

# MAGNESIUM

the critical and underrated mineral essential for optimal health

- The necessity of magnesium & consequences of deficiency
- Supplementation absorption & pharmacological properties
- The tight homoeostatic regulation of magnesium
- Evidence-based magnesium indications table
- Study highlights
- Practitioner & patient resources





***‘According to the medical literature, we are currently experiencing two concomitant phenomena: (i) a “neglected epidemic of chronic disease” and (ii) a widespread deficiency of selected nutrients.’<sup>1</sup>***

***‘Many studies have reported that reduced levels of magnesium are associated with a wide range of chronic diseases.’<sup>2</sup>***

***‘Dietary data suggest that the average magnesium intake has declined markedly over the last 100 years.’<sup>3</sup>***

1. Schwalfenberg GK, Genius SJ. The importance of magnesium in clinical healthcare. Scientifica (Cairo). 2017:4179326.

2. Al Alawi AM, Majoni SW, Falhammar H. Magnesium and human health: Perspectives and research directions. Int J Endocrinol. 2018:9041694.

3. Vormann J. Magnesium: Nutrition and homoeostasis. AIMS public health. 2016;3(2):329-40.

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### DISCLAIMER

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# Magnesium - a critical mineral for health

Magnesium plays numerous fundamental roles in the body, it is essential for every cell, and has been quoted as one of the most underrated minerals. Overall, it is the fourth most abundant cation in the body, but intracellularly it is the second most abundant cation; hence, its critical importance for human health.<sup>1</sup>

In this clinical guide you will learn the essential roles of magnesium, how deficiency is linked to numerous chronic diseases and how the body attempts to maintain homeostatic control, even when studies show magnesium is a deficient mineral in our diets. You will discover and understand how magnesium deficiency and supplementation affects chronic disease prevention and treatment, as well as the best form of magnesium supplementation for optimal absorption and intracellular functions. And finally, access some valuable resources for both practitioner and patient.

## The many essential roles of magnesium

**Magnesium is required as a cofactor in over 300 enzymes that regulate various functions, including:<sup>2</sup>**

**Muscle contraction • Neuromuscular conduction • Glycaemic control • Myocardial contraction • Blood pressure regulation • Protein synthesis**

### Other functions of magnesium, include: <sup>2</sup>

#### Role in active transport

Facilitates active transport of calcium and potassium ions across cell membranes, which is essential for the conduction of nerve impulses, muscle contraction, maintaining vasomotor tone, and normal heart rhythm.

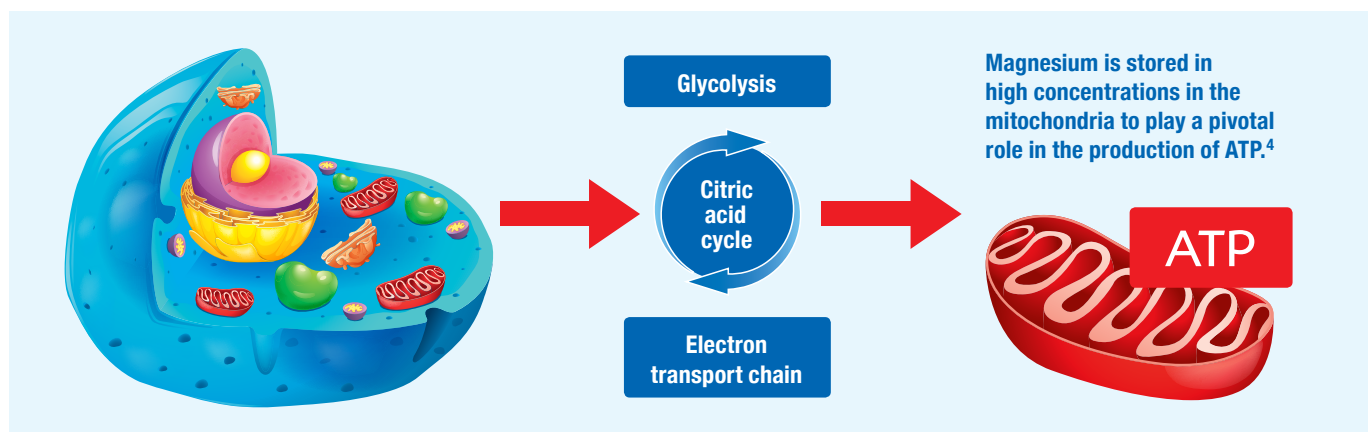
#### Structural roles

Important for the structure of bones, proteins, many enzymes, mitochondria, DNA and RNA.

