

Magnesium a Multifunctional Therapeutic Agent: Recent Updates on Mechanisms and Clinical Implications beyond Electrolyte Homeostasis

Jyoti Mahadev Benni^{1*}, Varsha Mahesh Shindhe²,
Reshma Nadaf³, Savita Hiremath⁴ and Fareedabanu Balikai⁵

¹Department of Pharmacology, Jawaharlal Nehru Medical College, KLE Academy of Higher Education and Research (KAHER), Deemed-to-be-University, Belagavi, Karnataka, India.

²Department of Physiology, Jawaharlal Nehru Medical College, KLE Academy of Higher Education and Research (KAHER), Deemed-to-be-University, Belagavi, Karnataka, India.

³Department of Pharmacology, Karnataka Medical College and Research Institute, Hubballi, Karnataka, India.

⁴Department of Physiology, SSPM Medical College and Lifetime Hospital, Padve, Shindudurga, Maharashtra, India.

⁵Department of Physiology, Universiti Sains Malaysia- KLE, International Medical Programme, Belagavi, Karnataka, India.

*Corresponding Author E-mail: drjyotibenni@jnmcc.edu

<https://dx.doi.org/10.13005/bpj/3487>

(Received: 13 January 2026; accepted: 08 June 2026)

Magnesium is a vital divalent cation involved in more than 300 enzymatic reactions crucial for cellular metabolism, neuromuscular transmission, and cardiovascular (CV) stability. Traditionally regarded as an electrolyte required for physiological homeostasis, magnesium is now increasingly recognized as a multifunctional modulator influencing diverse biochemical and pharmacological pathways. This narrative review examines the evolving pharmacological significance of magnesium supplementation beyond electrolyte balance, with emphasis on its mechanisms of action, therapeutic roles, and clinical implications. A targeted literature search was performed in PubMed, Scopus, and Google Scholar to retrieve relevant experimental and clinical studies published in English up to the year 2025. Articles addressing magnesium's physiological actions, deficiency states, and therapeutic interventions were critically reviewed and synthesized. Evidence indicates that magnesium exerts pleiotropic effects on cellular signalling, vascular tone, immune modulation, and neuronal excitability. Therapeutically, magnesium supplementation has been explored in CV disorders, metabolic syndrome, neurological conditions, inflammatory diseases, and oncology. Experimental studies further demonstrate its role in reducing oxidative stress, regulating apoptosis, and maintaining genomic stability. Overall, magnesium's pharmacological potential extends well beyond its classical role in electrolyte homeostasis. A deeper understanding of its diverse mechanisms may inform therapeutic innovation. However, further translational and clinical studies are desirable to find the optimal dosing strategies, formulations, and disease-specific applications.

Keywords: Cardioprotection, Magnesium, Metabolic syndrome, Neuroprotection, Oxidative stress, Pharmacological mechanisms, Pleiotropic effects.

Magnesium serves as a crucial mediator in a wide range of enzymatic and metabolic processes. Conventionally recognized for maintaining

neuromuscular and cardiac stability, its growing pharmacological significance in chronic diseases such as diabetes, hypertension, migraine, and

depression has garnered substantial attention in recent years. Magnesium is the fourth most abundant cation overall in the human body and the second most abundant within cells, following potassium.¹ It serves as a cofactor in more than 300 enzymatic reactions and functions as an essential electrolyte for neuromuscular excitability and cardiac rhythm—its physiological significance extends well outside ionic homeostasis.^{2,3}

Magnesium is a critical mineral and involved in approximately 80% of known metabolic functions, according to Workinger.⁴ Subclinical magnesium deficiency is now recognized as a widespread global issue, including in India, where 15–30% of the population reportedly fails to achieve suggested dietary intake levels.^{5,6} Contributing factors include poor dietary habits, frequent consumption of processed foods, and the usage of medicines such as diuretics, proton-pump inhibitors, and certain antibiotics that predispose to hypomagnesemia.⁷ Also, magnesium deficiency has been linked to various diseases like metabolic syndrome, insulin resistance, hypertension, migraine and mood disorders.⁸

Pharmacologically, magnesium exhibits diverse actions that underlie its extensive therapeutic applications across multiple organ systems. FDA-approved indications of magnesium formulations include the management of constipation, hypomagnesemia, seizure prevention in preeclampsia/eclampsia, acute nephritis in paediatric patients, and cardiac arrhythmias secondary to magnesium deficiency, as well as for use in soaking minor cuts and bruises.^{5,9} In addition, magnesium is used off-label in conditions such as acute asthma exacerbations, Torsades de pointes during advanced cardiac life support (ACLS), and as a tocolytic agent to prevent preterm labour.⁹

Recent research continues to elucidate magnesium's diverse biological roles, emphasizing its influence on oxidative stress, inflammation, and cellular signalling pathways.¹⁰ Mechanistically, magnesium functions as a natural calcium antagonist, modifies N-methyl-D-aspartate (NMDA) receptor actions, and supports endothelial nitric oxide synthesis and mitochondrial function.¹¹ These actions link magnesium status to the pathogenesis of CV, metabolic, and neuropsychiatric disorders.^{12,13} Growing clinical

evidence highlights magnesium supplementation as an effective adjunct therapy in several chronic diseases. Randomized controlled trials and meta-analyses report several benefits, including reduced blood pressure, improved glycaemic regulation, and relief of migraine and depressive symptoms.^{12, 14–16} Owing to its safety, low cost, and broad physiological effects, magnesium is now viewed not only as an essential nutrient but also as a promising pharmacological adjuvant in modern medicine.¹⁷

This review seeks to synthesize current evidence on the pharmacological significance of magnesium supplementation beyond its traditional role in electrolyte balance. It studies magnesium's physiological functions, deficiency-related disorders, therapeutic applications, and underlying mechanisms across various body systems. Also, mentions the observed common adverse drug reactions with magnesium supplementation. By integrating classical physiological understanding with recent clinical advances, the review underscores magnesium's evolution from a basic electrolyte to a multifunctional therapeutic agent with wide-ranging systemic benefits.

Search strategy

A focused literature exploration was conducted in PubMed, Scopus, and Google Scholar using the specified keywords “magnesium,” “supplementation,” “pharmacology,” “therapeutic applications,” “mechanisms,” and “clinical benefits.” Appropriate original research articles, reviews, and meta-analyses published in English up to October 2025 were referred to. Additional references were identified by reviewing the bibliographies of key papers. The selection emphasized studies that explored the pharmacodynamic and pharmacokinetic aspects of magnesium, its mechanistic roles across physiological systems, and emerging therapeutic applications beyond its traditional role in electrolyte balance.

Pharmacological basis of the therapeutic applications of magnesium

The subsequent sections outline its physiological role and pharmacological basis for its clinical potential in metabolic, cardiovascular, neurological, obstetric, respiratory, gastrointestinal, and musculoskeletal systems, along with emerging therapeutic indications supported by contemporary

evidence. The diverse therapeutic applications of magnesium supplementation are summarized in Table 1, which outlines the mechanisms of action, clinical indications, dosage used and key references.

