

REVIEW PAPER

Review on MgO nanoparticles multifunctional role in the biomedical field: Properties and applications

Heba Mohamed Fahmy ^{1*}, Mohamed Hamdy El-Hakim ¹, Doaa Sayed Nady ², Yomna Elkaramany ³, Fatima Adel Mohamed ⁴, Alaa Mohamed Yasien ¹, Mariam Ahmed Moustafa ⁵, Bothaina Ezzat Elmsery ⁶, Hesham A Yousef ⁷

¹Biophysics Department, Faculty of Science, Cairo University

²Chemistry Department, Faculty of Science, Cairo University

³Biotechnology Program, Faculty of Science, Cairo University

⁴Chemistry Department, Faculty of Science, Cairo University

⁵Zoology Department, Faculty of Science, Cairo University

⁶Department of Physics, Basic Science Center, Misr University for Science and Technology (MUST), Giza, Egypt.

⁷Entomology Department, Faculty of Science, Cairo University

ABSTRACT

Nanotechnology has introduced many useful uses to people's lifestyles in various fields such as health care, agriculture, the food industry, and separate industries during the previous few decades, and it is now available to the majority of the world's population. Among these applications, nanotechnology is critical in the realm of medical therapy. Many forms of studies indicate that nanoparticles, particularly metal oxide, can make a significant contribution to this field. In the current work, we examined one of them, MgO, a critical inorganic oxide used in a variety of applications. MgO is a multilateral oxide material with several properties, including great thermodynamic stability and a low refractive index and dielectric constant. The wide bandgap allows for a variety of uses in ceramics, catalysis, hazardous waste remediation, and antibacterial materials as a refractory additive paint and as a superconductor product. MgO NPs have been used in a variety of disciplines due to their extensive properties and functions, which we will discuss in this article.

Keywords: Antibacterial activity, Cancer treatment, Catalysis, Nanoparticles cytotoxicity, Tissue engineering

How to cite this article

Fahmy HM, El-Hakim MH, Nady DS, Elkaramany Y, Mohamed FA, Yasien AM, Moustafa MA, Elmsery BE, Yousef HA. Review on MgO Nanoparticles Multifunctional Role in the Biomedical Field: Properties and applications. *Nanomed J.* 2022; 9(1):1-14. DOI: 10.22038/NMJ.2021.60646.1629

INTRODUCTION

Nanotechnology has made significant development in terms of preparation, characterization, and application during the last several years. Nanomaterials are commonly used in scientific study due to their intriguing features and benefits over bulk materials. Many researchers with diverse interests and specialties have been drawn to nanomaterials in order to improve the quality of their study work while using nanomaterials. Many metal oxide Nanoparticles possess numerous advantages and are used in the medical research [1-4] such as Ag₂O [5, 6], CaO [7, 8], CuO [9-11], ZnO [12-14], SiO₂ [15-17], NiO [18, 19], CrO [20], Fe₃O₄ [21-23], Fe₂O₃ [24, 25], Al₂O₃

[26-29], CdO [30-32], and CeO₂ [33, 34]. Similarly, MgO nanoparticles have a high potential for use in nanomedical research [35], as well as numerous other applications in agriculture [36-38], chemical reaction catalysis [39-41], dye removal [42-44], and lithium batteries [45-47]. The interesting properties of MgO nanoparticles, such as stability, easy and inexpensive preparation methods, including green ones, magnetization, crystallinity, absorptivity, electrical and thermal conductivity, stoichiometry, large surface area, and reactivity, are attributed to their wide range of applications. All of these amazing capabilities propelled MgO nanoparticles to the forefront of nanomedical research. Our review will show the many preparation procedures that can produce MgO NPs with a uniform size distribution, various forms, and variable Dimensions.

* Corresponding Author Email: heba_moh_fahmi@yahoo.com
Note. This manuscript was submitted on September 2, 2021; approved on November 8, 2021

The shape of MgO nanoparticles

Understanding shapes is fundamental to cognitive development; it is significant because it has practical applications in medicine, industry, agriculture, and scientific study.

MgO nanoparticles come in a variety of morphologies, including spherical nanocubes, nanocrystals, nanofibrous nanowires, nanotubes, and nanosheets. This variety of MgO NPs shapes has resulted in a wide range of applications that exploit each shape in a variety of fields. Table 1 depicts several shapes of MgO nanoparticles.

The morphological structures of MgO nanoparticles were examined using a variety of analytical techniques. X-ray Diffraction is used to determine the crystallinity and size of the MgO nanoparticle (XRD). Transmission electron microscopy is used to determine the size and shape of the particles (TEM). Using Fourier transform infrared microscopy, the sample's infrared spectrum was acquired, revealing its powdered nature. UV-Visible spectroscopy was used to evaluate the optical properties of the NPs [48].

Table 1. shapes and sizes obtained from different preparation methods

Method of preparation	Size	Shape	Reference
Sonication method	15 nm	Nanocrystal	[60]
Sol-gel method	9.5 nm - 15.5 nm	Nanoplates	[61]
Hydrothermal method	10 nm in diameter 18-20 nm length	Nano wire	[62]
Co-precipitation method	21 nm	Nanocube	[63]
Green method	60-70 nm	spherical	[64]
Sol-gel method	200-300 nm	coralline	[65]
Wet chemical method	30-50 nm 50-80 nm 70-130	Dense flakes Irregular flakes Irregular porous	[66]
Green method	13 nm	spherical	[67]
Wet chemical method	25 nm	Nanocrystal	[68]
Quick precipitation method	50 nm length 20 nm thickness	Nanocrystal	[69]
Green method	Less than 10 nm	spherical	[70]
Green method	Less than 20 nm	spherical	[71]
Co-precipitation	28-64 nm	Nanocrystal	[72]
Green method	Less than 20 nm	spherical	[73]
Hydrothermal method	6 nm diameters 10 micro length	Nano wire	[74]
Cationic surfactant based microemulsion	8-10 nm	Anisotropic	[75]
Chemical precipitation	5-30 μm at 100 C Less than 1 μm at 960 $^{\circ}\text{C}$ Less than 500 nm at 1200 $^{\circ}\text{C}$	Powders	[76]
The wet chemical reaction method	Average 16 nm. size distribution of 7-38 nm	spherical	[77]
Thermal decomposition of the hydroxide	1-100 nm	nanocrystal	[78]
hydrothermal calcination	40-60 nm in diameter thickness ~ 5 nm	nanoplates	[79]
Chemical precipitation	10-20nm thickness up to 100 nm length	nanoplates	[80]
The reaction of magnesium powder with water at a very low temperature	~ 40 nm width ~20 nm thickness up to 1 μm length.	nanoflakes	[81]
Preparation is done by torch flame of an oxygen microwave plasma	10-50 nm	Various shapes (hexahedrons, plates, and rectangles)	[82]

MgO nanoparticles size

MgO NPs have a long history of use in a variety of sectors for a variety of reasons [49]. Depending on the fabrication circumstances, different sizes have different properties: calcinations and temperature rate in the thermal decomposition method; conditions of gel preparation such as the heating rate for gel formation, pH, gelling agents, and temperature of gel calcination in the sol-gel method. The bactericidal characteristics of MgO fluctuate with particle size, with the bactericidal efficacy of MgO Nanoparticles increasing as particle size decreases [50]. The optical properties of MgO nanocubes, as measured by UV diffuse reflectance and photoluminescence spectroscopy, also reflect the change of the ratio between corner and edge ions [51]. The diameters of the MgO particles ranged from micro- to nano-sizes [52] or variable grain sizes [53]. Dynamic light scattering [54], disc centrifugation [55], nanoparticle tracking analysis [56], tunable resistive pulse sensing [57], atomic force microscopy [58], and electron microscopy are some of the techniques used to measure their size. The BET method can be used to calculate the surface areas of MgO particles, which have a high surface area of about 100 m²/g [51]. The size of MgO nanoparticles measured by various preparation processes is shown in Table 1.

MgO nanoparticles role in cancer therapy

Cancer is one of the top causes of death in all countries [83]. A cancer tumor develops when a person's cells begin to divide rapidly into surrounding tissues. Tumors can occur because of these excess cells. Cancer is a hereditary disease caused by genes that regulate cell processes, particularly growth and division. Because cancer cells can ignore signals telling them to stop proliferating, they can divide forever or initiate the process of programmed cell death, or apoptosis, which is a procedure used by the body to eliminate undesired or damaged cells. Because cancer is a lethal disease with over 100 different types of cancer for different tissues and organs, we need simple and inexpensive treatments. The utilization of oxide nanoparticles biogenic sources to substitute harmful compounds has become the current intriguing challenge. Nanoparticles less than 100 nm in size can interact with proteins, nucleic acids, and lipids both inside and outside the cell, which may aid in cancer diagnosis and treatment. MgO nanoparticles are one type of

nanoparticle that uses *sargassum wightii* (marine brown algae) as a capping and reducing agent. MgO NPs were tested against lung cancer cell lines in this study. MgO NPs produced lung cancer cytotoxicity, which might be attributed to elevated ROS levels as the mitochondrial membrane potential was altered, initiating the apoptotic process and ultimately leading to cell death [84]. The cytotoxicity test confirmed that the produced nanostructures are non-poisonous to normal healthy RBCs. MgO nanorods have potential applications such as a powerful chemotherapeutic agent for the rapid detection and identification of all cancer types [85]. The cytotoxic effects of MgO NPs on normal lung fibroblast cells and various malignant cells revealed that they had a magical power to destroy cancerous cells, including HeLa, AGS, and SNU-16 cells. In addition, MgO NPs were implied in hyperthermia and nano cryosurgery to cure cancer. These discoveries broaden the scope of MgO Nanoparticles' possible use in nanomedicine for a cancer cure as a viable alternative to chemotherapy because of their toxicity to cancer cells via apoptosis induced by ROS [86]. Measuring the heating efficiency of Fe/MgO magnetic shell nanoparticles and their *in vitro* application in hyperthermia was examined in human breast cancer cell lines. This study might be considered the first key principle for *in vitro* hyperthermia.