#### Role in immunological functions

Involved in macrophage activation, adherence and bactericidal activity of granulocyte oxidative burst, lymphocyte proliferation, and endotoxin binding to monocytes.

## Key role of magnesium in cellular physiology



## Why magnesium is also called the 'relaxing and stress blocking mineral'

Magnesium is a divalent cation ( $Mg^{2+}$ ), which means it is capable of attaching to and protecting the negatively charged surface of the cell membrane. By doing so magnesium can cause a drop in neuromuscular, muscular and cardiac excitability.

Magnesium is also a calcium antagonist, inhibiting the release and action of calcium-induced 'excitatory' transmitters, such as adrenaline, noradrenaline, acetylcholine, prostaglandins, bradykinin and histamine.<sup>3</sup>

# Magnesium deficiency is widespread with health consequences

With magnesium being essential to every cell in the human body, deficiency needs to be avoided for optimal health; however, various sources show magnesium deficiency is widespread globally, with some population studies showing nearly 1/4 of the population have a daily dietary intake less than 50% of the recommendations. Research also shows that magnesium deficiency occurs in between 1.7% and 36% of the population, with estimates of up to 42% in young adults; therefore, supplementation is often required. The following chart shows the potential causes and signs and symptoms of magnesium deficiency, and the consequences on cell function with potential disease risks.<sup>3-5</sup>

## CAUSES OF POTENTIAL MAGNESIUM DEFICIENCIES

- Hospitalisation & surgery
- Drugs
- Poor nutrition
- Stress
- Chronic alcoholism
- Prolonged heat - exercise
- Pregnancy and lactation
- Burns
- Endocrine disorders
- GIT disorders
- Kidney dysfunction
- Metabolic acidosis

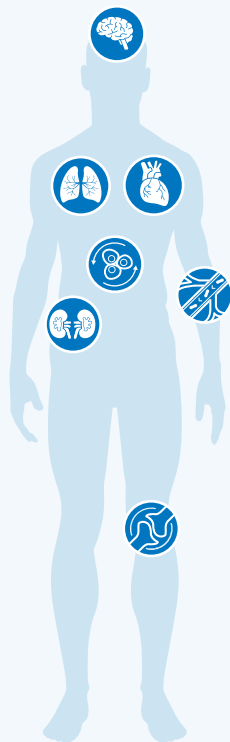
## FUNCTIONS AFFECTED BY MAGNESIUM DEFICIENCY

- >300 enzymes
- Heart rhythm & vascular tone
- Nerve function and NT release
- Muscle contraction & relaxation
- Energy metabolism
- Blood glucose regulation
- Vitamin D metabolism
- Protein, nucleic acid & mitochondria structure
- Immune function
- Bone formation
- Membrane function
- Insulin secretion

## DIETARY DEFICIENCY SIGNS & SYMPTOMS

- Can be asymptomatic in mild deficiency
- Weakness
- Fatigue
- Low mood & anxiety
- Hyperexcitability
- Agitation & hyperirritability
- Headaches
- Muscle twitches and spasms
- Loss of appetite
- Dizziness
- Nausea
- Low stress tolerance

