Fullscript

REFERENCE SHEET:

Magnesium

Pronunciation

Magnesium (mag-nee-zee-um)
Mg2+

Summary

Magnesium (Mg) is an element and essential mineral. It is a cofactor in over three hundred enzymatic reactions involved in protein synthesis, muscle contraction, nerve function, blood pressure, glucose regulation, hormone receptor binding, cardiac conduction, transmembrane ion flux, and calcium channel gating. It is required for the production of ATP and the synthesis of RNA and DNA. The food sources with the highest amounts of Mg include hemp seeds, pumpkin seeds, flax seeds, Brazil nuts, spinach, avocado, and whole grains. Dark chocolate, cashews, shelled peas, and green lentils are also excellent sources. It is estimated that approximately 68% of adults in western countries consume less than the recommended dietary allowance (RDA) of Mg, possibly attributed to declining mineral content in soil and other modern dietary challenges. Magnesium deficiencies are common and may lead to many physical and mental health complications.

Main Medical Uses

Supplemental Mg is often administered to correct a nutritional deficiency in the mineral. Supplementation with Mg may provide several cardiovascular benefits and has been shown to be effective in the treatment of hypertension, pre-eclampsia, eclampsia, mitral valve prolapse, and heart failure. Magnesium may also prevent and treat coronary artery disease and reduce post-operative cardiac arrhythmias, including atrial fibrillation, supraventricular arrhythmias, ventricular arrhythmias, and supraventricular tachycardia.

Magnesium may be used to reduce gastrointestinal complications after cardiac surgery, as well as reduce constipation. It can be used in metabolic syndrome and diabetes. Evidence also supports its use in asthma, chronic obstructive pulmonary disease, muscle cramps in pregnancy, nocturnal leg cramps, tetanus, and migraines. Magnesium may improve insomnia, periodic limb movements during sleep (PLMS), and restless leg syndrome, as well as physical performance and sleep in aging adults. It can assist in chronic fatigue syndrome and fibromyalgia. It is used for kidney stones, chronic kidney disease, premenstrual syndrome, glaucoma and prevention of osteoporosis. Magnesium may be effective in the treatment of depression, attention deficit hyperactivity disorder, anxiety, stress, mania in bipolar disorder, chronic alcoholism, and smoking cessation.

Recommended Dietary Allowance (RDA) for Mg:

- Ages 0-6 months 30 mg (adequate intake)
- Ages 7-12 months 75 mg (adequate intake)
- Ages 1-3: 80 mg
- Ages 4-8: 130 mg
- Ages 9-13: 240 mg
- Ages 14-18: 410 mg (males), 360 mg (females)
- Ages 19-30: 400 mg (males), 310 mg (females)
- Ages 31+: 420 mg (males), 320 (females)
- Pregnancy: 400 mg (ages 14-18); 350 mg (ages 19-30); 360 mg (ages 31-50)
- Lactation: 360 mg (ages 14-18); 310 mg (ages 19-30); 320 mg (ages 31-50)

The adequate intake for adults is estimated to be between 320-420 mg per day. However, intake deficiencies (serum concentrations below 0.85 mmol/L) are often masked as the body draws from Mg reserves in the bone.

Forms

There are several forms of Mg that can be broadly classified as inorganic and organic salts. Studies have evaluated the bioavailability of several popular forms of Mg. For the most part, organic Mg salts are more soluble, improving bioavailability compared to inorganic salts. Magnesium can also be classified by amino acid chelates, such as magnesium glycinate, magnesium bis-glycinate, magnesium lysinate, magnesium orotate, and magnesium taurate.

Administering divided doses of Mg may lead to increased bioavailability compared with large bolus doses. Slow-release or effervescent formulations may also improve bioavailability. While varying methodologies and dosing between studies make it difficult to compare relative bioavailabilities between forms, the following table provides available information on the bioavailability of various forms of Mg in humans.