Role of Magnesium in Glucose Homeostasis and Diabetes Mellitus (DM)

Magnesium mediates a vital part in insulin secretion, glucose utilization, and cellular glucose transport.¹⁸ It functions as an insulin sensitizer by facilitating autophosphorylation of insulin receptors and regulating tyrosine kinase activity at the receptor level.¹⁹ A decline in intracellular magnesium concentrations permits excessive calcium entry into adipocytes, triggering oxidative stress and inflammation and thereby exacerbating insulin resistance, which contributes to the development of metabolic syndrome.²⁰ Persistent hypomagnesemia has been linked to the development of DM, suboptimal glycaemic control in type 2 DM (T2DM), and a heightened risk of both microvascular and macrovascular complications.²¹

Magnesium supplementation has improved the insulin sensitivity and glycaemic control in T2DM patients.²² Meta-analyses have demonstrated that oral magnesium intake reduces fasting plasma glucose levels, improves glycaemic control, and enhances HOMA-IR indices.²³ Trials have used varied doses (200–400 mg elemental magnesium per day) over 4–24 weeks.²³ Other studies report small but statistically significant control in fasting glucose and insulin-sensitivity markers among individuals with diabetes or insulin resistance, with greater effects observed in those with lower baseline magnesium levels.^{24,25}

The proposed mechanisms of magnesium include, modulation of insulin receptor phosphorylation, activation of the phosphatidylinositol 3'-kinase (PI3K)-Akt (PI3K/Akt) signalling pathway, and suppression of systemic inflammation.²⁶ Magnesium serves as an essential cofactor for numerous enzymes involved in glycolysis and oxidative metabolism, influencing key steps of carbohydrate utilization.¹⁸ It regulates ATP-dependent enzymatic reactions and glucose transport across cell membranes, stabilizing membrane potential and enhancing insulin-mediated glucose uptake.²⁷ Collectively, these findings indicate that maintaining adequate

magnesium status may serve as a preventive and adjunctive therapeutic strategy in diabetes and related metabolic disorders.

Role of Magnesium in Lipid Metabolism, and Cardiac Diseases

Magnesium supports CV health through multiple harmonizing mechanisms, including vasodilation, antiarrhythmic activity, and protection of endothelial function. It counteracts vascular smooth muscle contraction by antagonizing calcium influx through voltage-gated calcium channels and reduces oxidative stress and inflammation within endothelial cells.²⁸ It also modulates vascular tone and nitric oxide synthesis, thereby improving endothelial reactivity.²⁹ In addition, magnesium limits ischemic cellular injury by preventing calcium overload in cardiomyocytes and coronary vasculature.³⁰ Also, magnesium exhibits intrinsic antiplatelet and anticoagulant properties. By acting as a natural calcium antagonist, it inhibits platelet activation, decreases thromboxane A₂ synthesis, and enhances prostacyclin production, thereby reducing the risk of thrombosis.³¹

Hypomagnesemia has been linked to dyslipidaemia, characterized by decreased high-density lipoprotein (HDL) cholesterol and increased triglyceride and total cholesterol levels.³² In addition, low magnesium status is associated with an increased risk of heart failure, cardiac arrhythmias, and sudden cardiac death, highlighting its critical role in maintaining myocardial electrical stability and vascular health.³³ Multiple prospective cohort studies have confirmed that lower circulating magnesium levels are predictive of increased risk for atrial fibrillation, ventricular arrhythmias, and mortality from sudden cardiac death.³⁴

A randomized controlled trial reported that, supplementation with magnesium has been linked with enhanced exercise tolerance in stable coronary artery disease patients, along with enhancements in insulin sensitivity, lipid metabolism, and reduced platelet aggregation and thrombosis.³⁵ A recent umbrella meta-analysis concluded that, magnesium supplementation of e"300–400 mg/day in individuals with hypertension and magnesium deficiency, significantly reduced systolic and diastolic blood pressure.³⁶ In acute cardiac care, intravenous magnesium sulphate remains the preferred drug for the treatment of Torsade's de Pointes (polymorphic ventricular

tachycardia), even with normal serum magnesium levels.³⁷ This antiarrhythmic action is mediated by the modulation of inward calcium and outward potassium currents, leading to stabilization of cardiac membrane potentials and suppression of early afterdepolarizations.³⁸ Growing evidence indicates that sufficient magnesium intake may lower the risk of atrial fibrillation, heart failure, and sudden cardiac death.³⁹

These findings support that magnesium has vasodilatory, anti-thrombotic, antiarrhythmic and metabolic-modulating roles in cardiac health. Hence, maintaining optimal magnesium status—through diet or supplementation—may serve as both a preventive and adjunctive therapeutic strategy in cardiovascular disorders.

Neuroprotective and Psychotropic Roles of Magnesium

Magnesium produces notable neuroprotective and psychotropic effects by modulating neuronal excitability, regulating neurotransmitter activity, and attenuating neuroinflammatory processes.^{40,41} As a physiological NMDA receptor antagonist, magnesium limits excessive calcium influx, thereby preventing excitotoxic neuronal injury and promoting synaptic plasticity and cognitive stability. It also modulates GABAergic and glutamatergic transmission, contributing to anxiolytic and antidepressant effects.⁴¹ Moreover, magnesium inhibits microglial activation and the release of proinflammatory cytokines such as interleukin-6 (IL-6) and Tumor Necrosis Factor alpha (TNF- α), thereby attenuating oxidative stress and neuroinflammation implicated in Alzheimer's disease as well as mood and cognitive disorders.⁴²

Hypomagnesemia has been connected with an augmented incidence of migraines, peripheral neuropathies, neuroinflammation, neurodegenerative disorders, and impairments in cognitive function and mood.⁴³ Additionally, deficient magnesium levels also disturb the hypothalamic–pituitary–adrenal (HPA) axis, resulting in disruption of cortisol regulation, increased stress response activation, and involvement in the pathogenesis of anxiety and depression.⁴⁴ Magnesium deficiency also augments excitotoxic neuronal injury through unchecked NMDA receptor–mediated calcium influx.⁴⁵

Randomized controlled trials have shown

that oral magnesium supplementation improves mood in individuals with mild to moderate depression, producing effects comparable to those of low-dose antidepressant therapy.⁴⁶ Both clinical and preclinical evidence support magnesium's role in alleviating depressive symptoms, reducing anxiety, and enhancing cognitive function, particularly in individuals with hypomagnesemia or stress-related disorders.^{46,47} Intake of Magnesium has also been shown to decrease the frequency and severity of migraine.⁴⁶ In Parkinson's disease, altered magnesium levels are associated with transporter dysfunction and their supplementation helps to stabilize these mechanisms and potentially slow disease progression.⁴⁸

At the molecular level, magnesium modulates the NMDA receptor complex, blocking excessive calcium influx to prevent excitotoxic neuronal injury and promoting synaptic plasticity.^{41,45} Additionally, magnesium reduces neuroinflammation by inhibiting microglial activation and lowering proinflammatory cytokine release, including IL-6 and TNF- α .⁴² Collectively, these findings indicate that maintaining optimal magnesium status supports neuroprotection, stress resilience, and mood stability.

Anti-inflammatory and Antioxidant Mechanisms of Magnesium

Magnesium plays a pivotal role in maintaining immune and redox homeostasis. Hypomagnesemia leads to a state of low-grade systemic inflammation through nuclear factor kappa B (NF- κ B) activation and upsurge in inflammatory mediators, C-reactive protein (CRP) and IL-6.⁴⁹ It also elevates intracellular calcium levels and reactive oxygen species (ROS) generation, leading to mitochondrial dysfunction and reduced activity of antioxidant enzymes such as superoxide dismutase and glutathione peroxidase, thereby enhancing oxidative stress and endothelial dysfunction.⁵⁰

Conversely, magnesium supplementation downregulates NF- κ B activity, reduces circulating CRP and IL-6 levels, restores antioxidant enzyme activity, and improves nitric-oxide–mediated vasodilation.^{20,51} Clinical studies show that magnesium supplementation most consistently reduces CRP and improves endothelial function, with additional benefits on cardiometabolic biomarkers such as blood pressure and insulin

sensitivity, particularly in individuals with low baseline magnesium or elevated inflammatory status.⁵²

Through its anti-inflammatory and antioxidant mechanisms, magnesium exerts beneficial effects in conditions associated with oxidative and inflammatory stress including the metabolic syndrome, type 2 DM, hypertension, and cardiovascular diseases.⁵⁰ Additionally, by enhancing mitochondrial efficiency and reducing oxidative stress, magnesium supplementation has shown symptomatic benefits in disorders such as fibromyalgia, chronic fatigue syndrome and migraine.⁵³