## THE POTENTIAL ADVERSE EFFECTS OF HYPOMAGNEAEMIA



### BRAIN

- ↑ Risk of migraine
- ↑ Risk of seizure
- ↑ Risk of stroke

### LUNG

- ↑ Severity of COPD

### KIDNEY

*In patients with CKD, hypomagnesaemia is associated with the following:*

- ↑ Risk of osteoporosis
- ↑ Cardiovascular morbidity & an all-cause mortality

### PANCREAS & METABOLISM

- ↑ Insulin resistance
- ↑ Risk of type 2 diabetes mellitus
- ↑ Triglycerides & total cholesterol
- ↓ HDL
- ↑ Oxidative stress

### HEART

- ↑ Risk of cardiac arrhythmia
- ↑ Risk of digoxin toxicity
- ↑ Risk of coronary artery disease
- ↑ Mortality in patient with heart failure
- ↑ Mortality and morbidity post AMI

### VASCULAR SYSTEM

- ↑ Risk of atherosclerosis
- ↑ Risk of hypertension
- ↑ Vascular tone & resistance

### BONES

- ↑ Risk of osteoporosis
- Increased risk of bone fragility
- Reduces the vascular supply of bones
- Increases inflammatory cytokines
- Reduces PTH levels
- Increase in tissue resistance to PTH
- Decrease in vitamin D levels

*Causes of magnesium-dependent vitamin D-resistant rickets:*

- Reduction of the synthesis of vitamin D
- Reduction of PTH levels

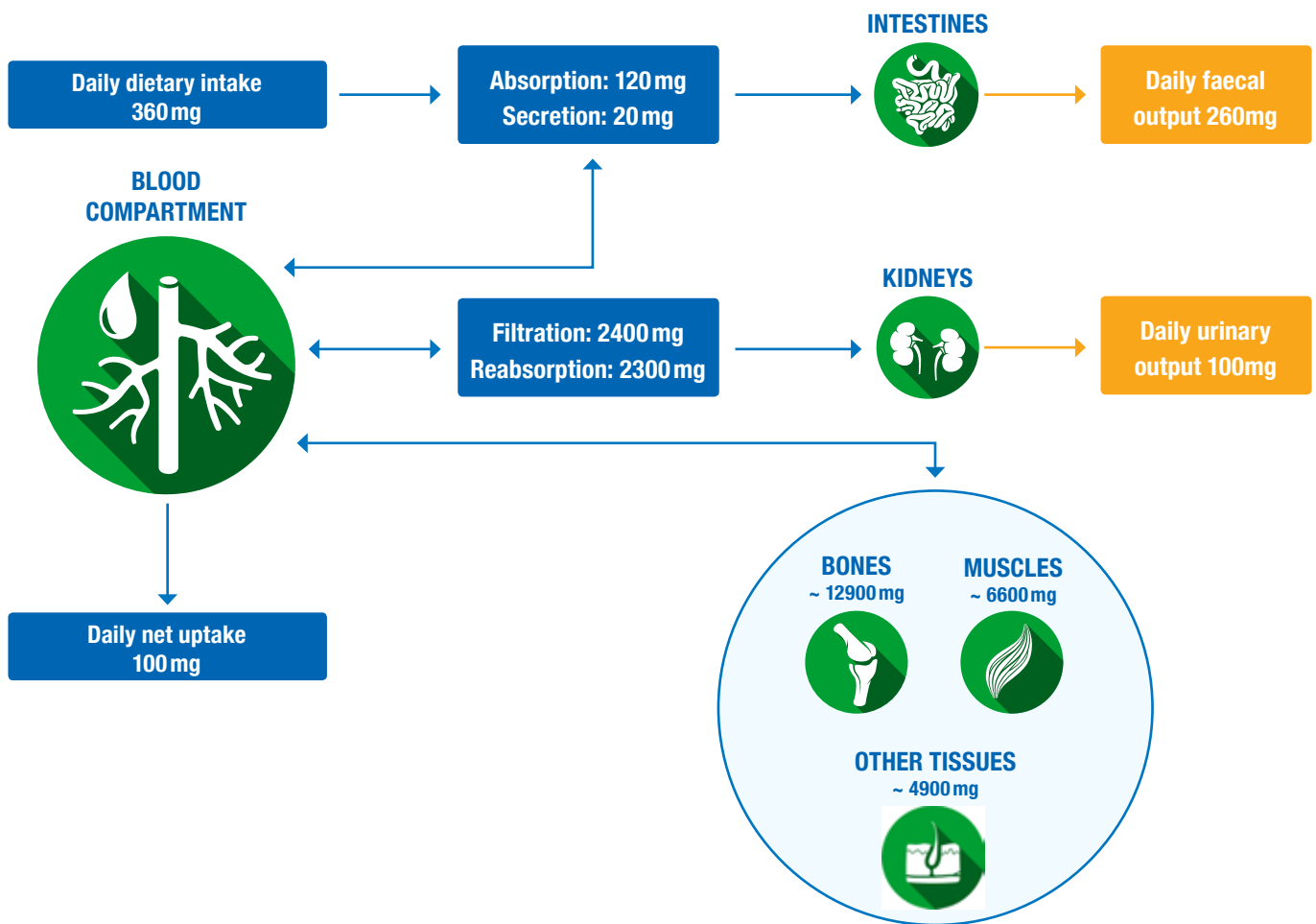
# The intricate balance of magnesium in the body