Forms	Percent of absorption	Other comments
Magnesium aspartate	41.7-44.5%	Good solubility Increases urinary magnesium excretion more than magnesium oxide compared to control
Magnesium lactate	42.3%	Excellent solubility Magnesium lactate dihydrate bioavailability was 20.26% (fasted) and 12.49% (fed) in serum, and 38.11% (fasted) and 40.99% (fed) in urine compared with intravenous magnesium sulfate
Magnesium citrate	29.64%	Very good solubility Greater solubility and bioavailability compared with magnesium oxide measured by urinary content Greater serum Mg compared with magnesium oxide and magnesium amino acid chelate after 24 hours and 60 days of administration Higher urinary and serum concentrations compared with magnesium oxide, but both groups had no change in monocyte and lymphocyte magnesium concentration
Magnesium glycinate	23.50%	Good solubility No difference in serum and urinary profile between solution, slow-release tablets and magnesium gluconate Magnesium diglycinate was tolerated compared with oral magnesium oxide, but only had significantly greater absorption (23.5%) in patients with greatest impairment of magnesium oxide absorption after ileal resection

Forms	Percent of absorption	Other comments
Magnesium chloride	19.68%	High solubility Equal Mg concentration in urine compared with tablets containing magnesium hydroxide, magnesium citrate/lactate, or magnesium citrate/lactate + hydroxide No difference in serum magnesium compared with magnesium gluconate
Magnesium gluconate	19.25%	Moderate solubility No difference in serum and urinary profile with solution and slow-release magnesium glycinate No difference in serum magnesium compared with magnesium chloride
Magnesium hydroxide	14.9%	Insoluble Equal Mg concentration in urine compared with tablets containing magnesium citrate/lactate, magnesium citrate/lactate + hydroxide, or a magnesium chloride solution
Magnesium oxide	4.00%	Very low solubility Oral absorption of 22.8% in patients with ileal resection
Magnesium sulfate	4.00-7.00%	Moderate solubility Low absorption causing laxative effects
Magnesium fumarate	No data	Good solubility

Dosing and Administration

Condition	Dosing & Administration	Outcome	Class of Evidence	MOA
Age-related decline in physical performance	300 mg (Mg oxide) per day for 12 weeks	↑ short physical performance battery score & walking speed; ↓ chair stand times	B	Positive association of Mg with muscle mass, leg power, & hs-CRP
Asthma	1.2-2.0 g (i.v. Mg sulfate) over 15-30 minutes adjunct to standard therapy	↑ pulmonary function; ↓ hospital admission rate in severe cases	A	↓ FEV1; ↑ PEF rate ↓ bronchial reactivity, antigen response ↑ reduced glutathione; ↓ methaemoglobin, hemichrome & hemoglobin ↓ histamine-induced broncho-constriction, lipopolysaccharide-induced neutrophil influx, ovalbumin-induced asthma, macrophages
	170 mg twice per day for 6.5 months	↑ methacholine required to decrease FEV1, peak expiratory flow (PEF) rate, QoL & control scores	B	
	200-290 mg (Mg citrate) per day for 12 weeks in children	↓ bronchodilator use	B	
	300 mg per day for 2 months in children	↑ methacholine PC20 required to test bronchial reactivity; ↓ asthma exacerbations, used less salbutamol, antigen response on skin	C	
Attention-deficit hyperactivity disorder	200 mg per day for 6 months in children	↓ hyperactivity	B	↑ reward system ↑ erythrocyte Mg

Condition	Dosing & Administration	Outcome	Class of Evidence	MOA
<u>Cardiac conditions</u>				
Atrial fibrillation (AF)	100 mg/kg (i.v. Mg sulfate) during aortic cross-clamp	↓ AF incidence after coronary artery bypass graft surgery, ICU stay length	B	↑ rate control & rhythm control ↑ calcium channel inhibition
	4.5 g (i.v. Mg sulfate) with AV nodal blocking agents in emergency rapid AF	↓ ventricular rate; ↑ rhythm control rate	B	↓ calcium levels in myocardial cells exposed to LPC ↑ PR interval, QRS duration, intra-atrial and atrioventricular (AV) nodal conduction times, atrial and AV refractory periods
Post-operative cardiac arrhythmias	Up to 14.6 g bolus post-cardiac surgery	↓ AF risk, ventricular arrhythmias risk	A	
	30 mg/kg (i.v. Mg sulfate) post cardiac surgery	↓ arrhythmia incidence	B	↑ tachycardia cycle length, AH interval ↑ left ventricular stroke index
	2 g (i.v. Mg chloride) intraoperatively post cardiopulmonary bypass surgery	↓ ventricular dysrhythmias, supraventricular dysrhythmias, mechanical ventilatory support required; ↑ postoperative cardiac indices	B	
Premature ventricular and supraventricular complexes	3 g (Mg pidolate) per day for 30 days	↓ premature complex density and symptoms	B	
Supraventricular tachycardia (SVT)	5 g (i.v. Mg sulfate) per day, intraoperatively and post thoracic surgery for 2 days	↓ SVT incidence in px undergoing pneumonectomy	B	
Chronic alcoholism	200 mg twice per day for 8 weeks	↓ aspartate-aminotransferase, alanine-aminotransferase, gamma-glutamyl-transpeptidase; ↑ Na, Ca, P, K, Mg	B	No data