Immunoregulatory Roles of Magnesium

Magnesium is a vital immunoregulatory micronutrient that influences both innate and adaptive immune responses by serving as a cofactor in over 300 enzymatic reactions.² It maintains ionic homeostasis in immune cells and acts as a physiological calcium antagonist,³¹ thereby regulating lymphocyte activation and T-cell receptor (TCR) signalling. Adequate intracellular magnesium is crucial for phosphorylation–dephosphorylation processes mediated by tyrosine kinases and phosphatases such as calcineurin, which are central to T-cell activation and cytokine regulation.⁵⁴ Mechanistically, magnesium supports immune tolerance by improving the differentiation and function of regulatory T-cells (Tregs), by shifting macrophage polarization from the pro-inflammatory toward the anti-inflammatory phenotype, and downregulating endothelial adhesion molecules—thereby reducing leukocyte infiltration and tissue inflammation.⁵⁵ It also facilitates mitochondrial ATP generation in immune cells, ensuring sufficient energy for phagocytosis and antigen presentation.⁵⁵

Magnesium deficiency disrupts these processes, leading to decreased cytotoxic function in CD8⁺ T cells and natural killer (NK) cells, hyperactivation of NF- κ B and the NLRP3 inflammasome, and elevated levels of pro-inflammatory cytokines such as IL-6, IL-1 α , and TNF- α .^{56,57} Conversely, magnesium supplementation restores immune balance by inhibiting NF- κ B translocation, enhancing antioxidant defences, and promoting the anti-inflammatory cytokines synthesis.⁵⁰

Clinically, magnesium exhibits immunomodulatory benefits across a range of inflammatory and allergic conditions. In asthma, intravenous magnesium sulphate is employed as adjunct therapy owing to its mast cell–stabilizing and bronchodilatory effects. In metabolic and cardiovascular diseases, magnesium supplementation mitigates systemic inflammation, oxidative stress, and endothelial dysfunction, leading to reductions in circulating CRP and IL-6.⁵² Emerging evidence also highlights its potential to attenuate COVID-19–related cytokine storm, enhance immune homeostasis, and improve vaccine responsiveness.⁵⁸ Collectively, these findings underscore magnesium as a critical micronutrient linking immunoregulation, redox balance, and clinical protection against inflammatory, allergic, and infectious diseases.

Magnesium role in musculoskeletal health and pain modulation

Magnesium is essential for muscle contraction–relaxation cycles, ATP production, and maintenance of bone integrity. It plays a central role in neuromuscular transmission, muscle relaxation, and modulation of pain perception.² It functions as a physiological calcium antagonist at voltage-gated calcium channels and NMDA receptors, thereby preventing excessive calcium influx into neurons.^{31,41} This action inhibits central sensitization and the propagation of nociceptive signals in the spinal cord, explaining its analgesic and anti-hyperalgesic effects.^{59,60} Magnesium additionally stabilizes neuronal membranes and promotes the release of endogenous pain-modulating mediators, including nitric oxide and gamma-aminobutyric acid (GABA).⁶⁰

Hypomagnesemia causes muscle cramps, tremors, and neuromuscular irritability. Supplementation helps normalize muscle excitability and decreases both the frequency and severity of muscle cramps in conditions such as pregnancy, diabetes, and among athletes.⁶¹ Moreover, magnesium supports bone health by enhancing vitamin D activation and parathyroid hormone (PTH) secretion, facilitating calcium incorporation into bone. Chronic magnesium deficiency is associated with osteoporosis and sarcopenia, and magnesium supplementation has been shown to improve associated with

Table 1. Major therapeutic indications of magnesium, underlying mechanisms of action, clinical applications, and commonly employed doses

Indications	Mechanism of Action	Therapeutic Use	Dose
Type 2 Diabetes ^{18,22,25}	Improves insulin sensitivity, glucose uptake, glycemic control, HOMA-IR, and reduces oxidative stress.	Adjunct in glycemic control and metabolic syndrome.	Oral Mg oxide or citrate 200–400 mg/day.
Cardiovascular Disorders ^{32,33,36,39}	Modulates myocardial excitability; inhibits Ca ²⁺ influx; antiarrhythmic, antihypertensive, antithrombotic, and cardioprotective.	Adjunct in arrhythmia, hypertension, myocardial ischemia and heart failure	IV MgSO ₄ , 1–2 g bolus in arrhythmia; Oral Mg citrate 300–400 mg/day.
Metabolic Syndrome ^{14,18,20,94,95}	Enhances insulin signalling, GLUT-4 translocation, reduces oxidative stress and inflammation, improves lipid profile.	Adjunct strategy in insulin resistance and related metabolic disorders	Oral Mg. chloride ~400 mg/day elemental Mg.
Neuroprotective & Psychotropic activity ^{41–48}	Suppresses oxidative stress, neuroinflammation, and IL-6/TNF- α release. NMDA antagonist; modulates GABA and glutamate neurotransmission	Adjunct in anxiety, mood disorders, migraine, neuropathy, and neurodegenerative diseases	Oral Mg. supplements 100–400 mg/day elemental Mg.
Anti-inflammatory / Antioxidant activity ^{20,51–53}	Downregulates NF- κ B, reduces IL-6/CRP, enhances antioxidant defences, improves NO-mediated vasodilation, and enhances mitochondrial function.	Adjunct in metabolic syndrome, T2DM, hypertension, CVD, chronic fatigue, and fibromyalgia	Oral Mg. 250–400 mg/day elemental Mg for 6–8 weeks
Immunoregulatory Roles ^{50,52,54,56–58}	Modulates immunity, reduces inflammation, supports phagocyte function, and stabilizes mast cells.	Adjunct in inflammatory, allergic, and infectious diseases (e.g., asthma, COVID-19)	Oral 250–400 mg elemental magnesium per day for 8–16 weeks
Musculoskeletal and pain modulation ^{53,63,64,66}	NMDA antagonism; enhances GABA/NO signalling, reduces pain transmission, and improves bone health.	Adjunct in chronic pain, migraine, fibromyalgia, osteoporosis, and neuropathic pain.	Oral Mg citrate/oxide 250–500 mg bedtime; IV MgSO ₄ , 1–2 g in refractory cases.
Eclampsia / Pre-eclampsia ^{45,68–71}	NMDA antagonism with cerebral vasodilation and anticonvulsant effects.	Severe preeclampsia and eclamptic seizures.	IV MgSO ₄ , loading 4–6 g; maintenance 1 g/hr infusion (Pritchard or Zuspan regimen).
Asthma (Acute Severe/Refractory) ^{52,72–74}	Ca ²⁺ channel blockade, bronchodilation, and mast cell stabilization.	Adjunct in severe or refractory asthma.	IV MgSO ₄ , 2 g over 20–30 min; nebulized 150 mg with β 2-agonist.
Constipation ^{77,79,80}	Promotes gastrointestinal motility (releases cholecystokinin), osmotic action in intestine	Treatment of acute and chronic constipation.	Oral Mg hydroxide 30–60 mL (400 mg/5 mL) or Mg citrate 240 mL single dose.
Migraine ^{41,81–84}	NMDA antagonism, Ca ²⁺ channel blockade, and modulation of CGRP/serotonin.	Migraine prevention and acute treatment.	Oral MgO 400–600 mg/day; IV MgSO ₄ , 1–2 g over 15–30 min for acute attack.

osteoporosis and sarcopenia, and magnesium supplementation has been shown to improve the bone mineral density.⁶²

Therapeutically, intravenous magnesium sulphate is employed as an adjunct analgesic in perioperative settings to reduce anaesthetic and opioid requirements, thereby improving postoperative pain control.⁶³ Oral magnesium supplementation has demonstrated benefits in long-term aching conditions such as fibromyalgia, chronic fatigue syndrome, migraine, tension-type headaches, chronic low back pain, and neuropathic pain syndromes, where altered neuronal excitability, impaired mitochondrial function, and magnesium's muscle relaxant effects contribute to pain modulation.^{53,64} Magnesium has also shown efficacy in sleep-related movement disorders and idiopathic Restless Legs Syndrome (RLS), particularly when serum magnesium levels are low. In a study, oral administration of magnesium citrate led to significant improvements in restless legs syndrome (RLS) symptoms and sleep efficiency following oral administration of magnesium citrate (250–500 mg/day) or parenteral magnesium sulphate (1–2 g slow intravenous infusion at bedtime for 4–6 weeks).⁶⁵ Furthermore, a randomized crossover trial reported that magnesium supplementation significantly reduced the periodic limb movement index and improved subjective sleep quality, particularly in individuals with baseline magnesium deficiency.⁶⁶

Through these multifaceted mechanisms, calcium antagonism, NMDA blockade, antioxidant action, and membrane stabilization, magnesium serves as a key modulator of pain and musculoskeletal integrity.