The magnesium content in the blood (extracellular) is less than 1% of the body's total magnesium, with the majority (about 99%) stored in bone, muscles and non-muscular soft tissue. Approximately 50-60% of magnesium forms part of the hydroxyapatite component of bone. Intracellularly, magnesium is in higher concentration in cells with the highest metabolic activity; hence, within mitochondria for ATP production.<sup>3</sup>

## Maintaining the crucial homeostatic balance of magnesium in the body

Being such a critical nutrient for health, the body has mechanisms to maintain adequate tissue and intracellular levels. This homeostatic process is regulated by the intestines, bones and kidneys, with the kidneys playing a major role.<sup>2</sup>

*'Magnesium balance in the body is controlled by a dynamic interplay among intestinal absorption, exchange with bone and renal excretion.'*<sup>3</sup>



- Around 24-76% of the ingested magnesium is absorbed in the gut with the remainder eliminated in the faeces. If the body is low in magnesium up to 80% can be absorbed.
- The kidneys filter around 2400mg of magnesium per day with 95% reabsorbed by the loop of Henle and the distal tubules. Only about 100mg of magnesium is excreted under normal physiological conditions. The kidneys play a major role in magnesium balance by regulating excretion.
- The muscles store around 6600mg, bone approximately 12900mg and other tissues around 4900mg.<sup>2,7</sup>

Adapted from: Al Alawi AM, Majoni SW, Falhammar H. Magnesium and human health: Perspectives and research directions. Int J Endocrinol. 2018;9041694.

# Where do we get magnesium from?

## Magnesium in foods

Magnesium is in a wide range of foods with good sources including green leafy vegetables, legumes, nuts, seeds and whole grains. Foods naturally contain magnesium in an organic form, such as magnesium citrate, which is also available as a supplement to the diet.

### Rich food sources of magnesium

#### per 100gm serving

- Hemp seeds - 700mg
- Pumpkin seeds - 525mg
- Flax seeds - 392mg
- Brazil nuts - 376mg

#### per serving

- Spinach, boiled (1/2 cup) - 78mg
- Whole wheat bread (2 slices) - 46mg
- Avocado (1 cup) - 44mg
- Baked potato - 43mg
- Kidney beans (1/2 cup) - 35mg

## How much magnesium do we need?

The recommended daily intakes (RDIs) for magnesium in adolescents, adult men and women, and pregnant women are between 360 to 420mg every day for healthy individuals not at risk of magnesium deficiency. For those with hypomagnesaemia or at risk of magnesium deficiency, additional supplementation may be required.