More research on the hyperthermal response is required before moving on to *in vivo* approaches [87]. MgO NPs have the potential to be exploited as a drug transporter and releaser. Furthermore, bimetal oxide nanoparticles with a multifunctional attitude will play a prominent role in DDS as a favourable drug vehicle [88]. *Penicillium* fungi were employed in the manufacture of MgO nanoparticles, which resulted in Stable Nanoparticles with outstanding anticancer properties and low influence on normal cells. Nanoparticles stimulated apoptotic activity and DNA damage, although more cytotoxicity experiments are needed to establish the Nanoparticles' potential toxicity [89]. Nanoparticles have a strong reciprocal effect with biomolecules, which can improve the way anticancer drugs are recognized. They can overpower cellular and noncellular strategies of blocking foreign bodies, making it easy for the drug to target the cancer cells and decreasing its dangerous effects on normal cells [90]. MgO

nanoparticles could be used in the freezing method of nano cryosurgery, using their advantages as they are non-poisonous, biodegradable, and have a few bad consequences on humanity. According to experiments on animal and nucleation analysis, the bringing of MgO nanoparticles with their slight weight and good thermal features to the marked tissue would enhance the result of the cryosurgery as thermal features help shape the ice ball in the freezing method quickly and effectively [91]. The need to use nanomaterials in medications for humans is crucial to examine them clinically and study their interactions with plasma proteins as human serum albumin (HSA) and their cytotoxic effects on normal and cancer cell lines. It was found that MgO nanoparticles build an inactive, unplanned combination with HSA molecules by actions lacking attraction for water. Docking study dependent upon the size of the Nanoparticles showed that there are varying connections that can be constructed between MgO Nanoparticles and HSA. The circular dichroism spectroscopy Shows that MgO Nanoparticles did not change the secondary composition of HAS. They showed cytotoxicity instead of the K562 cell line, which made it an original anticancer, as their moderating of cell death begins with the production of ROS in the cancer cells [92].

MgO nanoparticles as an antibacterial

There are two types of bacteria depending on their impact on humans; Commensal bacteria[93], which are beneficial and essential for our survival, and harmful bacteria[94], which threaten our health. We used to get rid of the harmful bacteria by using antibiotics. However, due to the unselective use of antibiotics, bacteria are progressively resistant to several antibiotics at a very large rate over time [95-97], leading to the rapid development of antibiotic-resistant strains due to their potential antibacterial activity against Gram-positive and Gram-negative bacteria [98]. They are proposed to slow the growth rate of more resistant bacteria because they target multiple biomolecules simultaneously [99]. MgO is a metal oxide nanoparticle with antibacterial properties. Its properties depend on shape and size. Where small-sized MgO NPs had better antibacterial activities towards gram-negative (*E. coli*) bacteria and gram-positive (*S. aureus*) [100]. MgO nanoparticles have dosage-dependent antibacterial activity [101]. Frequency

affects the activity too, where increasing shaking rate increased the death of bacteria in the slurry, suggesting that the active oxygen generated from the MgO powder slurry was one of the main factors in its activity [102]. MgO nanoparticles can be metabolized properly inside the body compared to heavy metal oxide nanoparticles (silver and zinc), where it is easy for the degraded ions to be removed [103]. MgO nanoparticles showed unique antibacterial properties against several common foodborne pathogens. Their contact with bacterial cells leads to leakage from the cellular membrane and oxidative stress induction, causing cell death [104]. MgO nanoparticles were prepared at various temperatures for thermal decomposition, resulting in various sizes and surface areas. The antibacterial effect was studied by diffusion method using *E. coli*, then introducing MgO nanoparticle suspensions. The MgO nanoparticles showed remarkable bactericidal activity producing a large inhibitory zone surrounding the nanoparticles, and stronger activity against gram-positive bacteria than gram-negative ones was noticed. The antibacterial activity was more related to the surface area than the resulting nanoparticle size [105].

Size impact was also noticed when using Gram-positive (*S. aureus*) and gram-negative (*E. coli*) bacteria. The antibacterial efficacy of nanoparticles has been examined. Smaller MgO nanoparticles are discovered to have both gram-positive and gram-negative adverse antimicrobial activity, while larger MgO nanoparticles have a gram-negative adverse impact only [66]. Decreasing the size of the nanoparticles will lead to an increasing in the surface area. Consequently, a larger number of surface hydroxyl groups will help destroy the bacterial protein contributing to the antibacterial effect of the MgO nanoparticles [106]. In another experiment, different concentrations of MgO nanoparticles were inoculated with cultures of *Escherichia coli* overnight. MgO nanoparticles were found to have potent antibacterial properties against foodborne pathogens (*E. coli*). The MgO NPs application injures the cell membrane, resulting in intracellular contents leakage consequently; bacterial cell death [107]. The same activity toward (*E. coli*) was shown when a simple green chemistry procedure was used to synthesize MgO NPs, coat them with cotton fabric, and test them with the agar diffusion method [108]. The antibacterial property of MgO NPs was evaluated

as the Inhibitory zones appear around the MgO powder slurry when there is direct contact with nutrient agar plates inoculated with (*E. coli*) or (*S. aureus*). However, no zone appeared when they were isolated from each other by a penicillin cup [109]. The direct interaction between NPs and (*E. coli*) was prone to attack the cell membrane. MgO nanoparticles prepared by sol-gel and calcination techniques had a high tendency to inactivate (*E. coli*) and remove heavy metal ions. When the cell membrane was damaged, heavy metal ions entered easily into a bacterial cell and thus induced bacterial inactivation [110]. Increasing the shaking rate resulted in increasing the death rate of (*E. coli*) in the slurry, showing that the contact frequency between bacterial cells and MgO powders affected the antibacterial activity. Chemiluminescence research revealed that active oxygen produced from the MgO powder slurry and that changes in antibiotic sensitivity in *E. coli* treated with MgO powder matched those seen in *E. coli* treated with active oxygen. So, it was suggested that the active oxygen generated from the MgO powder slurry was a primary factor aiding in its antibacterial activity [109]. Reactive oxygen species generation was also noticed when using MgO antibacterial against gram-negative bacteria *Escherichia coli* and *Pseudomonas aeruginosa* as well as the gram-positive bacterium *Staphylococcus aureus* with resazurin as an indicator of cell growth. The minimal inhibitory concentration of 1,000 µg/mL for *P. aeruginosa* & *S. aureus* and 500 µg/mL against *E. coli* was observed. MgO NPs increased ultrasound-induced lipid peroxidation in the liposomal membrane [111]. Natural synthesis is a new method used to eliminate the chances of toxins contaminating; the MgO NPs were prepared using extracts from the three different leaves: *Amaranthus tricolor*, *Amaranthus blitum*, and *Andrographis paniculata*, then inoculating in *E. coli* culture. The nanoparticles made from *A. blitum* had the strongest antibacterial activity and the largest inhibition zone [112]. MgO nanoparticles prepared with microwaves and hydrothermal methods showed a noticeable antibacterial activity towards the *A. hydrophila* [113]. The *Vibrio Cholerae* bacterial system was used for antibacterial properties investigation of the nanoparticles where significant inhibition of bacterial growth is noticed, and insignificant cytotoxicity was found in Human intestinal or tumor cells [114]. Different MgO nanoparticles

were synthesized using different methods and compared its bactericidal activity to the TiO₂ nanoparticles on *Bacillus subtilis*. The results showed that the bactericidal ability of MgO was inversely related to the particle size. Magnesium oxide nanoparticles have better bactericidal effects than TiO₂ nanoparticles in both the absence and presence of light. The activity was related to the high concentrations of O₂ found, which is highly active and can react with the peptide linkages in the surrounding walls of the spores. The spores are destroyed by the resulting damage to their structure [115]. Magnesium oxide showed great efficiency against *P. aeruginosa* bacteria isolated from Urine tract infection; it showed an inhibition zone diameter of 24 mm [116]. Study of antibacterial activity of MgO against water found bacteria (*Pseudomonas aeruginosa* and *Staphylococcus aureus*) revealed the effectiveness of MgO nanoparticle is greater against gram-positive than the gram-negative pathogens; this is attributed to the absence of outer membrane within the cell wall, unlike the gram-negative bacteria, which have a complex wall [117]. Apart from the antibacterial resistance, MgO NPs also aid in disease prevention in some veggies. In tomatoes, MgO was used to prevent the infection with *Ralstonia solanacearum*. inducing systemic resistance [118]. MgO also conducted antifungal activity in *Saccharomyces cerevisiae*, *Aspergillus niger*, *Candida albicans*, and *Rhizopus stolonifer*. Evaluation of antifungal activity was done via measuring the electrical conductivity changes resulted from the fungal metabolism. MgO nanoparticles show a noticeable effect against all fungi used in this study [119]. MgO nanoparticles doped with silver were tested for their antibacterial effect. This doping process led to a MgO nanoparticles size decrease. Also, the bactericidal effect of the MgO NPs was improved greatly due to increased ROS production and the probability of interactions between the nanoparticles and Bacteria [120].