Condition	Dosing & Administration	Outcome	Class of Evidence	MOA
Chronic kidney disease	365 mg (Mg oxide) for 3 months in obese pre-diabetic px with hypo-magnesemia	↓ uric acid; ↑ albumin, Mg	B	↓ intestinal phosphate absorption, vascular calcification ↓ uric acid; ↑ albumin, Mg
	360 mg (Mg hydroxide) twice per day for 8 weeks	↑ T50 propensity (delaying crystalline nanoparticle formation)	C	↓ rate of crystalline nanoparticle formation
Chronic obstructive pulmonary disease	1.2 g (i.v. Mg sulfate) over 20 minutes after 2.5 mg nebulized albuterol	↑ peak expiratory flow (PEF) over 45 mins	B	↓ FRC; ↑ inspiratory capacity, MIP, MEP ↓ FRC, residual volume, MAP, cardiac double product at rest; ↑ max exercise load reached (& inspiratory capacity), respiratory expiratory ratio ↑ PEF, FEV, FVC
	2 g (i.v. Mg sulfate)	↓ functional respiratory capacity (FRC); ↑ inspiratory capacity, max inspiratory pressure (MIP), max expiratory pressure (MEP)	C	
	2 g (i.v. Mg sulfate) alongside cycle ergometer exercise. Test performed 100 minutes after infusion	↓ FRC, residual volume (RV), mean arterial pressure (MAP), cardiac double product at rest; ↑ max exercise load reached (& inspiratory capacity), respiratory expiratory ratio	C	↓ bronchial reactivity, antigen response ↓ elastin degradation & vascular calcification
	2 g (i.v. Mg sulfate) with bronchodilator therapy	↑ forced expiratory volume over 2 hours, forced vital capacity	C	
	151 mg (nebulized Mg sulfate) per dose with 500 µg ipratropium bromide	↓ dyspnea; ↑ PEF rates	C	

Condition	Dosing & Administration	Outcome	Class of Evidence	MOA
Coronary artery disease	365 mg total Mg (Mg citrate or oxide) twice per day for 6 months	↑ endothelium-dependent brachial artery flow-mediated vasodilation (FMD), exercise tolerance & duration, VO2 max, HR response, left ventricular ejection fraction (LVEF), QoL; ↓ frequency of ischemic ST-segment changes, arrhythmias, & chest pain during exercise	B	↑ FMD; ↓ frequency of ischemic ST-segment changes and arrhythmias during exercise ↑ VO2max, HR response & LVEF during exercise ↓ platelet dependent thrombosis
	800-1200 mg (Mg oxide) per day for 3 months	↓ platelet dependent thrombosis	C	↑ cardiac index; ↓ MAP, systemic vascular resistance, epinephrine, isolated ventricular premature complexes, couplets & nonsustained ventricular tachycardia frequency Stabilizes cardiac repolarization
Depression	320 mg per day	↓ risk for depression	A	↑ NMDA receptor antagonism
	500 mg (Mg oxide) per day for 8 weeks	↑ Mg levels; ↓ Beck score	B	↑ synaptic sprouting & synaptic strengthening
	50 ml (Mg chloride 5% solution = 450 mg elemental Mg) in type II diabetics with depression & hypomagnesia	↓ Yasavage and Brink Scores of depression equivalently to 50mg of imipramine; ↑ serum Mg	C	↑ reward systems ↑ BDNF, GluN2B, P-S831 & P-S845 proteins in the olfactory bulb