Age	Male	Female	Pregnancy	Lactation
0 – 6 months	<b>30 mg</b>	<b>30 mg</b>		
7 – 12 months	<b>75 mg</b>	<b>75 mg</b>		
1 – 3 years	<b>80 mg</b>	<b>80 mg</b>		
4 – 8 years	<b>130 mg</b>	<b>130 mg</b>		
9 – 13 years	<b>240 mg</b>	<b>240 mg</b>		
14 – 18 years	<b>410 mg</b>	<b>360 mg</b>	<b>400 mg</b>	<b>360 mg</b>
19 – 30 years	<b>400 mg</b>	<b>310 mg</b>	<b>350 mg</b>	<b>310 mg</b>
31 – 50 years	<b>420 mg</b>	<b>320 mg</b>	<b>360 mg</b>	<b>320 mg</b>
51+ years	<b>420 mg</b>	<b>320 mg</b>		

## Magnesium in supplements

There are many commonly prescribed magnesium supplements; however, the organic forms found naturally in the body, such as magnesium citrate, have been shown to be superior to inorganic magnesium salts, such as magnesium oxide. Water solubility is an important issue in absorption and utilisation of magnesium supplements, with magnesium citrate shown to have superior solubility and therefore, greater absorption than magnesium oxide.<sup>3,6</sup>

Research has also revealed the actual absorption mechanism of magnesium, showing that it is absorbed only as free unbound ions. This means that tightly bound magnesium salts will be harder to absorb, unlike magnesium citrate, which freely dissociates into separate magnesium and citrate molecules at the intestinal wall.<sup>7</sup> However, not all citrates are the same, as will be revealed later in this guide.

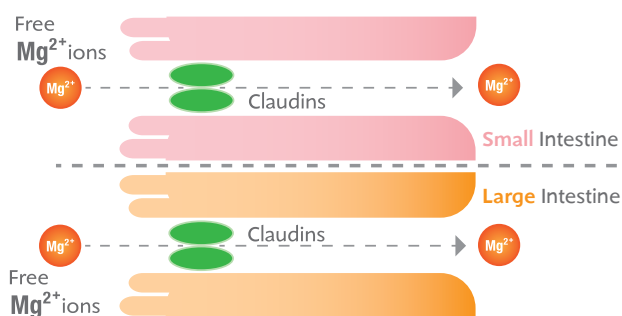
**The next section of this clinical guide will discuss the beneficial properties of magnesium citrate.**

# Free unbound magnesium is the key to magnesium absorption from supplements

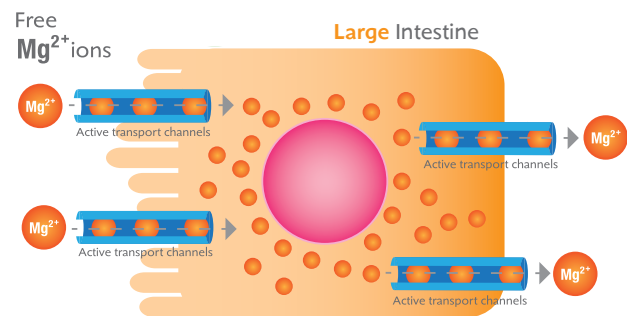
'Mg<sup>2+</sup> absorption in the gut depends on two separate pathways; paracellular transport is responsible for bulk Mg<sup>2+</sup> absorption and takes place mostly in the small intestine, whereas fine-tuning occurs in the cecum and colon via transcellular transport.'<sup>7</sup>

In a comprehensive 2015 review, the authors revealed that the **key requirement for magnesium absorption through both paracellular and transcellular pathways is free unbound magnesium.** This is also required for intracellular absorption.<sup>7</sup>

## 1. Paracellular absorption (between the cells)



## 2. Transcellular (active transport)



Optimal absorption requires **free unbound magnesium** at the intestinal and cell wall. In other words, tightly bound magnesium salts will hinder magnesium absorption.<sup>7</sup>

**Magnesium citrate is one form that easily dissociates to release free Mg<sup>2+</sup> for optimal absorption in the intestines and into the cells, where it is most needed.**



