ***P* ≤0.001]

declined in these discrete brain regions (F=30.8-266, *P* ≤0.001) (Fig. 4G). The ACh levels also showed a dose-dependent elevation (F=26.5-97.8, *P* ≤0.001) (Fig. 4H).

Antioxidants and Antioxidant enzymes

After receiving MgO NPs for 30 days, the mice exhibited a significant, dose-dependent decrease in reduced glutathione (F=36.7-113, *P* ≤0.001) and elevation in the TBARS levels (F=23.9-63, *P* ≤0.001) in C, CC, MO, and OB (Fig. 4 I & J). The activity of antioxidant enzymes, glutathione peroxidase (F=17.2-50.2, *P* ≤0.001), SOD (F=6.4-54.4, *P* ≤0.05-0.001), as well as catalase (F=27-45.9, *P* ≤0.001), exhibited a significant and dose-dependent decline in C, CC, MO, and OB (Fig. 4 K&L).

Discussion

Nanoparticle synthesis is accomplished by various methods and techniques which is a known fact. The study reveals that the MgO NPs obtained have a specific shape and size, as revealed through SEM, TEM, and XRD. The XRD peaks indicate crystalline nature, while the FTIR spectra correspond to the Magnesium-oxygen (Mg-O) stretching vibration modes. Additionally, the Zeta potential analysis showed that the produced MgO NPs had strong anionic properties and good stability[15].

Histological examination helps in identifying cytoarchitectural changes caused by any toxicant or any foreign substances. The study found that exposure to MgO NPs in mice caused pathological changes in discrete brain regions, causing neurotoxicity and altering anatomy through oxidative stress as suggested byBoukholda[16]. In particular, these MgO NPs caused Purkinje cell degeneration, potentially disrupting cerebellum signals to higher centres, as these cells are the sole efferent neurons in the cerebellum[17]. Granular cells receive and interpret mossy fiber inputs, allowing C and OB to make finer distinctions. MgO NPs degenerated and impaired granular cells, affecting their functions and obstructing input reception and interpretation[18].

Damage to pyramidal cells in CC impairs excitation hence, damage caused by MgO NPs directly affects the extent of excitation loss[19]. CC glial cells surround neurons, provide nutrients, and oxygen, and insulate them, destroy pathogens, phagocytose dead neurons, and assist in synaptic connections. Degeneration of these cells by MgO NPs could impact these functions[20]. MgO NPs' injury to nerve rootlets in MO disrupts brain-to-hypoglossal nerve impulse transmission, accessory nerves, glosso-pharyngeal nerves, and vagus nerves, affecting organ function and nerve-associated organs.

Mitral cells are olfactory system neurons that receive inputs from receptor neurons and form synapses. They transfer information to various brain areas and form a relay for olfactory information. Damage to these cells by MgO NPs affects input receptors, interpretations, relay to other brain regions, and cognizance[21]. The deposition of MgO NPs in histological sections confirmed their entry into the brain after crossing the BBB. MgO NPs cause dystrophic calcification in mice's cerebellum due to neuronal damage and inflammation, potentially disrupting enzyme activities, neurotransmitters, and trace metal homeostasis, eventually leading to neurodegenerative diseases.