Role of Magnesium in treatment of pre-eclampsia and eclampsia

Magnesium sulphate is the preferred medication for both preventing and treating eclampsia, a severe and potentially life-threatening complication of pre-eclampsia.⁶⁷ Its therapeutic efficacy arises from its anticonvulsant, vasodilatory, and neuroprotective properties.⁴⁵ The primary mechanism involves noncompetitive antagonism of NMDA receptors in the CNS, thereby reducing neuronal excitability and preventing seizure generation.^{41,68} Additionally, magnesium acts as a physiological calcium antagonist, reducing presynaptic calcium influx and acetylcholine

release at neuromuscular junctions, thereby producing anticonvulsant and muscle-relaxant effects. It also promotes endothelial-dependent vasodilation by enhancing nitric oxide synthesis and inhibiting calcium-mediated vasoconstriction, thereby improving cerebral and uteroplacental perfusion.⁶⁹

Large-scale randomized controlled trials, particularly the Magpie Trial involving over 10,000 women, have shown that magnesium sulphate significantly reduces the risk of eclampsia by 58% and maternal mortality by 45%, compared with placebo and other anticonvulsants such as diazepam and phenytoin.⁶⁸ Furthermore, its use is associated with lower neonatal morbidity, fewer recurrent seizures, and better maternal outcomes, with minimal foetal adverse effects. Magnesium sulphate also has a role in neuroprotection of preterm infants, where antenatal administration before anticipated early delivery (<32 weeks) reduces the risk of cerebral palsy in surviving neonates.⁷⁰

In obstetric practice, magnesium sulphate is administered for both seizure prophylaxis in severe preeclampsia and seizure control in eclampsia. The most widely used regimens are the Pritchard (intramuscular and intravenous) and Zuspan (intravenous) protocols. The Pritchard regimen consists of a 4 g intravenous loading dose administered over 5–10 minutes, followed by 10gm intramuscularly (5 g in each buttock), with a maintenance dose of 5gm intramuscularly every 4 hours. The Zuspan regimen involves a 4 g intravenous loading dose, followed by a continuous IV infusion at 1 g per hour. Serum magnesium levels are maintained between 4–7 mEq/L for therapeutic effectiveness and higher levels may cause loss of deep tendon reflexes, respiratory depression and cardiac conduction abnormalities.⁷¹

Magnesium sulphate remains the drug of choice for the management of eclampsia and pre-eclampsia. Adherence to standard treatment protocols with strict clinical and biochemical monitoring minimizes adverse effects. Regular assessment of serum magnesium levels, respiratory rate, deep tendon reflexes, and urine output is essential to ensure safe therapy. As magnesium is predominantly eliminated by the kidneys, dose adjustment and vigilant monitoring are required in patients with renal impairment or oliguria. In

cases of magnesium toxicity, intravenous calcium gluconate serves as the specific antidote to rapidly reverse neuromuscular and cardiac effects.^{69,70}

Role of Magnesium in Acute Severe (Refractory) Asthma

Magnesium relaxes bronchial smooth muscle by inhibiting voltage-gated calcium channels, thereby lowering intracellular Ca^{2+} levels and promoting bronchodilation.⁹ Additionally, it shows anti-inflammatory and membrane-stabilizing effects by preventing the degranulation of mast cells and reducing the release of inflammatory mediators.⁵² Magnesium also modulates NMDA receptor activity in airway sensory pathways, helping to reduce central sensitization related to cough and bronchospasm, while improving endothelial and airway microvascular function—all contributing to faster relief in refractory asthma episodes.⁷²

Systematic reviews and a Cochrane meta-analysis have shown that administering magnesium sulphate 1.2–2 gm as a single intravenous dose for over 15–30 minutes, improves lung function in patients with acute severe asthma who are unresponsive to initial therapy.^{73,74} Some clinical guidelines and emergency medicine references also mention nebulized magnesium sulphate as a potential adjunct treatment in selected patients, though evidence for its effectiveness remains inconsistent.⁷³

Magnesium sulphate should only be used after first-line therapies, i.e. oxygen, high-dose inhaled β_2 -agonists, ipratropium bromide, and systemic corticosteroids, have been initiated, and it should be continued along with standard care. When administering frequently or large IV doses, blood pressure and deep tendon reflexes should be monitored.⁷¹ Rapid administration may cause flushing or transient hypotension, and must be used cautiously or avoided in patients with renal impairment.⁷⁵

Role of magnesium in Gastrointestinal disorders

Magnesium promotes gastrointestinal motility primarily by stimulating the release of cholecystokinin (CCK), which enhances intestinal peristalsis and increases luminal secretions. Because magnesium ions are only partially absorbed from the gastrointestinal tract, they increase the osmotic pressure in the intestinal

lumen, leading to water retention that softens stool and facilitates bowel movements.⁷⁶ Consequently, magnesium salts are widely employed as osmotic laxatives in the treatment of constipation.^{9,77}

Common formulations include magnesium sulphate, magnesium hydroxide (milk of magnesia) and magnesium citrate. Magnesium hydroxide is generally given in doses of 30–60 mL (400 mg/5 mL suspension) at bedtime. Magnesium-containing laxatives are particularly useful for occasional or short-term constipation, opioid-induced constipation, and bowel preparation before diagnostic procedures.⁷⁸ Magnesium should be used with caution or avoided in patients with renal impairment, as reduced magnesium excretion may lead to hypermagnesemia, presenting with hypotension, muscle weakness, and cardiac arrhythmias.^{75,79}

Recent trials and meta-analyses support their efficacy and safety when used within recommended doses for functional constipation, and they remain an important component of first-line management alongside dietary fibre and hydration.^{77,80}

Magnesium in Migraine Prophylaxis

Magnesium acts as a physiological calcium channel blocker, stabilizing vascular smooth muscle and preventing excessive vasoconstriction, which contributes to the throbbing pain of migraine.^{28,41} Furthermore, magnesium regulates serotonergic and nitric oxide (NO) pathways, decreases the release of substance P, vasoactive neuropeptides and thereby decreases neurogenic inflammation.⁸¹

Hypomagnesemia has been consistently observed in migraineurs, particularly during acute attacks, suggesting a pathogenic link.⁸² Deficiency of magnesium leads to neuronal hyperexcitability, platelet aggregation, and vasospasm, mechanisms implicated in both migraine with and without aura.⁸³

Magnesium plays a crucial role in the pathogenesis and prevention of migraine, acting through multiple mechanisms that involve neuronal excitability, vascular tone, and neurotransmitter regulation.⁴⁵ Supplementation helps restore vascular and neuronal stability, thereby reducing attack frequency and severity.⁴⁶ Clinical studies and meta-analyses demonstrate that magnesium supplementation, especially magnesium oxide

(MgO) and magnesium citrate, can significantly reduce the frequency of migraine attacks when administered prophylactically.^{46,81,83}

Magnesium exerts its beneficial effects primarily by antagonizing NMDA receptors, thereby inhibiting cortical spreading depression, the electrophysiological associate of migraine aura.⁸⁴ Magnesium sulfate 1–2 g IV over 15–30 minutes is effective for aborting acute migraine attacks, particularly in patients with aura or menstrual migraine.⁸⁵ Oral Magnesium oxide 400–600 mg/day (elemental magnesium ~240–360 mg) is recommended for migraine prevention, usually taken in divided doses for 8–12 weeks and is especially useful in menstrual migraine, migraine with aura, and patients with magnesium deficiency.^{82,84}

In summary, magnesium's NMDA antagonism, calcium channel blockade, and modulation of serotonergic and NO signalling form the pharmacological basis for its efficacy in migraine. Both oral prophylactic supplementation and intravenous magnesium sulphate for acute attacks are safe, cost-effective therapeutic options supported by substantial clinical evidence.