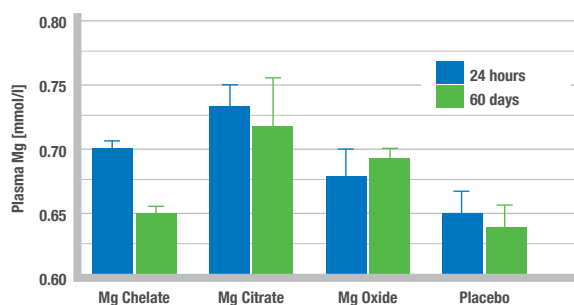
# Magnesium citrate - the ideal magnesium carrier

Citrate is the ideal carrier for magnesium through the upper GIT tract, as it easily dissociates at the intestines, allowing free unbound magnesium ions to be rapidly absorbed. As an organic anion (negatively charged molecule), citrate increases the bioavailability of cations (positively charged molecules), such as magnesium.

## Magnesium citrate shows optimal absorption

In a randomised, double-blind, placebo-controlled study, 46 healthy individuals were supplemented with 300mg of elemental magnesium per day from magnesium citrate, magnesium amino acid chelate or magnesium oxide. The magnesium citrate group showed significantly higher absorption than all other groups at 24hrs and after 60 days.

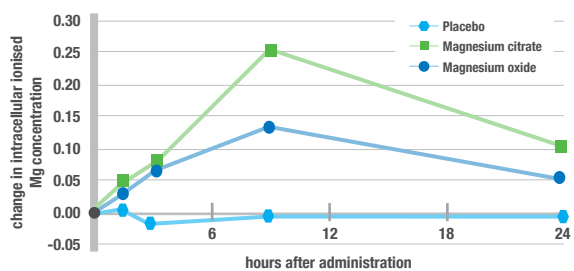
Walker AF, Marakis G, Christie S, et al. Mg citrate found more bioavailable than other Mg preparations in a randomised, double-blind study. *Magnesium Res.* 2003;16(3):183-91.



## Water-soluble magnesium citrate increases intracellular magnesium status

In a placebo-controlled, randomised study, 51 healthy individuals received 300mg of water soluble TMDC anhydrous magnesium citrate, magnesium oxide or placebo. The magnesium citrate group had significantly greater increases in intracellular magnesium levels.

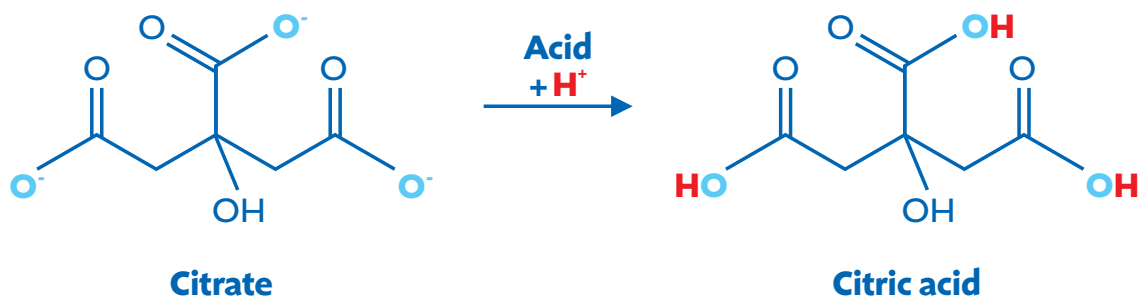
Nestler A, Vormann J, Kolisek M. Mg supplementation acutely affects intracellular mg<sup>2+</sup> in human leukocytes. *The FASEB Journal.* 2012;26(1\_supplement):lb278-lb.



## Magnesium citrate is also beneficial for balancing acid-base balance

The additional action of citrate in metabolism is due to its ability to absorb acid (hydrogen ions) and in turn forming citric acid. This helps to reduce the effects of an excess acidity; therefore, maintaining the physiological acid-base balance.