The enzyme activity of the mice changed dramatically after being exposed to MgO NPs for 30 days. The brain's ACP activity increases as a result of the MgO NPs' injury to the cells in neural tissues. It is generally known that increased levels of the lysosomal enzyme ACP are associated with increased cell/tissue necrosis[22]. The increased vacuolar space sizes in neural tissue indicate injury[23], corresponding to increased ACP activity, are observed in histochemical studies of neuronal tissue exposed to MgO NPs. The decrease in ALP activity may be due to reduced protein synthesis, altered membrane transport, and electrolytic imbalance caused by tissue after dehydration, as well as injury to neuronal membranes, as ALP is a membrane-bound enzyme[24]. The decline in SGPT and SGOT enzyme activities indicates disturbed protein synthesis, promoting oxidative deamination and intermediary metabolism disturbances. This decrease affects cerebral blood flow (CBF), altering neural mechanisms underlying cognition and memory[25]. MgO NPs may have caused stress on the ionic balance, leading to increased Na^+-K^+-ATPases, impulse transmission, Na^+- influx, and K^+- efflux in extracellular fluid, thereby elevating Na^+- concentration in neurons and K^+- in extracellular fluid[26]. MgO NPs also cause acute energy shortages by disrupting oxidative phosphorylation, leading to a decrease in Mg^{+2}- ATPases and Ca^{+2}- ATPases[27]. All of the aforementioned alterations in the enzyme activity imply that the MgO NPs damage the integrity of the cell membrane. These findings lead us to believe that long-term exposure to MgO NPs may have negative effects on organ systems throughout the body, such as the liver, kidneys, and lungs.

The neurotransmitter and its release in the correct amounts are vital for brain communication within and to the animal's body. Dopamine is a crucial neurotransmitter in the brain, produced and secreted by dopaminergic neurons. It plays a significant role in the reward system and hormone control[28]. Damage to the brain can obstruct dopamine synthesis and release, leading to decreased levels. This decline in dopamine levels in the present study indicates brain injury, potentially causing paralysis, movement difficulties, altered behaviour, and disturbed hormonal release. Serotonin, a neurotransmitter responsible for mood swings, sleep, hunger, learning, and memory[29], is

depleted when brain neurons, particularly serotonergic ones, are injured. Inhibition in serotonin pathway enzymes, such as tryptophan hydroxylase and amino acid decarboxylase, may also contribute to serotonin depletion[30]. However, MgO NPs' action on these enzymes cannot be entirely ruled out as this decrease can lead to depression, anxiety, and constipation[31].

Glutamate, an excitatory neurotransmitter, is responsible for memory, speech, learning, and cognition, and its metabolism involves enzymes viz.; GS, GDH, SGPT and SGOT. Brain astrocytes are key sites for the GS enzyme, which regulates glutamate and ammonia detoxification. This enzyme helps in metabolizing glutamate and ammonia into glutamine[32]. So, decline in GS levels indicates an impact on the conversion process, leading to excess glutamate levels. GDH, a crucial brain mitochondrial enzyme, links protein and carbohydrate metabolism in the brain, facilitating the conversion of α-keto glutarate to glutamate. In the study, GDH levels were found to be elevated, potentially causing excess glutamate synthesis during stress caused by NPs[33]. The study reveals that decreased SGPT and SGOT activity affects glutamate interconversion, leading to elevated levels, causing excitotoxicity, promoting inflammation, and cell death, which are recorded in the presence of MgO NPs[32]. The study reveals that NPs can affect the conversion of glutamate to GABA, a neurotransmitter responsible for calming the brain and relaxing thoughts, processes, and speech[34]. Despite increased glutamate levels, the inhibition in GABA levels indicates that these NPs also affect this conversion process[32]. MgO NPs may influence cholinergic neurons to synthesize ACh from acetyl-CoA fraction of pyruvate and choline, potentially stimulating the enzyme choline acetyltransferase[35]. Ca^{+2}- and pyruvate levels regulate ACh production, while stressors from MgO NPs might have affected larger cholinergic areas, leading to excessive Ach release in the basal forebrain. Further elevated ACh levels may be triggered by the inhibition of the AChE enzyme, leading to brain excitation, cholinergic crisis, paralysis, and respiratory failure[36].

The brain is highly susceptible to oxidative damage due to its high concentration of peroxidable unsaturated fatty acids, and high oxygen consumption[37]. Glutathione (GSH) is a crucial antioxidant in cells, protecting against reactive oxygen species (ROS) like peroxides, heavy metals, and free radicals. In its reduced form, it scavenges free radicals and is used by enzymes like GSH peroxidase and GSH reductase. The ratio of GSH to oxidized form measures oxidative stress. Chronic exposure to MgO NPs decreases reduced GSH content, potentially due to the formation of complexes between radical species and cellular proteins or biomolecules. This decline may be due to NPs complex with thiol groups or increased GSH use to tone down free radicals' effect. TBARS, a crucial biomarker for lipid peroxidation and membrane conditions, was elevated by MgO NPs, potentially causing excessive lipid peroxidation and oxidative stress that can be attributed to the depletion of the antioxidant system and decreased antioxidant enzyme activities[37].