Condition	Dosing & Administration	Outcome	Class of Evidence	MOA
<u>Diabetes</u>				
Type I diabetes (TID)	300 mg per day for 5 years in TID with chronic Mg depletion	↑ erythrocyte Mg; ↓ polyneuropathy in 39% of participants, no change in 49%, or worsening in 12%	B	↓ fasting glucose ↑ post-ischemic endothelial- dependent flow-mediated dilation
Type II diabetes (TIID)(237)	360 mg per day for 12 weeks in TIID	↓ FBG; ↑ HDL-C	A	↓ HbA1C, insulin, C-peptide, HOMA-IR, HOMA-B
	50 mL ($MgCl_2$ 5% solution = 450 mg) per day for 4 months in hypertensive TIID with Mg deficiency	↓ SBP & DBP; ↑ HDL-C	B	↓ FBG, total cholesterol, LDL-C, TGs, SBP; ↑ HDL-C ↑ insulin dependent glucose disappearance, glucose disposal & oxidation
	374 mg (unspecified form) for 4 weeks in TIID	↑ insulin dependent glucose disappearance, glucose disposal & oxidation	B	↓ SBP & DBP ↑ HMG-CoA reductase acyltransferase, & desaturase activities
	4.5 g (Mg pidolate) per day for 1 month in TIID	↓ total-C, LDL-C; ↑ HDL-C	C	
Gestational diabetes (GD)	250 mg (Mg oxide) per day for 6 weeks in GD	↓ FBG, insulin, HOMA-IR, HOMA-B, hs-CRP, MDA, newborn hyperbilirubinemia & newborn hospitalization, LDL receptor expression; ↑ insulin sensitivity, TGs, PPAR-γ & GLUT-1 expression	B	↓ FBG, insulin, HOMA-IR, HOMA-B, hs-CRP, MDA; ↑ insulin sensitivity, TGs ↑ PPAR-γ & GLUT-1 expression; ↓ LDL receptor expression
Diabetic foot ulcers (DFU)	250 mg (Mg oxide) per day for 12 weeks in px with diabetic foot ulcers	↓ ulcer length, width, & depth, FBG, insulin, HBA1C, & hs-CRP; ↑ insulin sensitivity, total antioxidant capacity	B	↓ ulcer length, width, & depth, FBG, insulin, HBA1C, & hs-CRP; ↑ insulin sensitivity, total antioxidant capacity

Condition	Dosing & Administration	Outcome	Class of Evidence	MOA
Prediabetes	30 mL ($MgCl_2$ 5% solution = 382 mg elemental Mg) per day for 4 months in prediabetes px with Mg deficiency	↓ fasting & post-load glucose, HOMA-IR, TGs; ↑ glycemic status, HDL-C	C	↓ fasting & post-load glucose, HOMA-IR, TGs; ↑ glycemic status, HDL-C
Heart failure	8 g (i.v. Mg sulfate) over 12 hours	↓ ventricular ectopic beats, couplets & nonsustained ventricular tachycardia	B	↑ rate control & rhythm control
	6000 mg (Mg orotate) for 1 month and 3000 mg for 11 months	↑ survival rate, improvement in NYHA scale	B	↑ calcium channel inhibition ↓ calcium levels in myocardial cells exposed to LPC
	365 mg (Mg chloride) per day for 6 weeks	↓ mean arterial pressure (MAP), systemic vascular resistance, epinephrine, isolated ventricular premature complexes, couplets & nonsustained ventricular tachycardia frequency	C	↑ PR interval, QRS duration, intra-atrial and atrioventricular (AV) nodal conduction times, atrial and AV refractory periods stabilizes cardiac repolarization
	970 mg over 24 hours (i.v. Mg sulfate)	Stabilizes cardiac repolarization	C	↓ MAP, systemic vascular resistance, epinephrine, isolated ventricular premature complexes, couplets & nonsustained ventricular tachycardia frequency
	800 mg (Mg oxide) per day for 3 months	↑ small arterial compliance	C	↑ serum & intracellular Mg; ↓ serum CRP ↑ small arterial compliance