### Neutralisation of acid by citrate



# Magnesium citrate improves magnesium status in muscle, brain and serum

In a 2019 experimental study, magnesium citrate, when dissolved in water at a dose of 405mg (405mg/70kg), was shown to significantly improve levels of magnesium in the:

## MUSCLE TISSUE



## BRAIN

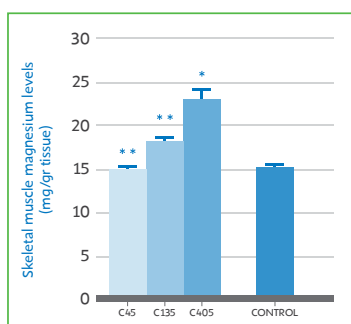


## SERUM



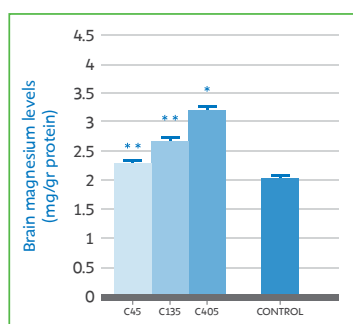
### In muscle tissue

In skeletal muscle, the dose of 405mg/kg of magnesium citrate statistically improved magnesium tissue levels



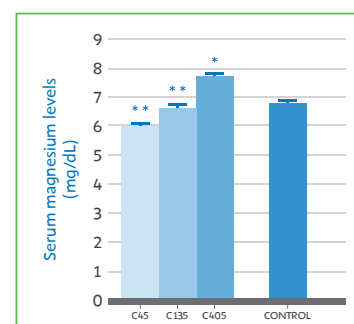
### In the brain

In the brain, the dose of 405mg/kg of magnesium citrate statistically improved magnesium tissue levels



### In the serum

In the 405mg/kg of magnesium citrate group, serum magnesium levels were statistically improved.



In each chart above: C = magnesium citrate; C45 = 45mg/70 kg dose; C135=135 mg/70 kg dose; C405=405 mg/70 kg dose

Ates M, Kizildag S, Yuksel O, et al. Dose-dependent absorption profile of different magnesium compounds. Biological Trace Element Research. 2019.

The above data show the benefits of using magnesium citrate for optimal magnesium absorption; however, it is not well known that not all magnesium citrate supplements are the same.

**The next section will discuss the differences and provide a checklist for the optimal magnesium supplement.**

## Not all magnesium citrates are the same

**When a product states magnesium citrate it does not state whether it is trimagnesium dicitrate (TMDC) or whether it is anhydrous, nonahydrate or dodecahydrate. What's the difference?**

**Magnesium citrate supplements occur in different forms:**

- They vary in the number of magnesium ions to citrate ions
- They vary in their solubility, ranging from poor to excellent

### Magnesium to citrate ion ratio

1. Magnesium citrate dibasic tetrahydrate contains a 1:1 ratio of magnesium to citrate
2. Trimagnesium dicitrate (TMDC) is the optimal form providing 3 magnesium ions to 2 citrate (3:2).  
This ratio provides more magnesium per complex.

### TMDC occurs in different solubility forms

1. TMDC anhydrous— provides excellent water solubility. This the best form and can only be delivered in watertight packaging due to its highly soluble ability to attract water (i.e. not tubs, gelatin or veg capsules)
2. TMDC nonahydrate— providing less magnesium and poor solubility
3. TMDC dodecahydrate— providing even less magnesium and poor solubility

**The best form of magnesium citrate is TMDC anhydrous, with high solubility and easy dissociation in the gut for optimal absorption**



### Ensuring the optimal delivery of magnesium citrate for absorption

1. The preferred delivery choice of magnesium citrate is the highly water soluble TMDC anhydrous form, in a liquid drink.
2. This therapeutic magnesium travels rapidly through the stomach reducing interaction with other substances and lessening competition for absorption.
3. Other delivery forms can have slower transit time, so they break open in the stomach, which means the released free magnesium ions may bind with fatty acids, amino acids and phosphates, reducing their bioavailability.
4. At the intestinal wall, before absorption, magnesium easily dissociates from citrate providing unbound absorbable magnesium ions.