Emerging and Novel Therapeutic Applications of Magnesium

Support of magnesium in Oncology and Chemotherapy treatment

Magnesium has attracted oncological interest for its diverse biological roles and use as an adjunct in cancer care. It supports DNA repair, regulates key pathways such as PI3K/AKT/mTOR and NF- κ B, and influences apoptosis in tumour cells. Optimal Mg²⁺ levels protect against DNA damage and mutations, while deficiency increases vulnerability of precancerous cells.⁸⁶ By stabilizing the genome and modulating cell proliferation, differentiation, and apoptosis, magnesium helps reduce tumorigenesis and may improve cancer prognosis.⁸⁷ Chronic magnesium deficiency results in immune dysfunctions and greater baseline inflammation along with oxidative stress, which are linked to several age-related diseases and cancer.⁸⁶ In addition, several anticancer therapies can induce hypomagnesemia, often requiring magnesium supplementation during treatment, to relieve symptoms and maintain the general health of the patient.⁸⁸

Magnesium ions are currently used as

anti-tumor implant materials in interventional therapies. During degradation, magnesium produces magnesium hydroxide, hydrogen gas, and magnesium ions. Magnesium hydroxide neutralizes the acidic tumor microenvironment, whereas hydrogen gas and magnesium ions exert notable anti-inflammatory and antioxidant effects.⁸⁹

Role of magnesium in gut microbiome and colorectal cancer prevention

A groundbreaking 2025 randomized trial demonstrated that magnesium supplementation favourably altered the gut microbiota, increasing *Faecalibacterium prausnitzii* and *Carnobacterium maltaromaticum*, bacteria linked to enhanced vitamin D metabolism and lower colorectal-cancer risk.⁹⁰ Magnesium's ability to maintain epithelial integrity, modulate bile acid metabolism, and reduce oxidative DNA damage underlies its preventive role in colorectal carcinogenesis. The gut–magnesium–microbiome axis is now a promising target for nutritional chemoprevention.^{90,91}

Role of magnesium in Polycystic Ovary Syndrome (PCOS)

In women with PCOS, a randomized clinical trial (250 mg/day Mg oxide for 2 months) showed improvements in insulin levels and HOMA-IR compared with placebo.⁹² The use of magnesium supplementation in patients with PCOS, irrespective of disease aetiology or stage, can significantly improve metabolic status by enhancing insulin sensitivity and modulating lipid profile levels.²³ Magnesium supplementation can improve insulin resistance, lipid profiles, and glycaemic control, and may therefore contribute to better clinical results in patients with PCOS.^{92,93}

Magnesium for management of metabolic syndrome

Magnesium deficiency is frequent in obese subjects and is a highly prevalent condition in patients with diabetes. It has gained renewed attention for its impact on glucose metabolism, insulin sensitivity, and metabolic syndrome.^{18,20} In addition, it regulates the activity of lipoprotein lipase (LPL) and lecithin–cholesterol acyltransferase (LCAT), thereby maintaining lipoprotein homeostasis by lowering LDL cholesterol and triglycerides while increasing HDL cholesterol.¹⁴ Recent meta-analysis involving over 90,000 participants showed an opposite relationship between intake of magnesium

supplements and development of metabolic syndrome. Mechanistically, magnesium enhances insulin receptor phosphorylation, promotes GLUT-4 translocation, and reduces oxidative stress and inflammation.⁹⁴ A randomized, double-blind, placebo-controlled clinical trial demonstrated that oral magnesium chloride (5% solution), providing approximately 382 mg of elemental magnesium daily for 16 weeks, led to significantly greater improvements in components of metabolic syndrome—including blood pressure, fasting glucose, and triglycerides—compared with placebo.⁹⁵ These findings advocate magnesium repletion as an adjunct strategy in insulin resistance and related metabolic disorders.

Adverse drug reactions (ADRS) with magnesium treatment

Magnesium supplements are generally well tolerated at recommended doses. The most common ADRs are gastrointestinal (diarrhoea, nausea, abdominal cramping) related to the laxative effects of unabsorbed magnesium salts.^{76,96} Excessive intake or reduced renal excretion may lead to hypermagnesemia, which manifests clinically as hypotension, flushing, nausea, hyporeflexia, muscle weakness, and, in severe cases, respiratory depression, cardiac arrhythmias and cardiac arrest.^{75,79} During intravenous administration, blood pressure and deep tendon reflexes should be carefully monitored.⁷¹ Such severe toxicity is uncommon in individuals with normal renal function but occurs more frequently in elderly patients and those with chronic kidney disease.⁷⁵ Additionally, magnesium supplements can reduce the absorption of certain medications, including tetracyclines, fluoroquinolones, bisphosphonates, and levothyroxine, necessitating appropriate dosing intervals to avoid clinically significant interactions.⁹⁶

CONCLUSION & FUTURE PERSPECTIVES

Magnesium exerts a broad spectrum of pharmacological actions that extend beyond its classical roles in electrolyte homeostasis and neuromuscular function. Gathering evidence underscores its multifaceted contributions to cellular signalling pathways, vascular regulation, immune modulation, neuronal excitability, and

antithrombotic, anti-inflammatory, analgesic, and anticancer mechanisms, thereby reinforcing its therapeutic relevance across multiple organ systems. Clinically, magnesium is predominantly employed as an adjunctive or preventive strategy, particularly in individuals with underlying magnesium deficiency. Forthcoming research must emphasize the detailed characterization of emphasise on the magnesium mechanism of action in specific diseases and provide standardized doses, formulations, and durations of magnesium supplementation. Well-designed randomized controlled trials and improved assessment of magnesium status may further strengthen its role in preventive and therapeutic medicine, nutritional interventions and chronic disease management.

ACKNOWLEDGEMENTS

Authors would like to express sincere gratitude to all the researchers whose published studies were referred to carry out this present review article. Their valued contributions have meaningfully enriched the present work.

Funding Sources

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of interest

The authors do not have any conflict of interest.

Data Availability Statement

This statement does not apply to this article.

Ethics Statement

This research did not involve human participants, animal subjects, or any material that requires ethical approval.

Informed Consent Statement

This study did not involve human participants, and therefore, informed consent was not required.

Clinical Trial Registration

This research does not involve any clinical trials.

Permission to reproduce material from other sources

Not Applicable

Authors Contribution

Jyoti Benni: Conceptualization,

methodology, Literature search, Manuscript writing and editing, overall supervision and submission to journal (corresponding author); Varsha Shindhe: literature search, Manuscript–Review; Reshma Nadaf: Manuscript–Review & Editing, supervision; Savitha Hiremath: Literature search, Resources, Supervision; Fareedabanu Balikai: Literature search and manuscript drafting.