Condition	Dosing & Administration	Outcome	Class of Evidence	MOA
Hypertension	365-450 mg for 1-6 months	↓ SBP & DBP	A	↓ systemic vascular resistance & left cardiac work indexes
	300 mg per day for 1 month minimum	↓ SBP & DBP	A	↑ arterial response to ACh-relaxation induced by NO
Insomnia/sleep	320 mg (Mg citrate) per day for 7 weeks	↑ serum Mg only in Mg-deficient px; ↓ plasma CRP only in px with >3.0 mg/L (an indicator of chronic inflammatory stress)	B	↑ slow-wave sleep ↑ renin, melatonin; ↓ cortisol
	500 mg (Mg oxide) twice per day for 8 weeks	↑ sleep time, sleep efficiency, serum renin & serum melatonin; ↓ ISI score, sleep onset latency, serum cortisol	C	↑ slow-wave sleep, delta & sigma power, renin, aldosterone; ↓ cortisol
	Effervescent tablets titrated from 10 mmol to 20 mmol for 3 days each, up to 30 mmol per day for 14 days in elderly subjects	↑ slow-wave sleep, delta & sigma power, renin, aldosterone; ↓ cortisol	C	
Metabolic syndrome	30 ml (Mg chloride 5% solution = 382 mg elemental Mg) per day for 4 months	↓ SBP, DBP, HOMA-IR, fasting glucose, TGs	B	↓ insulin resistance ↓ SBP, DBP, HOMA-IR, fasting glucose, TGs

Condition	Dosing & Administration	Outcome	Class of Evidence	MOA
Migraines	600 mg (Mg dicitrate) per day	↑ migraine prophylaxis	A	↑ inferolateral frontal, inferolateral temporal, insular blood flow
	600 mg (tri-Mg dicitrate) per day for 12 weeks	↓ attack frequency, number of days with migraine	B	↓ pain transmission & cortical spreading depression via blockade of NMDA receptors
	1000 mg (i.v. Mg sulphate) once	↓ photophobia & phonophobia intensity in px without aura; ↓ pain in px with aura	B	↓ visual evoked potential P1 amplitude
	600 mg (Mg citrate) per day for 3 months	↓ attack frequency, intensity, P1 amplitude; ↑ inferolateral frontal, inferolateral temporal, insular blood flow	C	
Muscle cramps	300 mg (Mg citrate) per day for 6 weeks	↓ mean number of nocturnal cramps during Mg use	C	↓ acetylcholine release from motor nerve terminals
Muscle cramps during pregnancy	120 mg in the morning, 240mg at night (Mg citrate or Mg lactate)	↓ leg cramps	A	Inhibition of ryanodine receptor calcium release channels
	300 mg (Mg bisglycinate chelate) per day for 4 weeks	↓ cramp frequency & intensity	B	
Osteoporosis prevention	150 mg (Mg oxide) twice per day for 1 year in girls aged 8-14	↑ hip bone mineral content	B	Suppress bone turnover via: ↓ serum iPTH, urinary deoxypyridinoline, PICP, ICTP, osteocalcin & ionized Mg2+
	1830 mg (Mg citrate) per day for 30 days in post-menopausal women	↓ serum iPTH, urinary deoxypyridinoline & ↑ serum osteocalcin	C	↑ PTH and bone density ↑ fracture prevention & bone mineral density

Condition	Dosing & Administration	Outcome	Class of Evidence	MOA
Pre-eclampsia & eclampsia	4-15 g (Mg sulfate i.v./i.m) + maintenance doses up to 2g/hour (i.m)	↓ initiation or recurrence of eclampsia at all doses	A	↓ platelet-derived growth factor-A (PDGF-A) mRNA expression in placenta ↓ seizure prophylaxis
	4 g (Mg sulfate i.v.) + 10 g (i.m.)	↓ recurrence of eclampsia to same extent as listed dose + 5.0g/4 hours (i.m)	A	↑ vasodilation of small intracranial & retinal vessels
	6 g (Mg sulfate i.v.)	↓ pulsatility index in central retinal, posterior ciliary blood vessels & middle cerebral artery	C	↓ BP (30) & serum MDA; ↑ serum ET-1, CGRP ↑ red blood cell deformability ↓ rate of pregnancy-induced hypertension, TBX2; ↑ PGF1a/TXB2 ratio
Premenstrual syndrome (PMS)	250 mg per day for 2 cycles	↓ depression, anxiety, water retention & somatic symptoms	B	↑ Mg in lymphocytes & polymorphonuclear cells alleviating mood changes and menstrual migraines
	360 mg (Mg pyrrolidone carboxylic acid) three times per day for 4 cycles	↓ menstrual Distress Questionnaire (MDQ) score, pain & negative affect score; ↑ Mg in lymphocytes & polymorphonuclear cells	C	
	360 mg (Mg pyrrolidone carboxylic acid) for 4 months	↓ pain, number of days with headache, MDQ score; ↑ Mg in lymphocytes & polymorphonuclear cells	C	
	200 mg (Mg oxide) per day for 2 cycles	↓ weight gain, extremity swelling, breast tenderness, bloating after 2nd month	C	