MgO nanoparticles as a biosensor

Because of its vast surface area, electrochemical processes at the nano-scale level play a vital role in generating various biosensors to detect very low concentrations of chemicals. It exemplifies high activity reactions, catalysis, and has a high absorption capacity in enzyme immobilization [121]. MgO NPs are electrodes

that detect hydrogen peroxide (H_2O_2) via catalase enzyme coupling (CAT). H_2O_2 is decomposed using CAT enzyme, while MgO NPs are utilized as an electrochemical transducer to assist and expedite electron transfer [122]. Another method of using nano MgO to detect H_2O_2 is by immobilizing Horseradish peroxidase (HRP) and preserving biological activity to a considerable extent, in which nano MgO is inoculated in a chitosan solution to form a nanocomposite as a stage in the manufacturing of an H_2O_2 biosensor [123]. Another biosensor used to detect H_2O_2 in hydroquinone as a mediator is prepared by adding MgO NPs prepared by the thermal evaporation method to the gold electrode. This biosensor is characterized by high sensitivity and rapid response [124]. Another one is the nonenzymatic sensor used to solve the problems of poor reproducibility and long-term operation. One of the nonenzymatic sensors is MgO nanoporous, which is eco-friendly and exhibits excellent electro-oxidation activity toward hydrogen peroxide. It can also be applied to detect H_2O_2 in the food as it has no potential risks to human health [125]. Another Biosensor depends on MgO nanobelts, which are highly sensitive towards ascorbic acid [126]. In the last years, Graphene was utilized to analyze ascorbic acid, dopamine, and uric acid, but this works well due to the overlapping of the oxidation peaks of these three acids. Recently, MgO nanobelts have been synthesized because of peak separation between analytes; therefore, the three acids can be detected by graphene-modified tantalum pelt with MgO NPs. [127,128]. The polyhedral nanocages and nanocrystals structures of MgO nanoparticles are used to produce high sensitive biosensors in a short time, glucose biosensors [121]. The biomolecule of MgO NPs, due to their biocompatibility, excessive sensitivity, and effective surface area, could be utilized as a good electrochemical biosensor material for detecting nucleic acid molecules [129]. Chitosan-modified nano MgO configure nanosensor for sensitive detection of *V. cholera* instead of conventional methods and costs a long time [130]. MgO nanoflowers are used to produce easy and low-cost biosensors for efficient detection of micro-RNA [131-132].

MgO role in tissue engineering

Tissue engineering is a field of research that employs living cells in a variety of ways to improve

tissue and organs by growing and assembling three-dimensional tissues from cultivated removing cells on bioactive degradable scaffolds [134]. Recently, tissue engineering has helped in orthopedic disorders treatment because it uses engineering principles, biology, and chemistry, so it is more effective than traditional methods [135]. Bones are characterized by pore interconnectivity and highly porous structure. To achieve that, we use the first 3D printing scaffolds of tricalcium phosphate (TCP) doped with SrO-MgO to improve bioactivity, bone formation, leading to early healing, increasing density, and reducing of the pore size of the bone. Also, doping improves bone modeling and mechanical strength of the TCP scaffolds [136-137]. Bioactive samples are used for bone regeneration applications because the hydroxyapatite layerable stimulates biological fluids. Researchers have been drawn to glass and glass-ceramics based on Ca, Mg, Si₂, and O₆ in recent years due to their exceptional properties, which include a low degradation rate, high mechanical strength, and low toxicity. It also attaches to the tissues of live organisms faster than the hydroxyapatite layer [138]. MgO nanoparticles are used in conjunction with poly (L-lactic acid) (PLLA) and hydroxyapatite (HA) nanoparticles to treat damaged bone; MgO NPs are used in orthopedic treatment by enhancing osteoblast union and spreading on HA-PLLA nanocomposites and making mechanical properties suitable for cancellous bone applications. Furthermore, MgO nanoparticles promote osteoblast growth and can be exploited to modify the mechanical properties of additive biomaterials [139].

MgO role in dental implantation

The dental implant is paramount to manage teeth loss [140]. It should be biocompatible, strong, inert, and tough [141]. Recently most modification has been designed to reduce time and improve dental implantation [142]. Nanotechnology is regarded as one of the most promising future tools in implant dentistry. Nano surface modification technologies are commonly utilized to improve the surface material properties of dental implants, resulting in faster osseointegration and bone healing [143]. Many experiments have been conducted in order to promote osseointegration and establish a thermal expansive confined match between two phases in bioactive glasses covered titanium implants. Magnesium oxide improved the

bioactivity, thermal characteristics, and structural qualities of glass by inhibiting crystallization, lowering the thermal expansion coefficient, and softening the glass temperature [144].

MgO Nanoparticle for bioactive glass

Bioactive glasses are reactive materials that may connect to mineralized bone tissue in a physiological environment and are used to restore damaged body parts in particular [145]. They accelerate tissue healing by inducing bone cell renewal and self-repair [146]. It has a wide range of applications in the biomedical field. It was first developed for middle ear surgery; it is now commonly utilized in the dentistry sector and is being researched for use in regenerative medicine and tissue engineering. The biocompatibility and bioactivity features of Bioactive glass are enhanced in nano-sized Biomaterials [147]. Many other composites have been created, but the most reactive materials inside the human body have significant CaO and Na₂O content [148]. The glass transition, melting commencement, endpoints, and temperature at which fusion occurs were all lowered when CaO was replaced with MgO. The activation energies for crystallization and glass transition were similarly reduced, indicating decreased bond length and enhanced strength. The thickness increased in direct proportion to the MgO content. The bioactivity test demonstrated that the greater the MgO concentration, the slower the reaction between the glass and bodily fluid [149]. The addition of MgO to a glass composite improves the bioactive glass's ability to behave as thermoseeds during hyperthermia [150]. The sol-gel process was used to create bioactive glasses containing MgO. This addition aided in the acceleration of the production of the hydroxyapatite layer [152]. Nanoparticles films with different formulations of chitosan blend with bioactive glass, including MgO NPs, were produced for system development have applicability in guided tissue regeneration. The inclusion of the inorganic component in the chitosan matrix improves the biological response of the membranes [153-155]. Bioactive Glass containing MgO nanoparticles exhibits potent antibacterial properties. Furthermore, they can aid in the repair of broken bones [156]. Using powder components allows for consistent precipitation, resulting in crack-free bioactive glass, as opposed to bulk materials [158]. Bioactive Glasses infused

with MgO have various advantages when used for orthopedic and dental coatings [159]. Bioactive glasses and ceramics have recently been discovered to have major uses in biomedicine, notably bone repair and substitution. Recent advances in tissue engineering have made it possible to improve the physical and biological efficiency of bioactive lenses and glass ceramics by including certain components into their compositions. These ingredients can improve the physiological, biological, and therapeutic qualities of bioactive glass [160].

MgO nanoparticles in medical imaging

Medical imaging plays a significant part in providing useful information to medical sciences and drugs. Imaging is frequently utilized to detect the presence of cancer and develop the cure plan by studying human tissues without entering any equipment into the body [161, 162]. Magnetic nanoparticles have piqued the interest of nanomedicine researchers due to their advantageous properties that can greatly facilitate their application in the medical field [163-165]. Magnetic nanoparticles can improve image contrast and provide higher-resolution scans, allowing for more precise diagnosis and therapy [166, 167]. The magnetic properties of MgO nanoparticles, as well as their ability to stay in the bloodstream for a long time, made them an ideal contrast agent for MRI [168]. Using MgO nanoparticles is overwhelming due to being Non-toxic, free of side effects, biocompatible, and quickly introduced into the human body [169]. Numerous medical applications for MgO Nanoparticles can be summarized through the Diagram as follows:

MgO cytotoxicity

In the preceding sections, we can obviously notice that Magnesium oxide nanoparticles are used in a wide range of applications and are widely manufactured around the world. However, concerns about its safety remain.

MgO Nanoparticles displayed a hemolytic activity, releasing their hemoglobin content [170]. Being of a high positive charge, MgO nanoparticles produces an increment of the blood level of K⁺ as progression for their hemolytic effect [171]. Using alcohols such as ethanol during MgO nanoparticles preparation can radically eliminate risks of MgO nanoparticles in terms of being

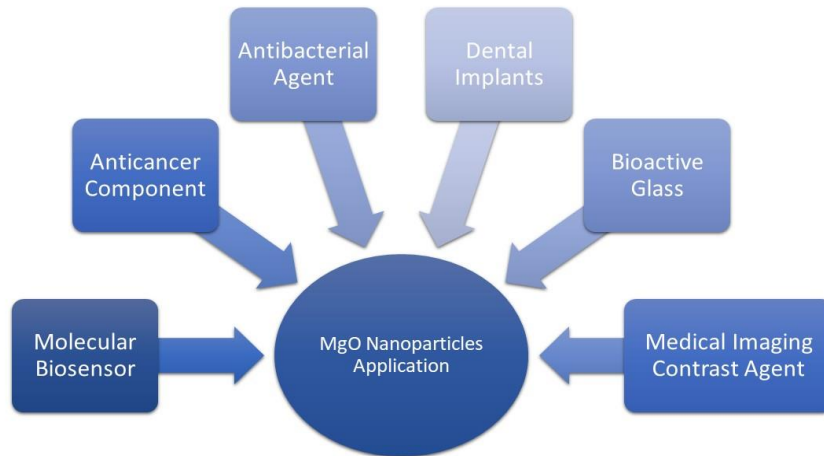


Fig 1. Diagram Represents the Different Medical applications of MgO nanoparticles

biocompatible with the components of the human blood [172]. Several histological and structural changes in Endothelial cells can occur following an exposure to MgO nanoparticles [173]. Vascular endothelial cells suffer from dysfunctional on treatment with MgO Nanoparticles which may contribute the formation of arteriosclerosis [174]. MgO Nanoparticles can do a severe damage to the respiratory system in the picture of triggering Lung Inflammation [175]. Pulmonary effect of MgO nanoparticles is strongly related to diminishing of cell viability accompanied by the elevation of the reactive oxygen Species [176]. MgO nanoparticles can generate oxidative stress inside the liver cells

which is associated with hepatocytotoxicity that can wholly affect all the liver functions [177]. The preceding toxic effect can be impressively eliminated when having the MgO nanoparticles conjugated with some natural proteins like Zein [178]. Glomerulus deformation is also observed after treatment with MgO nanoparticles which can lead to a renal function failure [179]. Toxic effects of MgO nanoparticles can be minimized to a low extent when low dosage is being used as per study carried out on the intestinal cells [180]. The following Figure is spotting the divergent cytotoxic effects of the MgO Nanoparticles.