Antioxidant enzymes like SOD, CAT, and GPx are crucial markers for oxidative stress and maintaining cell homeostasis. SOD converts toxic superoxide to hydrogen peroxide, CAT metabolizes hydrogen peroxide to oxygen and water, and GPx protects the lipid membrane from oxidative damage[38]. A balance between these enzyme activities is essential for organism health and survival. MgO NPs inhibited antioxidant enzymes, leading to brain region necrosis due to ROS production from stressors, indicating the inhibition of the antioxidant defense system. Our research demonstrates several common mechanisms of nanotoxicity, including apoptosis, oxidative stress, cytotoxicity, the generation of reactive oxygen species (ROS), and inflammation. This could be because NPs enter cells through endocytosis, interacting with the extracellular matrix or plasma membrane. They absorb and form endocytic vesicles, which are then delivered to intracellular trafficking compartments, causing damage[39]. This suggests that MgO NPs are transported through various mechanisms, including phagocytosis, pinocytosis, endocytosis, and caveolae-mediated endocytosis. The distribution of NPs is influenced by factors, such as size, surface qualities, and cell types, which can impact their intended application.

The distribution and toxicity of MgO NPs are influenced by their route of exposure as inhalation primarily causes respiratory effects, dermal contact leads to localized effects while ingestion targets the gastrointestinal tract, and so on. Ultimately, this indicates that different nanomaterials behave differently depending upon the route of exposure.

They enter the body through a "corona" of organic and inorganic molecules, causing serious physiological changes and interacting with different fluids, affecting excretion, metabolism, dispersion, and absorption pathways affecting organs and tissues[40].

MgO NPs through experimental pieces of evidence proved that they can create havoc in the brain, disrupting its mechanisms, leading to degenerative diseases and malfunctioning other organs and body systems, as the brain is the central control for body functioning. This study serves as a wake-up call to all scientists and individuals who once believed MgO NPs to be harmless but are now aware that this is no longer the case. Therefore, sufficient care must be taken before contemplating such NPs for any biomedical application because of the damage they might cause once they enter the brain, as this study has shown. Other organ systems may experience a similar situation, but perhaps with greater intensity, as they will be in direct contact with these NPs as they enter the body as opposed to the brain. As a result, extreme caution and safety measures should be used when handling these NPs or any items that contain them. Additionally, surface modification or encapsulation of the MgO NPs with discrete-sized polymers can reduce toxicity and enhance efficiency at reduced doses, as encapsulation is a crucial step in ensuring their safe use in various applications. Surface modifications in the shape and size will also change the properties of the particles in turn changing their toxicity. It might not only protect against potential harm but also allow for controlled release, targeted delivery, and prolonged stability of the NPs. Controlled or time-release systems can reduce acute toxicity, while biodegradable materials can facilitate gradual degradation and clearance. Furthermore, thorough testing and regular monitoring can effectively assess any potential risks associated with the use of these NPs or nanoparticle-containing products.

Conclusion

Magnesium oxide nanoparticles (MgO NPs) hold great promise for addressing a variety of problems in the disciplines of electronics, environmental remediation, and medicine but their potential toxicity has made it important to thoroughly investigate their safety before use. The current research findings reveal that oral exposure to MgO NPs for 30 days disrupts brain tissues, enzymes, antioxidants, and neurotransmitters, potentially leading to neuro degenerative disorders and impaired normal functioning. This can be prevented by modifying the NPs using appropriate entrapment, attachment or encapsulation into the matrix in order to deliver them safely and effectively.

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Conflict of Interest

Authors declare no competing interests.

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