REFERENCES

- de Baaij, JH, Hoenderop JG, Bindels RJ. Magnesium in man: implications for health and disease. *Physiol. Rev.* 2015; 95(1): 1–46. <https://doi.org/10.1152/physrev.00012.2014>
- Saris NE, Mervaala E, Karppanen H, Khawaja JA, Lewenstam A. Magnesium: An Update on Physiological, Clinical and Analytical Aspects. *Clin. Chim. Acta.* 2000;294:1-26. [http://dx.doi.org/10.1016/S0009-8981\(99\)00258-2](http://dx.doi.org/10.1016/S0009-8981(99)00258-2)
- Schwalfenberg GK, Genuis SJ. The Importance of Magnesium in Clinical Healthcare. *Scientifica.* 2017; 4179326. <https://doi.org/10.1155/2017/4179326>
- Workinger JL, Doyle RP, Bortz J. Challenges in the Diagnosis of Magnesium Status. *Nutrients.* 2018; 10(9): 1202. <https://doi.org/10.3390/nu10091202>
- Fatima G, Dzupina A, Alhmadi H, et al. Magnesium Matters: A Comprehensive Review of Its Vital Role in Health and Diseases. *Cureus.* 2024 Oct 13;16(10):e71392. <https://doi.org/10.7759/cureus.71392>
- Saboo B, Gupta A, Tiwaskar M, et al. Fortifying Micronutrient Supplementation in India: Indian Expert consensus. *J Assoc Physicians India.* 2024;72(4):81–90. <https://doi.org/10.59556/japi.72.0491>
- Gröber U. Magnesium and Drugs. *Int J Mol Sci.* 2019;20(9): 2094. <https://doi.org/10.3390/ijms20092094>
- Fang X, Wang K, Han D, et al. Dietary magnesium intake and the risk of cardiovascular disease, type 2 diabetes, and all-cause mortality: a dose-response meta-analysis of prospective cohort studies. *BMC Med.* 2016; 14(1): 210. <https://doi.org/10.1186/s12916-016-0742-z>
- Hicks MA, Tyagi A. Magnesium Sulfate. [Updated 2023 May 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK554553/> (accessed on 1-11-2025)
- Ashique S, Kumar S, Hussain A, et al. “A narrative review on the role of magnesium in immune regulation, inflammation, infectious diseases, and cancer.” *J Health Popul Nutr.* 2023;42:74. <https://doi.org/10.1186/s41043-023-00423-0>
- Romani AM. Magnesium in health and disease. *Metal Ions in Life Sciences.* 2013;13:49–79. https://doi.org/10.1007/978-94-007-7500-8_3
- Eby GA 3rd, Eby KL. Magnesium for treatment-resistant depression: a review and hypothesis. *Med Hypotheses.* 2010; 74(4): 649–660. <https://doi.org/10.1016/j.mehy.2009.10.051>
- Maier JA. Low magnesium and atherosclerosis: an evidence-based link. *Mol Aspects Med.* 2003;24(1-3):137-146. [https://doi.org/10.1016/s0098-2997\(02\)00095-x](https://doi.org/10.1016/s0098-2997(02)00095-x)
- Verma H, Garg R. Effect of magnesium supplementation on type 2 diabetes associated cardiovascular risk factors: A systematic review and meta-analysis. *J Hum Nutr Diet.* 2017;30(5): 621–633. <https://doi.org/10.1111/jhn.12454>
- Kandil M, Jaber S, Desai D, et al. MAGraïne: Magnesium compared to conventional therapy for treatment of migraines. *Am J Emerg Med.* 2021; 39:28–33. <https://doi.org/10.1016/j.ajem.2020.09.033>
- Li B, Lv J, Wang W, Zhang D. Dietary magnesium and calcium intake and risk of depression in the general population: A meta-analysis. *Aust N Z J Psychiatry.* 2017; 51(3): 219–229. <https://doi.org/10.1177/0004867416676895>
- Barbagallo M, Veronese N, Dominguez, L. J. Magnesium in Aging, Health and Diseases. *Nutrients.* 2021;13(2):463. <https://doi.org/10.3390/nu13020463>
- Piuri G, Zocchi M, Della Porta M, et al. Magnesium in Obesity, Metabolic Syndrome, and Type 2 Diabetes. *Nutrients.* 2021;13(2): 320. <https://doi.org/10.3390/nu13020320>
- Guerrero-Romero F, Rodríguez-Morán M. Magnesium improves the beta-cell function to compensate variation of insulin sensitivity: Double-blind, randomized clinical trial. *Eur J Clin Invest.* 2011;41: 405-410. <https://doi.org/10.1111/j.1365-2362.2010.02422.x>
- Nielsen FH. Magnesium deficiency and increased inflammation: current perspectives. *J Inflamm Res.* 2018; 11:25–34. <https://doi.org/10.2147/JIR.S136742>
- Alswat K. Type 2 diabetes control and complications and their relation to serum magnesium level. *Arch Med Sci.* 2021; 18;18(2):307-313. <https://doi.org/10.5114/aoms/102443>
- Feng J, Wang H, Jing Z, et al. Role of Magnesium in Type 2 Diabetes Mellitus. *Biol Trace Elem Res.* 2020;196(1):74–85. <https://doi.org/10.1007/>

- s12011-019-01922-0
23. Zamani M, Haghighat N. The Effects of Magnesium Supplementation on Serum Magnesium and Calcium Concentration in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Clin Nutr Res.* 2022;11(2):133-145. <https://doi.org/10.7762/cnr.2022.11.2.133>
24. Simental-Mendía LE, Sahebkar A, Rodríguez-Morán M, Guerrero-Romero F. A systematic review and meta-analysis of randomized controlled trials on the effects of magnesium supplementation on insulin sensitivity and glucose control. *Pharmacol Res.* 2016;111:272-282. <https://doi.org/10.1016/j.phrs.2016.06.019>
25. Veronese N, Dominguez LJ, Pizzol D, Demurtas J, Smith L, Barbagallo M. Oral Magnesium Supplementation for Treating Glucose Metabolism Parameters in People with or at Risk of Diabetes: A Systematic Review and Meta-Analysis of Double-Blind Randomized Controlled Trials. *Nutrients.* 2021 Nov 15;13(11):4074. <https://doi.org/10.3390/nu13114074>
26. Costello RB, Nielsen FH, Lukaski HC. Magnesium and insulin resistance: An update. *Magnes Res.* 2016; 29(1): 1–8. <https://doi.org/10.1684/mrh.2016.0400>
27. Barbagallo M, Dominguez LJ. Magnesium and type 2 diabetes. *World J Diabetes.* 2015;6(10):1152–1157. <https://doi.org/10.4239/wjd.v6.i10.1152>
28. Shechter M. Magnesium and cardiovascular system. *Magnes Res.* 2010; 23(2), 60–72. <https://doi.org/10.1684/mrh.2010.0202>
29. Verma H, Garg R. Effect of magnesium supplementation on blood pressure: a systematic review and meta-analysis. *Hypertens Res.* 2022;45(6):977–987. <https://doi.org/10.1038/s41440-022-00875-z>
30. Al Alawi AM, Majoni SW, Falhammar H. Magnesium and Human Health: Perspectives and Research Directions. *Int J Endocrinol.* 2018; 2018:9041694. <https://doi.org/10.1155/2018/9041694>
31. Siddiqui RW, Nishat S, Alzaabi AA, et al. The Connection Between Magnesium and Heart Health: Understanding Its Impact on Cardiovascular Wellness. *Cureus.* 2024;16(10):e72302. <https://doi.org/10.7759/cureus.72302>
32. Huang, JH., Lu, YF., Cheng, FC. et al. Correlation of magnesium intake with metabolic parameters, depression and physical activity in elderly type 2 diabetes patients: a cross-sectional study. *Nutrients.* 2012;11:41. <https://doi.org/10.1186/1475-2891-11-41>
33. Dong JY, Xun P, He K, Qin LQ: Magnesium intake and risk of type 2 diabetes: meta-analysis of prospective cohort studies. *Diabetes Care.* 2011; 34 (9): 2116-2122. <https://doi.org/10.2337/dc11-0518>
34. Peacock JM, Ohira T, Post W, Sotoodehnia N, Rosamond W, Folsom AR. Serum magnesium and risk of sudden cardiac death in the Atherosclerosis Risk in Communities (ARIC) Study. *Am Heart J.* 2010;160(3):464-470. <https://doi.org/10.1016/j.ahj.2010.06.012>
35. Shechter M, Bairey Merz CN, Stuehlinger HG, Slany J, Pachinger O, Rabinowitz B. Effects of oral magnesium therapy on exercise tolerance, exercise-induced chest pain, and quality of life in patients with coronary artery disease. *Am J Cardiol.* 2003;91(5):517-521. [https://doi.org/10.1016/s0002-9149\(02\)03297-6](https://doi.org/10.1016/s0002-9149(02)03297-6)
36. Argeros Z, Xu X, Bhandari B, Harris K, Touyz RM, Schutte AE. Magnesium Supplementation and Blood Pressure: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Hypertension.* 2025 Nov;82(11):1844-1856. <https://doi.org/10.1161/HYPERTENSIONAHA.125.25129>
37. Tzivoni D, Banai S, Keren A. Story of magnesium for torsade de pointes. *Heart Rhythm.* 2024;21(4):360–361. <https://doi.org/10.1016/j.hrthm.2024.01.013>
38. Negru AG, Pastorci A, Crisan S, Cismaru G, Popescu FG, Luca CT. The Role of Hypomagnesemia in Cardiac Arrhythmias: A Clinical Perspective. *Biomedicines.* 2022;10(10):2356. <https://doi.org/10.3390/biomedicines10102356>
39. Lutsey PL, Alonso A, Michos ED, et al. Serum magnesium, phosphorus, and calcium are associated with risk of incident heart failure: the Atherosclerosis Risk in Communities (ARIC) Study. *Am J Clin Nutr.* 2014;100(3):756-764. <https://doi.org/10.3945/ajcn.114.085167>
40. Moabedi M, Aliakbari M, Erfanian S, Milajerdi A. Magnesium supplementation beneficially affects depression in adults with depressive disorder: a systematic review and meta-analysis of randomized clinical trials. *Front Psychiatry.* 2023;14:1333261. <https://doi.org/10.3389/fpsy.2023.1333261>
41. Patel V, Akimbekov NS, Grant WB, Dean C, Fang X, Razzaque MS. Neuroprotective effects of magnesium: implications for neuroinflammation and cognitive decline. *Front Endocrinol.* 2024;15:1406455. <https://doi.org/10.3389/fendo.2024.1406455>
42. Varga P, Lehoczkai A, Fekete M, et al. The Role of Magnesium in Depression, Migraine,