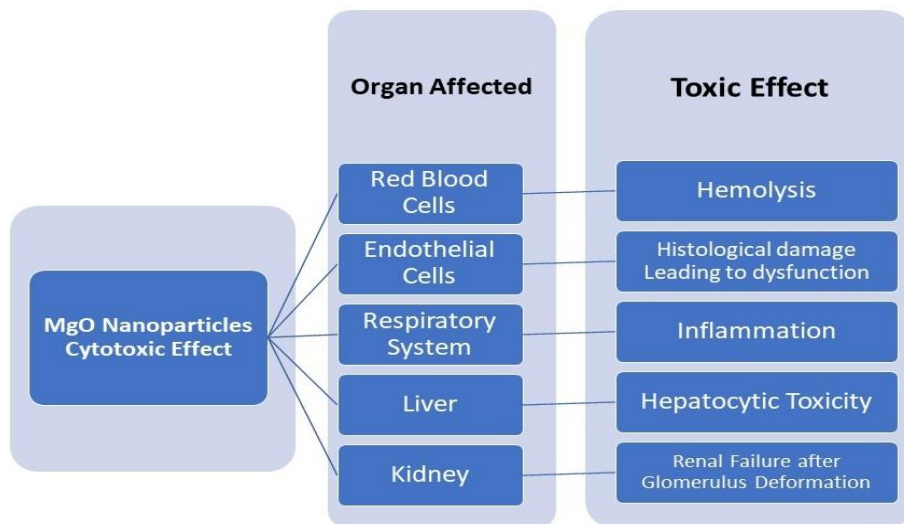


Fig 2. Systematic Representation for the toxic effects of MgO nanoparticles on different human body organs

CONCLUSION

Nanomaterials, particularly metal oxides, are useful in scientific research in a variety of domains because of their appealing features. In the medical field, for example, magnesium oxide is used. It comes in a variety of forms and sizes (varying from 6nm to 130nm), each with its own set of features. It's antimicrobial as well as anticancer. MgO nanoparticles are utilised in the creation of biosensors, the diagnosis of cancer, and the mentorship of the cure plan through medical imaging because of their active catalysis property, high reaction activity, and high absorption capability in enzyme immobilisation. Bioactive glass is being developed for application in surgery, dentistry, bacteria inhibition, bone mending, and tissue engineering. Because of its many properties, such as antibacterial, anticancer, biocompatibility, nontoxicity, biodegradability, and low cost, research findings justify adding MgO nanoparticles to a variety of medically useful compounds. In addition, MgO appears to be beneficial and safe in numerous medical uses. Considering the potential for harmful effects as a result of the exposure to MgO nanoparticles, we have to have the most proper way the get benefit of MgO nanoparticles and avoid its potential harmful effect simultaneously.

REFERENCES

1. Ficaí D, Oprea O, Ficaí A, Holban A. Metal Oxide Nanoparticles: Potential Uses in Biomedical Applications. *Curr Proteomics*. 2016;11(2):139-149.
2. Mallakpour S, Azadi E, Hussain CM. The latest strategies in the fight against the COVID-19 pandemic: the role of metal and metal oxide nanoparticles. *New J Chem*. 2021;45(14):6167-6179.
3. Alizadeh N, Salimi A. Multienzymes activity of metals and metal oxide nanomaterials: applications from biotechnology to medicine and environmental engineering. *J Nanobiotechnology*. 2021;19(1):1-31.
4. Kwon HJ, Shin K, Soh M, Chang H, Kim J, Lee J, et al. Large-Scale Synthesis and Medical Applications of Uniform-Sized Metal Oxide Nanoparticles. *J Adv Mater*. 2018; 30(42): 1704290-1704314.
5. Dharmaraj D, Krishnamoorthy M, Rajendran K, Karuppiah K, Annamalai J, Durairaj KR, et al. Antibacterial and cytotoxicity activities of biosynthesized silver oxide (Ag₂O) nanoparticles using *Bacillus paramycoides*. *J Drug Deliv Sci Technol*. 2021; 61:102111.
6. Flores-Lopez NS, Cervantes-Chávez JA, Téllez de Jesús DG, Cortez-Valadez M, Estévez-González M, Esparza R. Bactericidal and fungicidal capacity of Ag₂O/Ag nanoparticles synthesized with Aloe vera extract. *Environ Sci Eng Toxic Hazard Subst Control*. 2021;56(7):762-768.
7. Pagar T, Ghotekar S, Pansambal S, Oza R, Marasini BP. Facile plant extract mediated eco-benevolent synthesis and recent applications of CaO-NPs: A state-of-the-art review. *Chem. Rev*. 2020;2(3):201-210.
8. Marquis G, Ramasamy B, Banwarilal S, Munusamy AP. Evaluation of antibacterial activity of plant mediated CaO nanoparticles using *Cissus quadrangularis* extract. *J Photochem Photobiol B Biol*. 2016; 155:28-33.
9. Mohamed AA, Abu-Elghait M, Ahmed NE, Salem SS. Eco-friendly mycogenic synthesis of ZnO and CuO nanoparticles for in vitro antibacterial, antibiofilm, and antifungal applications. *Biol. Trace Elem. Res*. 2021;199(7):2788-2799.
10. Shaheen TI, Fouda A, Salem SS. Integration of cotton fabrics with biosynthesized CuO nanoparticles for bactericidal activity in the terms of their cytotoxicity assessment. *Ind Eng Chem Res*. 2021;60(4):1553-1563.
11. Javed R, Rais F, Kaleem M, Jamil B, Ahmad MA, Yu T, et al. Chitosan capping of CuO nanoparticles: Facile chemical preparation, biological analysis, and applications in dentistry. *INT J BIOL MACROMOL*. 2021; 167:1452-1467.
12. Thi Tran QM, Thi Nguyen HA, Doan VD, Tran QH, Nguyen VC. Biosynthesis of Zinc Oxide Nanoparticles Using Aqueous Piper betle Leaf Extract and Its Application in Surgical Sutures. *J Nanomater*. 2021; 2021:1-15.
13. Manimaran K, Balasubramani G, Ragavendran C, Natarajan D, Murugesan S. Biological applications of synthesized zno nanoparticles using *Pleurotus djamor* against mosquito larvicidal, histopathology, antibacterial, antioxidant and anticancer effect. *J Cluster Sci*. 2021;32(6):1635-1647.
14. Amuthavalli P, Hwang JS, Dahms HU, Wang L, Anitha J, Vasanthakumaran M, et al. Zinc oxide nanoparticles using plant *Lawsonia inermis* and their mosquitocidal, antimicrobial, anticancer applications showing moderate side effects. *Sci Rep*. 2021;11(1):1-3.
15. Kowalik P, Kaminska I, Fronc K, Borodziuk A, Duda MA, Wojciechowski T, et al. The ROS-generating photosensitizer-free NaYF₄: Yb, Tm@ SiO₂ upconverting nanoparticles for photodynamic therapy application. *J Nanotechnol*. 2021;32: 475101
16. Mohanan A, Sozharajan B, Karthikeyan R, Kannan S, Manakari V, Gupta M. Tribocorrosion Mechanisms of Pure Mg-SiO₂ Nano Syntactic Biodegradable Foams Against Bovine Bone in Artificial Saliva Solution. *Journal of Bio- and Tribo-Corrosion*. 2021;7(4):1-2.
17. Nikmah A, Taufiq A, Hidayat A, Sunaryono, Susanto H. Excellent Antimicrobial Activity of Fe₃O₄/SiO₂/Ag Nanocomposites. *Nano*. 2021;16(5):2150049.
18. Kalita C, Sarkar RD, Verma V, Bharadwaj SK, Kalita MC, Boruah PK, et al. Bayesian modeling coherenced green synthesis of NiO nanoparticles using *camellia sinensis* for efficient antimicrobial activity. *BioNanoScience*. 2021;11(3):825-837.
19. Al-Shawi SG, Andreevna AN, Aravindhan S, Thangavelu L, Elena A, Viktorovna Kartamysheva N, Rafkatovna Zakieva R. Synthesis of NiO nanoparticles and sulfur, and nitrogen co doped-graphene quantum dots/nio nanocomposites for antibacterial application. *J Nanostruct*. 2021;11(1):181-188.
20. Ghandali N, Mirnurollahi SM, Safarkar R. A review of applications and mechanisms nanoparticles on inhibiting the growth of pathogens. *Asian J Nano Sci. mater*. 2021;4(1):68-80.
21. Ranjbar M, Govahi M, Khakdan F. Green synthesis of Ag/ Fe₃O₄ nanocomposite utilizing *Eryngium planum* L. leaf extract and its potential applications in medicine. *J Drug Deliv Sci Technol*. 2021:102941.