Note: references provided in the "Condition" column link to the pathophysiology of the associated condition to help further understand the mechanisms of action (MOA) of the ingredient.

For an explanation of the classes of evidence, please see the Rating Scales for Evidence-Based Decision Support.

Adverse Effects

While Mg is generally well-tolerated, oral supplementation may cause diarrhea, nausea, or vomiting, while intravenous overdosing may cause thirst, hypotension, drowsiness, muscle weakness, respiratory depression, headaches, flushing, cardiac arrhythmia, coma, and death. Upper limits (UL) for supplemental magnesium have been established at 65 mg for healthy children aged 1-3, 110 mg for children aged 4-8, and 350 mg for ages nine and over, including during pregnancy and lactation. It is important to note that there is no UL for magnesium derived from food as there is no evidence of adverse effects from dietary sources. Magnesium may be used as an alternative to conventional pharmaceuticals for treating conditions such as migraines during pregnancy and lactation as there are no known maternal or fetal contraindications.

Associated Depletions

Class of Drug	Pharmaceutical	Effect	Class of Evidence
Alkylating Agents	Cisplatin, carboplatin	↑ incidence of hypomagnesemia & association with lower serum Mg	A
Aminoglycosides	Gentamicin, Tobramycin, Amikacin, and Sisomicin	↑ incidence of hypomagnesemia ↓ plasma total mg, ionized mg concentration; ↑ Mg excretion	D D
Antifungal	Amphotericin B	↑ hypomagnesemia by 2nd week after low cumulative doses (208 mg). Lowest serum and largest excretion achieved after 1 month. Mg status recovered 1 year after discontinuation	D
Antiprotozoal	Pentamidine	↑ cases of severe hypomagnesemia and torsade de pointes	D
Antiviral	Foscarnet	↑ hypomagnesemia incidence; reversible with i.v. Mg sulfate (3.0 g)	C
Beta 2-adrenoceptor agonists	Salbutamol, rimiterol, terbutaline	↓ serum Mg ↑ hypomagnesemia (dose-related)	C/D D
Cardiac glycoside	Digoxin	↑ hypomagnesemia; ↓ serum Mg with digoxin toxicity	D

Class of Drug	Pharmaceutical	Effect	Class of Evidence
Epidermal growth factor receptor inhibitors	Panitumumab, cetuximab	↑ incidence of hypomagnesemia, & risk ↓ serum Mg, & effectiveness of Mg supplementation on raising Mg levels	A D
Estrogens	Estrogen therapy	↓ hypermagnesemia in postmenopause	B
	Oral contraceptives	↓ serum Mg with oral contraceptives & nonpregnant women	D
Immunosuppressant	Tacrolimus	↑ hypomagnesemia incidence ↓ serum magnesium after 1 week with 10% of patients with levels <1.8mg/dL ↑ hypomagnesemia incidence, & excretion of Mg	A C D
	Cyclosporin-A	↑ hypomagnesemia incidence	D
Loop diuretics	Furosemide, piretanide, bumetanide, and torasemide	↑ hypomagnesemia risk	A
Proton pump inhibitors	Dexlansoprazole, esomeprazole, ilaprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole	↑ risk of hypomagnesemia	A
Saline laxatives	Sodium phosphate	↓ postoperative serum Mg after sodium phosphate bowel cleanse; ↑ hypomagnesemia in rabbits	D
Thiazide diuretics	Chlorthiazide, chlorthalidone, hydrochlorothiazide, indapamide, metalazone	↓ plasma Mg, mononuclear cell Mg; ↑ incidence of hypomagnesemia	D
Xanthines	Theophylline	↓ intracellular Mg	D