- Alzheimer's Disease, and Cognitive Health: A Comprehensive Review. *Nutrients*. 2025;17: 2216. <https://doi.org/10.3390/nu17132216>
43. Kumar A, Mehan S, Tiwari A, et al. Magnesium (Mg²⁺): Essential Mineral for Neuronal Health: From Cellular Biochemistry to Cognitive Health and Behaviour Regulation. *Curr Pharm Des*. 2024;30(39):3074-3107. <https://doi.org/10.2174/0113816128321466240816075041>
 44. Sartori SB, Whittle N, Hetzenauer A, Singewald N. Magnesium deficiency induces anxiety and HPA axis dysregulation: modulation by therapeutic drug treatment. *Neuropharmacology*. 2012; 62(1): 304–312. <https://doi.org/10.1016/j.neuropharm.2011.07.027>
 45. Kirkland AE, Sarlo GL, Holton KF. The Role of Magnesium in Neurological Disorders. *Nutrients*. 2018;10(6):730. <https://doi.org/10.3390/nu10060730>
 46. Tarleton EK, Littenberg B, MacLean CD, Kennedy AG, Daley C. Role of magnesium supplementation in the treatment of depression: A randomized clinical trial. *PloS One*. 2017;12(6): e0180067. <https://doi.org/10.1371/journal.pone.0180067>
 47. Boyle NB, Lawton C, Dye L. The effects of magnesium supplementation on subjective anxiety and stress—a systematic review. *Am J Clin Nutr*. 2024;119(3):671-683. <https://doi.org/10.1016/j.ajcnut.2023.12.015>
 48. Ray S. The neuroprotective potential of magnesium in Parkinson's disease. *Magnes Res*. 2024;36(4):69–81. <https://doi.org/10.1684/mrh.2024.0523>
 49. Costello R, Wallace TC, Rosanoff A. Magnesium. *Adv Nutr*. 2016;7(1):199-201. <https://doi.org/10.3945/an.115.008524>
 50. Liu M, Dudley SC, Jr. Magnesium, Oxidative Stress, Inflammation, and cardiovascular disease. *Antioxidants (Basel)*. 2020; 9(10):907. <https://doi.org/10.3390/antiox9100907>
 51. Paolisso G, Barbagallo M. Hypertension, diabetes mellitus, and insulin resistance: the role of intracellular magnesium. *Am J Hypertens*. 1997;10(3):346–355. [https://doi.org/10.1016/s0895-7061\(96\)00342-1](https://doi.org/10.1016/s0895-7061(96)00342-1)
 52. Mazidi M, Rezaie P, Banach M. Effect of magnesium supplements on serum C-reactive protein: a systematic review and meta-analysis. *Arch Med Sci*. 2018;14(4):707-716. <https://doi.org/10.5114/aoms.2018.75719>
 53. Boulis M, Boulis M, Clauw D. Magnesium and Fibromyalgia: A Literature Review. *J prim care community health*. 2021; 12:21501327211038433. <https://doi.org/10.1177/21501327211038433>
 54. Tam M, Gómez S, González-Gross M, Marcos A. Possible roles of magnesium on the immune system. *Eur J Clin Nutr*. 2003;57(10): 1193–1197. <https://doi.org/10.1038/sj.ejcn.1601689>
 55. Gröber U, Schmidt J, Kisters K. Magnesium in Prevention and Therapy. *Nutrients*. 2015;7(9):8199–8226. <https://doi.org/10.3390/nu7095388>
 56. Mazur A, Maier JA, Rock E, Gueux E, Nowacki W, Rayssiguier Y. Magnesium and the inflammatory response: potential physiopathological implications. *Arch Biochem Biophys*. 2007; 458(1):48–56. <https://doi.org/10.1016/j.abb.2006.03.031>
 57. Zheltova AA, Kharitonova M V, Iezhitsa IN, Spasov AA. Magnesium deficiency and oxidative stress: an update. *BioMedicine*. 2016; 6(4): 20. <https://doi.org/10.7603/s40681-016-0020-6>
 58. Uwitonze AM, Razzaque MS. Role of Magnesium in Vitamin D Activation and Function. *J Am Osteopath Assoc*. 2018; 118(3): 181–189. <https://doi.org/10.7556/jaoa.2018.037>
 59. Begon S, Pickering G, Eschaliere A, Dubray C. Magnesium increases morphine analgesic effect in different experimental models of pain. *Anesthesiology*. 2002; 96(3): 627–632. <https://doi.org/10.1097/00000542-200203000-00019>
 60. Fawcett WJ, Haxby EJ, Male DA. Magnesium: physiology and pharmacology. *Br J Anaesth*. 1999;83(2):302–320. <https://doi.org/10.1093/bja/83.2.302>
 61. Garrison SR, Allan GM, Sekhon RK, Musini VM, Khan KM. Magnesium for skeletal muscle cramps. *Cochrane database of Syst Rev*. 2012; 2012(9): CD009402. <https://doi.org/10.1002/14651858.CD009402.pub2>
 62. Castiglioni S, Cazzaniga A, Albisetti W, Maier JAM. Magnesium and Osteoporosis: Current State of Knowledge and Future Research Directions. *Nutrients*. 2013; 5(8):3022-3033. <https://doi.org/10.3390/nu5083022>
 63. De Oliveira GS, Jr Castro-Alves LJ, Khan JH, McCarthy RJ. Perioperative systemic magnesium to minimize postoperative pain: a meta-analysis of randomized controlled trials. *Anesthesiology*. 2013; 119(1): 178–190. <https://doi.org/10.1097/ALN.0b013e318297630d>
 64. Park R, Ho AM, Pickering G, Arendt-Nielsen L, Mohiuddin M, Gilron I. Efficacy and Safety of Magnesium for the Management of Chronic Pain in Adults: A Systematic Review. *Anesth Analg*. 2020 Sep;131(3):764-775. <https://doi.org/10.1213/ANE.0000000000004673>
 65. Trenkwalder C, Stefani A, Bachmann CG, et al. Restless legs syndrome: abbreviated guidelines by the German sleep society and the German neurological society. *Neurol Res*