22. Hajalilou A, Ferreira LP, Jorge MM, Reis CP, Cruz MM. Superparamagnetic Ag-Fe₃O₄ composites nanoparticles for magnetic fluid hyperthermia. *J Magn Magn Mater.* 2021; 537:168242.
23. Salimi Z, Ehsani MH, Dezfuli AS, Alamzadeh Z. Evaluation of Iron and Au-Fe₃O₄ Ferrite Nanoparticles for Biomedical Application. *J Supercond Novel Magn.* 2021:1-8.
24. Abbas G, Singh KB, Kumar N, Shukla A, Kumar D, Pandey G. Efficient anticarcinogenic activity of α -Fe₂O₃ nanoparticles: *In-vitro* and computational study on human renal carcinoma cells HEK-293. *Mater. Today Commun.* 2021; 26:102175.
25. Raisi A, Asefnejad A, Shahali M, Doozandeh Z, Kamyab Moghadas B, et al. A soft tissue fabricated using a freeze-drying technique with carboxymethyl chitosan and nanoparticles for promoting effects on wound healing. *J Nanoanalysis.* 2022;7(4):262-274.
26. Jalilian Z, Salar-Amoli J, Jalousian F, Ali-Esfahani T, Dezfouli AB, Barin A. Mutation of p53 as a tumor suppressor gene in lung fibroblast cells exposed to nano-alumina and zinc oxide nanoparticles. *Iran Vet J.* 2021;17(1):15-23.
27. Sallal HA, Abdul-Hameed AA, Othman F. Preparation of Al₂O₃/MgO Nano-Composite Particles for Bio-Applications. *J Eng Technol.* 2020;38(4):586-593.
28. Ghandali N, Mirnurollahi SM, Safarkar R. A review of applications and mechanisms nanoparticles on inhibiting the growth of pathogens. *Asian J Nanosci Mater.* 2021;4(1):68-80.
29. Benu DP, Earnshaw J, Ashok A, Tsuchiya K, Saptiama I, Yuliarto B, Suendo V, Mukti RR, Fukumitsu N, Ariga K, Kaneti YV. Mesoporous Alumina-Titania Composites with Enhanced Molybdenum Adsorption towards Medical Radioisotope Production. *Bull Chem Soc Jpn.* 2021;94(2):502-507.
30. Kirthan BR, Prabhakara MC, Bhojyanaik HS, Viswanath R, Nayak PA. Optoelectronic, Photocatalytic and Biological studies of Mixed ligand Cd (II) Complex and its Fabricated CdO Nanoparticles. *J Mol Struct.* 2021; 1244:130917.
31. Abdulkareem SM, Hammadi AH, Majid H, Hassoni MH, Ali EM. Green Syntheses of CdO NPs and evaluation of their antimicrobial activities. *J Phys Conf Ser.* 2021;1963(1):12134.
32. Janani B, Syed A, Sruthi L, Sivaranjani PR, Elgorban AM, Bahkali AH, et al. Visible light driven photocatalytic activity and efficient antibacterial activity of ZnFe₂O₄ decorated CdO nanohybrid heterostructures synthesized by ultrasonic-assisted method. *Colloid Surf A-Physicochem ENG ASP.* 2021; 628:127307.
33. Nazaripour E, Mousazadeh F, Moghadam MD, Najafi K, Borhani F, Sarani M, et al. Biosynthesis of lead oxide and cerium oxide nanoparticles and their cytotoxic activities against colon cancer cell line. *Inorg Chem Commun.* 2021; 131:108800.
34. Hosseinalipour E, Karimipour M, Ahmadi A. Detrimental effects of cerium oxide nanoparticles on testis, sperm parameters quality, and in vitro fertilization in mice: An experimental study. *Int J Reprod Biomed.* 2021;19(9):801.
35. Yaqoob AA, Ahmad H, Parveen T, Ahmad A, Oves M, Ismail IM, et al. Recent Advances in Metal Decorated Nanomaterials and Their Various Biological Applications: A Review. *Front. Chem. Front Chem.* 2020; 8:341.
36. Wani AH, Shah MA. A unique and profound effect of MgO and ZnO nanoparticles on some plant pathogenic fungi. *J App Pharm Sci.* 2012;2(3):40-44.
37. Raliya R, Tarafdar JC, Singh SK, Gautam R, Choudhary K, Maurino VG, et al. MgO nanoparticles biosynthesis and its effect on chlorophyll contents in the leaves of clusterbean (*Cyamopsis tetragonoloba* L.). *Adv Sci Eng Med.* 2014;6(5):538-545.
38. Cai L, Chen J, Liu Z, Wang H, Yang H, Ding W. Magnesium oxide nanoparticles: effective agricultural antibacterial agent against *Ralstonia solanacearum*. *Front Microbiol.* 2018; 9:790.
39. Mirzaei H, Davoodnia A. Microwave assisted sol-gel synthesis of MgO nanoparticles and their catalytic activity in the synthesis of hantzsch 1, 4-dihydropyridines. *Chinese J Catal* 2012;33(9-10):1502-1507.
40. Layek K, Kantam ML, Shirai M, Nishio-Hamane D, Sasaki T, Maheswaran H. Gold nanoparticles stabilized on nanocrystalline magnesium oxide as an active catalyst for reduction of nitroarenes in aqueous medium at room temperature. *Green Chem.* 2012;14(11):3164-3174.
41. SAFAEI GJ, Zahedi S, Javid M, Ghasemzadeh MA. MgO nanoparticles: an efficient, green and reusable catalyst for the onepot syntheses of 2, 6-dicyanoanilines and 1, 3-diarylpropyl malononitriles under different conditions. *J Nanostruct.* 2015;5(2):153-160.
42. Venkatesha TG, Viswanatha R, Nayaka YA, Chethana BK. Kinetics and thermodynamics of reactive and vat dyes adsorption on MgO nanoparticles. *Chem Eng J* 2012; 198:1-10.
43. Haldorai Y, Shim JJ. An efficient removal of methyl orange dye from aqueous solution by adsorption onto chitosan/MgO composite: A novel reusable adsorbent. *Appl Surf Sci.* 2014; 292:447-453.
44. Moussavi G, Mahmoudi M. Removal of azo and anthraquinone reactive dyes from industrial wastewaters using MgO nanoparticles. *J Hazard Mater.* 2009;168(2-3):806-812.
45. Ponraj R, Kannan AG, Ahn JH, Kim DW. Improvement of cycling performance of lithium-sulfur batteries by using magnesium oxide as a functional additive for trapping lithium polysulfide. *ACS Appl Mater Interfaces.* 2016;8(6):4000-4006.
46. Xiang M, Wu H, Liu H, Huang J, Zheng Y, Yang L, Jing P, Zhang Y, Dou S, Liu H. A flexible 3D multifunctional MgO-decorated carbon foam@ CNTs hybrid as self-supported cathode for high-performance lithium-sulfur batteries. *Adv Funct Mater.* 2017;27(37):1702573.
47. Petnikota S, Rotte NK, Reddy MV, Srikanth VV, Chowdari BV. MgO-decorated few-layered graphene as an anode for Li-ion batteries. *ACS Appl Mater Interfaces.* 2015;7(4):2301-2309.
48. Sharma M, Sharma DG. Synthesis of Nanostructured Magnesium Oxide by Sol Gel Method and Its Characterization. *Int J Pharm Sci Res.* 2018;9(4):1576-1581.
49. Pilarska AA, Klapiszewski Ł, Jesionowski T. Recent development in the synthesis, modification and application of Mg(OH)₂ and MgO: A review. *Powder Technol.* 2017; 319:373-407.
50. Huang L, Li DQ, Lin YJ, Wei M, Evans DG, Duan X. Controllable preparation of Nano-MgO and investigation of its bactericidal properties. *J Inorg Biochem.* 2005;99(5):986-993.
51. Stankic S, Müller M, Diwald O, Sterrer M, Knözinger E, et al. Size-dependent optical properties of MgO nanocubes.