Associated Interactions

Class of Drug	Pharmaceutical	Effect	Class of Evidence
Anticonvulsants	Gabapentin (200 mg) once	↓ bioavailability of drug by 32%	C
	Carbamazepine (600 mg per day) for 4 weeks	↑ erythrocyte Mg concentration	D
	Sodium valproate (900 mg per day) for 4 weeks	↑ erythrocyte Mg concentration	D
Antihypertensives	General: 230 mg of Mg per day if treated with antihypertensive for more than 6 months; 460 mg of Mg per day if new to drug or if treatment paused for more than 4 weeks	↓ SBP & DBP in patients with Stage I hypertension but not normotensive patients	A
Antipsychotics	Haloperidol (8 mg per day) for 21 days	↑ erythrocyte Mg concentration	D
	Risperidone (6 mg per day) for 21 days	↑ erythrocyte Mg concentration	D
Antithrombotics	Acetylsalicylic acid for 7 months	↓ platelet-dependent thrombosis	C
	Acetylsalicylic acid (300 mg) once	↓ platelet aggregation synergistically	D
Anxiolytics	General	↓ anxiety	C
Calcium channel blockers	Verapamil (no dose)	↓ manic symptoms compared with drug monotherapy	C
Cardiac glycosides	Digoxin	↓ absorption of digoxin	D
H2 receptor antagonists	General	↓ laxative effect of Mg oxide	D
Hormones	Adrenocorticotropic hormone (25 U/day i.v.) for 3 weeks	↓ infantile spasm frequency over 24 weeks compared with drug monotherapy	C

Class of Drug	Pharmaceutical	Effect	Class of Evidence
Neuromuscular blockers	General	↓ neuromuscular blockade onset time, recovery time; ↑ clinical duration	A
	Propofol (1 mg/kg), rocuronium (0.6 mg/kg) & fentanyl (1 µg/kg)	↓ required doses of drugs during anesthesia via anesthetic, analgesic & muscle relaxation	B
	Rocuronium (0.45 mg/kg)	↓ onset time of drug in low dose group	B
NMDA receptor antagonists	Ketamine	↓ antinociceptive effectiveness when Mg sulfate applied first; ↑ antinociceptive effects when ketamine applied first in rats	D
		↑ drug effectiveness of lowering body temperature in rats	D
Proton pump inhibitors	General	↓ laxative effect of Mg oxide	D
Quinolones	Lomefloxacin	↓ drug in plasma from lowered absorption of Mg-lomefloxacin chelate complex	D
	Ciprofloxacin, sparfloxacin	↓ dissolution rate	E
Selective serotonin agonist	Cisapride (0.2 mg/kg/day) for 4 weeks	↑ stool passage frequency in pediatric functional constipation	D
Selective serotonin reuptake inhibitors	Sertraline (150 mg per day) for 21 days	↑ erythrocyte Mg concentration	D
Sulfonylureas	Glibenclamide (1.75 mg micronized or 2.5 mg non-micronized)	↑ micronized drug absorption rate (no effect on extent of drug absorbed, or insulin/glucose responses); ↑ drug AUC, total area, peak concentration, incremental insulin area, max insulin response	D
	Glipizide (5 mg)	↑ drug AUC, incremental insulin area; ↓ time to max insulin response, plasma glucose	D
Tetracyclines	General	↓ drug absorption	D

Class of Drug	Pharmaceutical	Effect	Class of Evidence
Tricyclic antidepressants	Amitriptyline (10 mg/day) for 8 weeks	↓ parameters of pain & pain threshold, fatigue, sleep disorders, irritability, number of tender points, tender point index, fibromyalgia impact, depression & anxiety	B
	Amitriptyline (25 mg three times/day) for 28 days	↑ erythrocyte Mg concentration	D
Vitamins	B6 (40-50 mg/day) for 1 cycle	↓ premenstrual symptoms synergistically	B
	D3 (2 µg/day) for 1 week	↑ Mg absorption in jejunum of healthy individuals	D