- Pract.* 2024;6:53. <https://doi.org/10.1186/s42466-024-00353-0>
66. Marshall NS, Serinel Y, Killick R, et al. Magnesium supplementation for the treatment of restless legs syndrome and periodic limb movement disorder: A systematic review. *Sleep Med Rev.* 2019;48:101218. <https://doi.org/10.1016/j.smrv.2019.101218>
 67. Sibai BM. Diagnosis, prevention, and management of eclampsia. *Obstet Gynecol.* 2005;105(2):402–410. <https://doi.org/10.1097/01.AOG.0000152351.13671.99>
 68. Altman, D., Carroli, G., Duley, L., et al. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomized placebo-controlled trial. *Lancet.* 2002;359(9321):1877–1890. [https://doi.org/10.1016/s0140-6736\(02\)08778-0](https://doi.org/10.1016/s0140-6736(02)08778-0)
 69. Euser AG, Cipolla MJ. Magnesium sulfate for the treatment of eclampsia: a brief review. *Stroke.* 2009; 40(4): 1169–1175. <https://doi.org/10.1161/STROKEAHA.108.527788>
 70. Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. *Cochrane Database of Syst Rev.* 2009;(1):CD004661. <https://doi.org/10.1002/14651858.CD004661.pub3>
 71. WHO Recommendations for Prevention and Treatment of Pre-Eclampsia and Eclampsia. Geneva: *World Health Organization.* 2011. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK140561/> Accessed on (11-11-2025)
 72. Song WJ, Chang YS. Magnesium sulfate for acute asthma in adults: a systematic literature review. *Asia Pac Allergy.* 2012 Jan;2(1):76-85. <https://doi.org/10.5415/apallergy.2012.2.1.76>
 73. Kew KM, Kirtchuk L, Michell CI. Intravenous magnesium sulfate for treating adults with acute asthma in the emergency department. *Cochrane Database of Syst Rev.* 2014; 5:CD010909. <https://doi.org/10.1002/14651858.CD010909.pub2> (Accessed 04 November 2025).
 74. Rosing AH, Savran O, Ulrik CS. Magnesium sulfate treatment for acute severe asthma in adults-a systematic review and meta-analysis. *Front Allergy.* 2023;4:1211949. <https://doi.org/10.3389/falgy.2023.1211949>
 75. Kwofie K, Wolfson AB. Intravenous Magnesium Sulfate for Acute Asthma Exacerbation in Children and Adults. *Am Fam Physician.* 2021;103(4):245–246.
 76. Schiller L. R. Review article: the therapy of constipation. *Aliment Pharmacol Ther.* 2001;15(6):749–763. <https://doi.org/10.1046/j.1365-2036.2001.00982.x>
 77. Mori H, Tack J, Suzuki H. Magnesium Oxide in Constipation. *Nutrients.* 2021;13(2):421. <https://doi.org/10.3390/nu13020421>
 78. Siegel JD, Di Palma JA. Medical treatment of constipation. *Clin Colon Rectal Surg.* 2005;18(2):76-80. <https://doi.org/10.1055/s-2005-870887>
 79. Cascella M, Vaqar S. Hypermagnesemia. [Updated 2023 Jun 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; Jan 2025. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK549811/>
 80. Suares NC, Ford AC. Systematic review: the effects of fibre in the management of chronic idiopathic constipation. *Aliment Pharmacol Ther.* 2011;33(8):895–901. <https://doi.org/10.1111/j.1365-2036.2011.04602.x>
 81. Mathew AA, Panonnumma R. ‘Magnesium’- the master cation-as a drug-possibilities and evidences. *Biomaterials.* 2021;34:955–986. <https://doi.org/10.1007/s10534-021-00328-7>
 82. Sun-Edelstein C, Mauskop A. Role of magnesium in the pathogenesis and treatment of migraine. *Expert Rev Neurother.* 2009;9(3):369–379. <https://doi.org/10.1586/14737175.9.3.369>
 83. Chiu HY, Yeh TH, Huang YC, Chen PY. Effects of Intravenous and Oral Magnesium on Reducing Migraine: A Meta-analysis of Randomized Controlled Trials. *Pain physician.* 2016;19(1): E97–E112.
 84. Mauskop A, Varughese J. Why all migraine patients should be treated with magnesium. *J Neural Transm.* 2012;119(5): 575–579. <https://doi.org/10.1007/s00702-012-0790-2>
 85. Bigal ME, Bordini CA, Tepper SJ, Speciali JG. Intravenous magnesium sulphate in the acute treatment of migraine without aura and migraine with aura. A randomized, double-blind, placebo-controlled study. *Cephalalgia.* 2002;22(5): 345–353. <https://doi.org/10.1046/j.1468-2982.2002.00364.x>
 86. Sambataro D, Scandurra G, Scarpello L, Gebbia V, Dominguez LJ, Valerio MR. A Practical Narrative Review on the Role of Magnesium in Cancer Therapy. *Nutrients.* 2025;17(14):2272. <https://doi.org/10.3390/nu17142272>
 87. Wolf FI, Maier JA, Nasulewicz A, et al. Magnesium and neoplasia: from carcinogenesis to tumor growth and progression or treatment. *Arch Biochem Biophys.* 2007;458(1):24-32. <https://doi.org/10.1016/j.abb.2006.02.016>
 88. Rosner MH, DeMauro Renaghan A. Disorders of Divalent Ions (Magnesium, Calcium, and Phosphorous) in Patients With Cancer. *Adv Chronic Kidney Dis.* 2021;28(5):447-459.e1. <https://doi.org/10.1053/j.ackd.2021.09.005>

89. Zan R., Wang H., Cai W., Ni J., Luthringer-Feyerabend B., Wang W., Peng H., Ji W., Yan J., Xia J., et al. Controlled release of hydrogen by implantation of magnesium induces P53-mediated tumor cells apoptosis. *Bioact. Mater.* 2022; 9:385–396. <https://doi.org/10.1016/j.bioactmat.2021.07.026>
90. Li Q, Chan H, Liu WX, et al. Carnobacterium maltaromaticum boosts intestinal vitamin D production to suppress colorectal cancer in female mice. *Cancer Cell.* 2023;41(8):1450-1465.e8. <https://doi.org/10.1016/j.ccell.2023.06.011>
91. Sun E, Zhu X, Ness RM, et al. Magnesium treatment increases gut microbiome synthesizing vitamin D and inhibiting colorectal cancer: results from a double-blind precision-based randomized placebo-controlled trial. *Am J Clin Nutr.* 2025;122(5):1185-1194. <https://doi.org/10.1016/j.ajcnut.2025.09.011>
92. Shahmoradi S, Chiti H, Tavakolizadeh M, Hatami R, Motamed N, Ghaemi M. The Effect of Magnesium Supplementation on Insulin Resistance and Metabolic Profiles in Women with Polycystic Ovary Syndrome: A Randomized Clinical Trial. *Biol Trace Elem Res.* 2024;202(3):941–946. <https://doi.org/10.1007/s12011-023-03744-7>
93. Li R, Li Z, Huang Y, Hu K, Ma B, Yang Y. The effect of magnesium alone or its combination with other supplements on the markers of inflammation, OS and metabolism in women with polycystic ovarian syndrome (PCOS): A systematic review. *Front Endocrinol (Lausanne).* 2022 Aug 5; 13:974042. <https://doi.org/10.3389/fendo.2022.974042>
94. Kim Y, Je Y. Intake or Blood Levels of Magnesium and Risk of Metabolic Syndrome: A Meta-Analysis of Observational Studies. *Nutrients.* 2025; 17: 1667. <https://doi.org/10.3390/nu17101667>
95. Rodríguez-Morán M, Simental-Mendía LE, Gamboa-Gómez CI, Guerrero-Romero F. Oral Magnesium Supplementation and Metabolic Syndrome: A Randomized Double-Blind Placebo-Controlled Clinical Trial. *Adv Chronic Kidney Dis.* 2018 May;25(3):261-266. <https://doi.org/10.1053/j.ackd.2018.02.011>
96. National Institutes of Health, Office of Dietary Supplements. Magnesium: Fact Sheet for Health Professionals. Bethesda (MD): NIH. 2023. Available from- Magnesium - Health Professional Fact Sheet