- Angew Chem Int Ed. 2005;44(31):4917-4920.
52. Azhar AZ, Mohamad H, Ratnam MM, Ahmad ZA. Effect of MgO particle size on the microstructure, mechanical properties and wear performance of ZTA-MgO ceramic cutting inserts. *Int J Refract Hard Met.* 2011;29(4):456-461.
 53. Ding Y, Wu H, Hai B, Wang L, Qian Y. Nanoscale magnesium hydroxide and magnesium oxide powders: control over size, shape, and structure via hydrothermal synthesis. *Chem Mater.* 2001;13(2):435-440.
 54. Sakho EH, Allahyari E, Oluwafemi OS, Thomas S, Kalarikkal N. Dynamic Light Scattering (DLS) in: Thermal and rheological measurement techniques for nanomaterials characterization. 2011.
 55. Bondoc LL, Fitzpatrick S. Size distribution analysis of recombinant adenovirus using disc centrifugation. *J Ind Microbiol Biotechnol.* 1998;20(6):317-322.
 56. Meijering E, Dzyubachyk O, Smal I. Methods for cell and particle tracking. *Methods Enzymol.* 2012; 504: 183-200.
 57. Bayley H, Martin CR. Resistive-pulse sensing from microbes to molecules. *Chem Rev.* 2000;100(7):2575-2594.
 58. Hiesgen R, Friedrich KA. Atomic force microscopy. In *PEM Fuel Cell Diagnostic Tools.* 2011:395-422.
 59. Wang L. Transmission electron microscopy of shape-controlled nanocrystals and their assemblies. *J Phys Chem. B.* 2000; 104:1153-1175.
 60. Tang ZX, Fang XJ, Zhang ZL, Zhou T, Zhang XY, Shi LE. Nanosize MgO as antibacterial agent: preparation and characteristics. *Braz. J Chem Eng.* 2012;29(4):775-781.
 61. Luo F, Lu J, Wang W, Tan F, Qiao X. Preparation and antibacterial activity of magnesium oxide nanoplates via sol-gel process. *Micro Nano Lett.* 2013;8(9):479-482.
 62. Al-Ghamdi AA, Al-Hazmi F, Alnowaiser F, Al-Tuwirqi RM, Al-Ghamdi AA, Alhartomy OA, et al. A new facile synthesis of ultra fine magnesium oxide nanowires and optical properties. *J Electroceram.* 2012;29(3):198-203.
 63. Rao KG, Ashok CH, Rao KV, Chakra CS. Structural properties of MgO nanoparticles: synthesized by co-precipitation technique. *Int J Sci Res.* 2014;3(12):43-6.
 64. Suresh J, Yuvakkumar R, Sundrarajan M, Hong SI. Green synthesis of magnesium oxide nanoparticles. *Adv Mater Res.* 2014; 952:141-144.
 65. Boddu VM, Viswanath DS, Maloney SW. Synthesis and characterization of coralline magnesium oxide nanoparticles. *J Am Ceram Soc.* 2008;91(5):1718-1720.
 66. Sundrarajan M, Suresh J, Gandhi RR. A comparative study on antibacterial properties of MgO nanoparticles prepared under different calcination temperature. *Dig J Nanomater Biostruct.* 2012;7(3):983-989.
 67. Vergheese M, Vishal SK. Green synthesis of magnesium oxide nanoparticles using *Trigonella foenum-graecum* leaf extract and its antibacterial activity. *J Pharmacogn Phytochem.* 2018;7:1193-1200.
 68. Kumaran RS, Choi YK, Singh V, Song HJ, Song KG, Kim KJ, et al. In vitro cytotoxic evaluation of MgO nanoparticles and their effect on the expression of ROS genes. *Int J Mol.* 2015;16(4):7551-7564.
 69. Meenakshi SD, Rajarajan M, Rajendran S, Kennedy ZR, Brindha G. Synthesis and characterization of magnesium oxide nanoparticles. *Elixir Int J.* 2012;50(9):10618-10620.
 70. Shikha M, Aakash S, Vipin K. Synthesis and Characterization of MgO Nanoparticles by Orange Fruit Waste through Green Method. *Int J Adv Res Chem Sci.* 2017;4(9):36-42.
 71. Abdallah Y, Ogunyemi SO, Abdelazez A, Zhang M, Hong X, Ibrahim E, et al. The green synthesis of MgO nano-Flowers using *Rosmarinus officinalis* L. (Rosemary) and the antibacterial activities against *Xanthomonas oryzae* pv. *oryzae*. *Biomed Res Int.* 2019;2019: 5620989.
 72. Chandran A, Prakash J, Naik KK, Srivastava AK, Dąbrowski R, Czerwiński M, et al. Preparation and characterization of MgO nanoparticles/ferroelectric liquid crystal composites for faster display devices with improved contrast. *J Mater Chem C.* 2014;2(10):1844-1853.
 73. Sharma G, Soni R, Jasuja D. Phytoassisted synthesis of magnesium oxide nanoparticles with *Swertia chirayaita*. *J Taibah Univ Sci.* 2017;11(3):471-477.
 74. Al-Hazmi F, Alnowaiser F, Al-Ghamdi AA, Al-Ghamdi AA, Aly MM, Al-Tuwirqi RM, et al. A new large-scale synthesis of magnesium oxide nanowires: structural and antibacterial properties. *Superlattices Microstruct.* 2012;52(2):200-209.
 75. Ganguly A, Trinh P, Ramanujachary KV, Ahmad T, Mugweru A, Ganguli AK. Reverse micellar based synthesis of ultrafine MgO nanoparticles (8–10 nm): Characterization and catalytic properties. *J Colloid Interface Sci.* 2011;353(1):137-142.
 76. Alvarado E, Torres-Martinez LM, Fuentes AF, Quintana P. Preparation and characterization of MgO powders obtained from different magnesium salts and the mineral dolomite. *Polyhedron.* 2000;19(22-23):2345-2351.
 77. Bindhu MR, Umadevi M, Micheal MK, Arasu MV, Al-Dhabi NA. Structural, morphological and optical properties of MgO nanoparticles for antibacterial applications. *Mater Lett.* 2016;166:19-22.
 78. Camtakan Z, Erenturk S, Yusan S. Magnesium oxide nanoparticles: preparation, characterization, and uranium sorption properties. *Environ. Prog. Sustainable Energy.* 2012;31(4):536-543.
 79. Duong TH, Nguyen TN, Oanh HT, Dang Thi TA, Giang LN, Phuong HT, et al. Synthesis of Magnesium Oxide Nanoplates and Their Application in Nitrogen Dioxide and Sulfur Dioxide Adsorption. *J Chem.* 2019;2019: 4376429
 80. Wang W, Qiao X, Chen J, Li H. Facile synthesis of magnesium oxide nanoplates via chemical precipitation. *Mater Lett.* 2007;61(14-15):3218-3220.
 81. Shah MA, Qurashi A. Novel surfactant-free synthesis of MgO nanoflakes. *J Alloys Compd.* 2009;482(1-2):548-551.
 82. Hong YC, Uhm HS. Synthesis of MgO nanopowder in atmospheric microwave plasma torch. *Chem. Phys. Lett.* 2006;422(1-3):174-178.
 83. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA: Cancer J Clin.* 2011;61(2):69-90.
 84. Pugazhendhi A, Prabhu R, Muruganathan K, Shanmuganathan R, Natarajan S. Anticancer, antimicrobial and photocatalytic activities of green synthesized magnesium oxide nanoparticles (MgONPs) using aqueous extract of *Sargassum wightii*. *J Photochem Photobiol. B, Biol.* 2019;190:86-97.
 85. Karthik K, Dhanuskodi S, Kumar SP, Gobinath C, Sivaramkrishnan S. Microwave assisted green synthesis of MgO nanorods and their antibacterial and anti-breast cancer activities. *Mater Lett.* 2017; 206:217-220.
 86. Krishnamoorthy K, Moon JY, Hyun HB, Cho SK, Kim SJ. Mechanistic investigation on the toxicity of MgO nanoparticles toward cancer cells. *J Mater. Chem.* 2012;22(47):24610-24617.
 87. Chalkidou A, Simeonidis K, Angelakeris M, Samaras T,