Pharmacokinetics

Absorption

Under normal conditions, the majority of Mg (56%) is absorbed in the ileum, followed by the jejunum (22%), the duodenum (11%), and colon (11%). At lower GI concentrations, 10-20% of Mg is uptaken through active transport (exchanging with effluxed sodium) via the saturable Transient Receptor Potential Channel Melastatin members (TRPM6 and TRPM7) in the distal small intestine and colon. These transporters are inhibited through their sensitivity to higher intracellular Mg concentrations, thereby shifting to passive paracellular transport mechanisms. Electrochemical gradient-generated passive diffusion accounts for 80-90% of all Mg absorption as it is not saturable. Claudin proteins allow for the passive diffusion of Mg between the tight junctions of intestinal epithelial cells. Similarly to TRPM6/TRPM7, these proteins have the ability to remove the hydration shells surrounding Mg, which may increase absorption of Mg through ion channels.

Distribution

After absorption, Mg is primarily distributed to bone (53%), muscle (27%), and soft tissues (27%). Only 0.8% is found in the blood, primarily in serum and red blood cells. In the serum, Mg can be found in free/ionized form, bound to proteins, or as complexes including Mg phosphate, bicarbonate, citrate, or sulfate. Total blood serum concentrations in healthy individuals may range between 0.65-1.05 mmol/L.

The body may draw Mg from bones, muscles, and soft tissues to keep serum concentrations under tight control. Therefore, limiting the diagnosis of Mg deficiencies to serum measurements may not reflect total body deficiency. This can lead to an increased risk for a cohort of chronic disease states as a true Mg deficiency may remain mistakenly undiagnosed. While they are convenient and relatively inexpensive, Mg assessments beyond serum measurements may be required. Other assessments can include measures of Mg in leukocytes and urine, as well as measures of free-Mg using fluorescent probes, dyes, ion-selective electrodes or nuclear magnetic resonance spectroscopy. Measuring Mg in the muscle is an appropriate indication of whole body Mg, however, it is expensive and invasive.

Metabolism

Magnesium is a cofactor in over three hundred enzymatic reactions and acts to stabilize enzymes involved in ATP synthesis. As a counter-ion to ATP and nucleic acids, Mg is required to metabolize glucose and synthesize fats and proteins. Disruptions of Mg status can lead to complications in body functions that require ATP, such as muscle contraction, heart function, bone formation, and neurotransmission.

Bone: Magnesium may be used in the formation of bone. Mg in the blood substitutes positions with the Mg in bone, increasing chondrocyte column development. It increases osteoblast proliferation in bone and decreases inflammatory molecules that increase osteoclast activity.

Brain: Magnesium may be used in the inhibition of postsynaptic NMDA receptor excitability when the membrane potential is below -60mV. The postsynaptic membrane potential is also lower in the presence of high Mg concentration as Mg stimulates GABA receptor uptake of chloride, resulting in a hyperpolarized neuron. This effect may also be achieved when Mg reduces presynaptic glutamate release by antagonizing calcium, thereby reducing neural signaling. Vasodilatory effects are also observed through Mg-related neuronal mechanisms, including increased calcitonin gene-related peptide and nitric oxide synthase activity.

Heart and Vascular System: In the heart and vascular system, Mg has multiple functions. Magnesium can inhibit ion channel activity and associated electrical potentials in the myocardium. It may antagonize calcium binding to cardiac muscle during contraction and overall calcium availability. Magnesium also provides anti-inflammatory and vasodilatory properties, which can prevent complications relating to atherosclerosis, vascular calcification, and thrombosis.

Muscle: In the muscle, Mg competes with calcium for ion channels and binding sites on troponin C and myosin that lead to muscular contraction. In the presence of adequate Mg, calcium displaces Mg causing contraction. But when Mg is low, less calcium is required to displace Mg, leading to hypercontractility.

Excretion

If not absorbed in the GI tract, between 20-70% of ingested Mg may be excreted in the feces. The half-life of Mg is approximately 1000 hours in humans. The kidney filters between 2000-2400 mg of Mg each day. In the proximal tubule, 10-30% of Mg is reabsorbed through passive paracellular pathways. In the thick ascending limb, 40-70% is reabsorbed via claudin proteins, whereas the final 5-10% of Mg is reabsorbed by active TRPM6 transport. Depending on many variables, 5-70% of magnesium filtered by the kidney can be excreted in the urine.