- Martinez-Boubeta C, Balcells L, et al. In vitro application of Fe/MgO nanoparticles as magnetically mediated hyperthermia agents for cancer treatment. *J Magn Magn Mater.* 2011;323(6):775-780.
88. Kumar R, Gokulakrishnan N, Kumar R, Krishna VM, Saravanan A, Supriya S, et al. Can Be a Bimetal Oxide ZnO—MgO Nanoparticles Anticancer Drug Carrier and Deliver? Doxorubicin Adsorption/Release Study. *J Nanosci Nanotechnol.* 2015;15(2):1543-1553.
 89. Majeed S, Danish M, Muhadi NF. Genotoxicity and apoptotic activity of biologically synthesized magnesium oxide nanoparticles against human lung cancer A-549 cell line. *Adv Nat Sci.: Nanosci Nanotechnol.* 2018;9(2):025011.
 90. Ciccarese F, Raimondi V, Sharova E, Silic-Benussi M, Ciminale V. Nanoparticles as Tools to Target Redox Homeostasis in Cancer Cells. *Antioxidants.* 2020;9(3):211.
 91. Di DR, He ZZ, Sun ZQ, Liu J. A new nano-cryosurgical modality for tumor treatment using biodegradable MgO nanoparticles. *Nanomed. Nanotechnol. Biol Med.* 2012;8(8):1233-1241.
 92. Behzadi E, Sarsharzadeh R, Nouri M, Attar F, Akhtari K, Shahpasand K, et al. Albumin binding and anticancer effect of magnesium oxide nanoparticles. *Int J Nanomedicine.* 2019; 14:257-270.
 93. Kelly D, Conway S, Aminov R. Commensal gut bacteria: mechanisms of immune modulation. *Trends Immunol.* 2005 ;26(6):326-333.
 94. Hui YH. *Handbook of fermented meat and poultry.* John Wiley & Sons; 2014.
 95. Raghunath A, Perumal E. Metal oxide nanoparticles as antimicrobial agents: a promise for the future. *Int J Antimicrob. Agents.* 2017;49(2):137-152.
 96. Amann S, Neef K, Kohl S. Antimicrobial resistance (AMR). *Eur J Hosp Pharm.* 2019;26(3):175-177.
 97. Gross M. *Antibiotics in crisis;* 2013.
 98. Azam A, Ahmed AS, Oves M, Khan MS, Habib SS, Memic A. Antimicrobial activity of metal oxide nanoparticles against Gram-positive and Gram-negative bacteria: a comparative study. *Int J Nanomed* 2012; 7:6003-6007.
 99. Slavin YN, Asnis J, Häfeli UO, Bach H. Metal nanoparticles: understanding the mechanisms behind antibacterial activity. *J Nanobiotechnology.* 2017;15(1):1-20.
 100. Tang ZX, Lv BF. MgO nanoparticles as antibacterial agent: preparation and activity. *Braz J Chem Eng.* 2014;31(3):591-601.
 101. Maji J, Pandey S, Basu S. Synthesis and evaluation of antibacterial properties of magnesium oxide nanoparticles. *Bull Mater Sci.* 2020;43(1):25.
 102. Mageshwari K, Mali SS, Sathyamoorthy R, Patil PS. Template-free synthesis of MgO nanoparticles for effective photocatalytic applications. *Powder Technol.* 2013; 249:456-462.
 103. Nguyen NY, Grelling N, Wetteland CL, Rosario R, Liu H. Antimicrobial activities and mechanisms of magnesium oxide nanoparticles (nMgO) against pathogenic bacteria, yeasts, and biofilms. *Sci Rep* 2018;8(1):1-23.
 104. He Y, Ingudam S, Reed S, Gehring A, Strobaugh TP, Irwin P. Study on the mechanism of antibacterial action of magnesium oxide nanoparticles against foodborne pathogens. *J Nanobiotechnol.* 2016;14(1):54-63.
 105. Vatsha B, Tetyana P, Shumbula PM, Ngila JC, Sikhwivhilu LM, Moutloali RM. Effects of precipitation temperature on nanoparticle surface area and antibacterial behaviour of Mg (OH) 2 and MgO nanoparticles. *J Biomater Nanobiotechnol.* 2013;4(4):365-372.
 106. Huang L, Li DQ, Evans DG, Duan X. Preparation of highly dispersed MgO and its bactericidal properties. *Eur Phys J D At Mol Opt Phys.* 2005;34(1-3):321-323.
 107. Jin T, He Y. Antibacterial activities of magnesium oxide (MgO) nanoparticles against foodborne pathogens]. *Nanoparticle Res.* 2011;13(12):6877-6885.
 108. Suresh J, Rajiv GR, Gowri S, Selvam S, Sundrarajan M. Surface modification and antibacterial behaviour of bio-synthesized mgo nanoparticles coated cotton fabric. *J. Biobased Mater. Bioenergy.* 2012;6(2):165-171.
 109. Sawai J, Kojima H, Igarashi H, Hashimoto A, Shoji S, Sawaki T, et al. Antibacterial characteristics of magnesium oxide powder. *World J Microbiol Biotechnol.* 2000;16(2):187-194.
 110. Cai Y, Li C, Wu D, Wang W, Tan F, Wang X, et al. Highly active MgO nanoparticles for simultaneous bacterial inactivation and heavy metal removal from aqueous solution. *Biochem. Eng J* 2017; 312:158-166.
 111. Krishnamoorthy K, Manivannan G, Kim SJ, Jeyasubramanian K, Premanathan M. Antibacterial activity of MgO nanoparticles based on lipid peroxidation by oxygen vacancy. *J Nanopart Res.* 2012;14(9):1063.
 112. Jeevanandam J, San Chan Y, Danquah MK. Evaluating the antibacterial activity of MgO nanoparticles synthesized from aqueous leaf extract. *Med One.* 2019;4(3):1-18.
 113. Karthik K, Dhanuskodi S, Gobinath C, Prabukumar S, Sivaramakrishnan S. Fabrication of MgO nanostructures and its efficient photocatalytic, antibacterial and anticancer performance. *J Photochem Photobiol, B.* 2019; 190:8-20.
 114. Patel MK, Zafaryab M, Rizvi M, Agrawal VV, Ansari ZA, Malhotra BD, et al. Antibacterial and cytotoxic effect of magnesium oxide nanoparticles on bacterial and human cells. *J Nanoeng Nanomanuf.* 2013;3(2):162-166.
 115. Huang L, Li D, Lin Y, Evans DG, Duan X. Influence of nano-MgO particle size on bactericidal action against *Bacillus subtilis* var. *niger*. *Chin Sci Bull.* 2005;50(6):514-519.
 116. Ibrahim EJ, Thalij KM, Badawy AS. Antibacterial potential of magnesium oxide nanoparticles synthesized by *Aspergillus niger*. *Biotechnol J Int* 2017;18(1):1-7.
 117. Schwechheimer C, Kuehn MJ. Outer-membrane vesicles from Gram-negative bacteria: Biogenesis and functions. *Nat Rev Microbiol.* 2015;13(10):605-619.
 118. Imada K, Sakai S, Kajihara H, Tanaka S, Ito S. Magnesium oxide nanoparticles induce systemic resistance in tomato against bacterial wilt disease. *Plant Pathol.* 2016;65(4):551-560.
 119. Sawai J, Yoshikawa T. Quantitative evaluation of antifungal activity of metallic oxide powders (MgO, CaO and ZnO) by an indirect conductimetric assay. *J Appl Microbiol.* 2004;96(4):803-809.
 120. Cai Y, Wu D, Zhu X, Wang W, Tan F, Chen J, et al. Sol-gel preparation of Ag-doped MgO nanoparticles with high efficiency for bacterial inactivation. *Ceram Int.* 2017;43(1):1066-1072.
 121. Umar A, Rahman MM, Hahn YB. MgO polyhedral nanocages and nanocrystals based glucose biosensor. *Electrochem Commun.* 2009;11(7):1353-1357.
 122. Aghebati-maleki L, Salehi B, Behfar R, Saeidmanesh H, Ahmadian F, Sarebanhassanabadi M, et al. Designing a hydrogen peroxide biosensor using catalase and modified electrode with magnesium oxide nanoparticles. *Int J Electrochem Sci.* 2014; 9:257-271.

123. Lu L, Zhang L, Zhang X, Wu Z, Huan S, Shen G, et al. A MgO nanoparticles composite matrix-based electrochemical biosensor for hydrogen peroxide with high sensitivity. *Electroanalysis*. 2010;22(4):471-477.
124. Zhao J, Qin L, Hao Y, Guo Q, Mu F, Yan Z. Application of tubular tetrapod magnesium oxide in a biosensor for hydrogen peroxide. *Microchim Acta*. 2012;178(3-4):439-445.
125. Dong XX, Li MY, Feng NN, Sun YM, Yang C, Xu ZL. A nanoporous MgO based nonenzymatic electrochemical sensor for rapid screening of hydrogen peroxide in milk. *RSC Adv*. 2015;5(105):86485-86489.
126. Li H, Li M, Qiu G, Li C, Qu C, Yang B. Synthesis and characterization of MgO nanocrystals for biosensing applications. *J Alloys Compd*. 2015; 632:639-644.
127. Zhao L, Li H, Gao S, Li M, Xu S, Li C, et al. MgO nanobelt-modified graphene-tantalum wire electrode for the simultaneous determination of ascorbic acid, dopamine and uric acid. *Electrochim Acta*. 2015; 168:191-198.
128. Li M, Guo W, Li H, Dai W, Yang B. Electrochemical biosensor based on one-dimensional MgO nanostructures for the simultaneous determination of ascorbic acid, dopamine, and uric acid. *Sens Actuators, B*. 2014; 204:629-636.
129. Patel MK, Agrawal VV, Malhotra BD, Ansari SG. Nanostructured magnesium oxide: a suitable material for DNA based biosensors. *Mater Focus*. 2014;3(1):1-11.
130. Patel MK, Ali MA, Zafaryab M, Agrawal VV, Rizvi MM, Ansari ZA, et al. Biocompatible nanostructured magnesium oxide-chitosan platform for genosensing application. *Biosens Bioelectron*. 2013; 45:181-188.
131. Mohammadi H, Yammouri G, Amine A. Current advances in electrochemical genosensors for detecting microRNA cancer markers. *Curr Opin Electrochem*. 2019; 16:96-105.
132. Shuai HL, Huang KJ, Zhang WJ, Cao X, Jia MP. Sandwich-type microRNA biosensor based on magnesium oxide nanoflower and graphene oxide-gold nanoparticles hybrids coupling with enzyme signal amplification. *Sens Actuators, B*. 2017; 243:403-411.
133. Lysaght MJ, Reyes J. The growth of tissue engineering. *Tissue Eng*. 2001;7(5):485-493.
134. Griffith LG, Naughton G. Tissue engineering--current challenges and expanding opportunities. *Science*. 2002;295(5557):1009-1014.
135. Boys AJ, McCorry MC, Rodeo S, Bonassar LJ, Estroff LA. Next generation tissue engineering of orthopedic soft tissue-to-bone interfaces. *MRS Commun*. 2017;7(3):289-308.
136. Tarafder S, Dernel WS, Bandyopadhyay A, Bose S. SrO- and MgO-doped microwave sintered 3D printed tricalcium phosphate scaffolds: Mechanical properties and in vivo osteogenesis in a rabbit model. *J Biomed. Mater. Res. Part B Appl. Biomater. J Biomed Mater Res B*. 2015;103(3):679-690.
137. Bandyopadhyay A, Bose S, editors. *Characterization of biomaterials*. Newnes; 2013.
138. Kaur P, Singh KJ, Yadav AK, Sood H, Kaur S, Kaur R, et al. Preliminary investigation of the effect of doping of copper oxide in CaO-SiO₂-P₂O₅-MgO bioactive composition for bone repair applications. *Mater Sci Eng C*. 2018; 83:177-186.
139. Hickey DJ, Ercan B, Sun L, Webster TJ. Adding MgO nanoparticles to hydroxyapatite-PLLA nanocomposites for improved bone tissue engineering applications. *Acta Biomater*. 2015; 14:175-184.
140. Pye AD, Lockhart DE, Dawson MP, Murray CA, Smith AJ. A review of dental implants and infection. *J Hosp Infect* 2009;72(2):104-110.
141. Osman RB, Swain MV. A critical review of dental implant materials with an emphasis on titanium versus zirconia. *Materials*. 2015;8(3):932-958.
142. Tomsia AP, Launey ME, Lee JS, Mankani MH, Wegst UG, Saiz E. Nanotechnology approaches for better dental implants. *Int J Oral Maxillofac Implants*. 2011; 26:25-49.
143. Gupta A, Singh G, Afreen S. Application of Nanotechnology in Dental Implants. *J Med Dent Sci*. 2017;16(11):77-81.
144. Al-Noaman A, Rawlinson SC, Hill RG. The role of MgO on thermal properties, structure and bioactivity of bioactive glass coating for dental implants. *J Non-Cryst Solids*. 2012;358(22):3019-3027.
145. Baino F, Hamzehlou S, Kargozar S. Bioactive glasses: where are we and where are we going?. *J Funct Biomater*. 2018;9(1):1-25.
146. Hench LL. Genetic design of bioactive glass. *J Eur Ceram. Soc*. 2009;29(7):1257-1265.
147. Carvalho SM, Moreira CD, Oliveira AC, Oliveira AA, Lemos EM, Pereira MM. Bioactive glass nanoparticles for periodontal regeneration and applications in dentistry. In *Nanobiomaterials in clinical dentistry*. 2019:351-383. Elsevier.
148. Siqueira RL, Peitl O, Zanutto ED. Gel-derived SiO₂-CaO-Na₂O-P₂O₅ bioactive powders: Synthesis and *in vitro* bioactivity. *Mater Sci Eng C*. 2011;31(5):983-991.
149. Massera J, Hupa L, Hupa M. Influence of the partial substitution of CaO with MgO on the thermal properties and in vitro reactivity of the bioactive glass S53P4. *J Non-Cryst Solids*. 2012;358(18-19):2701-2707.
150. Singh RK, Srinivasan A. Bioactivity of ferrimagnetic MgO-CaO-SiO₂-P₂O₅-Fe₂O₃ glass-ceramics. *Ceramics International*. 2010;36(1):283-290.
151. Agathopoulos S, Tulyaganov DU, Ventura JM, Kannan S, Karakassides MA, Ferreira JM. Formation of hydroxyapatite onto glasses of the CaO-MgO-SiO₂ system with B₂O₃, Na₂O, CaF₂ and P₂O₅ additives. *Biomaterials*. 2006;27(9):1832-1840.
152. Erol M, Özyuguran A, Çelebican Ö. Synthesis, characterization, and in vitro bioactivity of sol-gel-derived Zn, Mg, and Zn-Mg Co-doped bioactive glasses. *Chem Eng Technol*. 2010;33(7):1066-1074.
153. Correia CO, Leite AJ, Mano JF. Chitosan/bioactive glass nanoparticles scaffolds with shape memory properties. *Carbohydr Polym*. 2015; 123:39-45.
154. Mota J, Yu N, Caridade SG, Luz GM, Gomes ME, Reis RL, et al. Chitosan/bioactive glass nanoparticle composite membranes for periodontal regeneration. *Acta Biomater*. 2012;8(11):4173-4180.
155. Luz GM, Mano JF. Chitosan/bioactive glass nanoparticles composites for biomedical applications. *Biomed Mater*. 2012;7(5):1-9.
156. Imani AA, Hosseini HM, Hafezi F, Hosseinnejad F, Nourani MR. Sol-gel-derived bioactive glass containing SiO₂-MgO-CaO-P₂O₅ as an antibacterial scaffold. *J Biomed Mater Res Part A*. 2013;101(6):1582-1587.
157. Kansal I, Goel A, Tulyaganov DU, Rajagopal RR, Ferreira JM. Structural and thermal characterization of CaO-MgO-SiO₂-P₂O₅-CaF₂ glasses. *J Eur Ceram Soc*. 2012;32(11):2739-2746.

158. Harun WS, Kamariah MS, Muhamad N, Ghani SA, Ahmad F, Mohamed Z. A review of powder additive manufacturing processes for metallic biomaterials. *Powder Technol.* 2018; 327:128-151.
159. Lopez-Esteban S, Saiz E, Fujino S, Oku T, Suganuma K, Tomsia AP. Bioactive glass coatings for orthopedic metallic implants. *J Eur Ceram Soc.* 2003;23(15):2921-2930.
160. Rabiee SM, Nazparvar N, Azizian M, Vashae D, Tayebi L. Effect of ion substitution on properties of bioactive glasses: A review. *Ceram Int.* 2015;41(6):7241-7251.
161. Aerts HJ, Velazquez ER, Leijenaar RT, Parmar C, Grossmann P, Carvalho S, et al. Decoding tumour phenotype by noninvasive imaging using a quantitative radiomics approach. *Nat. Commun.* 2014;5(1):1-9.
162. Kurland BF, Gerstner ER, Mountz JM, Schwartz LH, Ryan CW, Graham MM, et al. Promise and pitfalls of quantitative imaging in oncology clinical trials. *Magn Reson Imaging.* 2012;30(9):1301-1312.
163. Guo T, Lin M, Huang J, Zhou C, Tian W, Yu H, et al. The recent advances of magnetic nanoparticles in medicine. *J Nanomater.* 2018;2018(1):7805147.
164. Stueber DD, Villanova J, Aponte I, Xiao Z, Colvin VL. Magnetic Nanoparticles in Biology and Medicine: Past, Present, and Future Trends. *Pharmaceutics.* 2021;13(7):943.
165. Fang C, Zhang M. Multifunctional magnetic nanoparticles for medical imaging applications. *J Mater Chem.* 2009;19(35):6258-6266.
166. Anderson SD, Gwenin VV, Gwenin CD. Magnetic functionalized nanoparticles for biomedical, drug delivery and imaging applications. *Nanoscale Res Lett.* 2019;14(1):1-6.
167. Blasiak B, van Veggel FC, Tomanek B. Applications of nanoparticles for MRI cancer diagnosis and therapy. *J Nanomater.* 2013;2013(1):148578.
168. Martinez-Boubeta C, Simeonidis K, Serantes D, Conde-Leborán I, Kazakis I, Stefanou G, et al. Adjustable Hyperthermia Response of Self-Assembled Ferromagnetic Fe-MgO Core-Shell Nanoparticles by Tuning Dipole-Dipole Interactions. *Adv Funct Mater.* 2012;22(17):3737-3744.
169. Martinez-Boubeta C, Balcells L, Cristófol R, Sanfeliu C, Rodríguez E, Weissleder R, et al. Self-assembled multifunctional Fe/MgO nanospheres for magnetic resonance imaging and hyperthermia. *Nanomed.: Nanotechnol Biol Med.* 2010;6(2):362-370.
170. Boro B, Nath AK, Barthakur M, Kalita P. Synthesis and characterization of MgO nanoparticle and its in vitro cytotoxic effect on erythrocytes. In *Advances in Bioprocess Engineering and Technology* 2021:199-207.
171. Baravkar PN, Sayyed AA, Rahane CS, Chate GP, Wavhale RD, Pratinidhi SA, et al. Nanoparticle Properties Modulate Their Effect on the Human Blood Functions. *BioNanoScience.* 2021;11:816-824.
172. Bhattacharya P, Swain S, Giri L, Neogi S. Fabrication of magnesium oxide nanoparticles by solvent alteration and their bactericidal applications. *J Mater Chem. B.* 2019;7(26):4141-4152.
173. Alsaleh NB. Adverse cardiovascular responses of engineered Nanomaterials: Current understanding of molecular mechanisms and future challenges. *Nanomed Nanotechnol Biol Med.* 2021:102421.
174. Wang Z, Tang M. Research progress on toxicity, function, and mechanism of metal oxide nanoparticles on vascular endothelial cells. *J Appl Toxicol.* 2021;41(5):683-700.
175. Arecheewakul S, Adamcakova-Dodd A, Givens BE, Steines BR, Wang Y, Meyerholz DK, et al. Toxicity assessment of metal oxide nanomaterials using *in vitro* screening and murine acute inhalation studies. *NanoImpact.* 2020; 18:100214.
176. Wang Z, Tang M. Research progress on toxicity, function, and mechanism of metal oxide nanoparticles on vascular endothelial cells. *J Appl Toxicol.* 2021;41(5):683-700.
177. Mekky G, Seeds M, Diab AE, Shehata AM, Ahmed-Farid OA, Alzebedeh D, et al. The potential toxic effects of magnesium oxide nanoparticles and valproate on liver tissue. *J Biochem Mol Toxicol.* 2021;35(3):22676.
178. Naguib GH, Abd El-Aziz GS, Mously HA, Bukhary SM, Hamed MT. Assessment of the dose-dependent biochemical and cytotoxicity of zein-coated MgO nanowires in male and female albino rats. *Ann Med.* 2021;53(1):1850-1862.
179. Mangalampalli B, Dumala N, Perumalla VR, Grover P. Genotoxicity, biochemical, and biodistribution studies of magnesium oxide nano and microparticles in albino Wistar rats after 28-day repeated oral exposure. *Environ Toxicol.* 2018;33(4):396-410.
180. Mittag A, Schneider T, Westermann M, Gleis M. Toxicological assessment of magnesium oxide nanoparticles in HT29 intestinal cells. *Arch Toxicol.* 2019;93(6):1491-1500.