### The optimal characteristics of a therapeutic magnesium include:

- ✓ High dose
- ✓ Highly water soluble
- ✓ Delivery through the gut with easy dissociation for absorption
- ✓ Improvement in blood magnesium status with use
- ✓ Bioavailability data
- ✓ Clinical trial support

# MAGNESIUM IN THERAPY

## A review of the evidence-based indications

Magnesium citrate has been shown to be beneficial in numerous clinical trials for various conditions.

This next section and table outline the areas of research and potential clinical indications for all forms of magnesium.

CONDITION	INDICATION	EVIDENCE		
		CLINICAL TRIALS*	SYSTEMATIC REVIEW/META-ANALYSIS*	EXPERIMENTAL TRIALS*
ADHD	Magnesium deficiency is common in ADHD Attention and hyperactivity improvements	●		
Alzheimer's disease	Magnesium levels are lower in Alzheimer's patients	●		
Asthma	Bronchospasm reduction Breathlessness and lung function improvement Hospitalisation reduction	●	●	●
Atopic dermatitis	Low magnesium levels found in AD sufferers Bathing in magnesium salt solution improves skin barrier function, enhances skin hydration, and reduces inflammation in atopic dry skin	●		
Cancer	Postmenopausal breast cancer risk reduction Colorectal cancer risk reduction Reduced hot flushes, fatigue and sweating in breast cancer therapy	●	●	●
CFS	Low RBC magnesium is associated with chronic fatigue syndrome; therapy improved energy levels, emotional state and pain	●		
Constipation	Osmotic laxative effect may be seen at certain types and doses	●	●	
COPD	Low serum magnesium is associated with chronic lung diseases	●		
CVD	Cardiovascular disease is linked to magnesium deficiency Improved dyslipidaemia, including lowered triglycerides and increased HDL Exercise tolerance and QoL in CAD Higher HDL, lower triglycerides and LDL in diabetics Improved vascular and endothelial function in diabetics Reduced sudden cardiac death rate Reduction in hypertension and arrhythmias Atrial fibrillation and angina Mitral valve prolapse symptom improvement Congestive heart failure symptom improvement and better survival outcome Improved mitochondrial function, reduced oxidative stress, and prevented cardiac diastolic dysfunction in diabetes Reduced risk of stroke Inflammatory marker reduction in CVD	●	●	●
Dementia	Memory improvement in dementia	●		●
Depression and anxiety	Depression and anxiety reduction and prevention	●	●	●
Diabetes and metabolic syndrome	T2D and metabolic syndrome are linked to magnesium deficiency T2D risk and incidence reduction Insulin sensitivity improvement and metabolic control Insulin resistance reduction in prediabetes and diabetes Fasting glucose and insulin improvements Metabolic syndrome prevention Systemic inflammatory marker reduction Increased HDL and reduced triglycerides total cholesterol and LDL in diabetes Peripheral neuropathy reduction Healthy renal function in T2D Depression reduction and prevention in diabetes Weight management in diabetes - lower waist circumference, body fat percentage and BMI Improved mitochondrial function, reduced oxidative stress, and prevented cardiac diastolic dysfunction in diabetes Beneficial effects on metabolic status and pregnancy outcomes in gestational diabetes	●	●	●
Fibromyalgia	Reduction in pain, depressive symptoms, tender points and life limitations	●		
Inflammation - general	Reduction in C-reactive protein and other inflammatory markers	●	●	●

\* Evidence is found on one or more of the indications within each condition subgroup from all magnesium types and delivery systems

COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; AD = atopic dermatitis; PD = Parkinson's disease;  
ADHD = attention deficit hyperactivity disorder; CKD = chronic kidney disease; CAD = coronary artery disease; LDL = low density lipoprotein; HDL = high density lipoprotein;  
QoL = quality of life; BMD = bone mass density; RBC = red blood cell

# MAGNESIUM IN THERAPY

## A review of the evidence-based indications

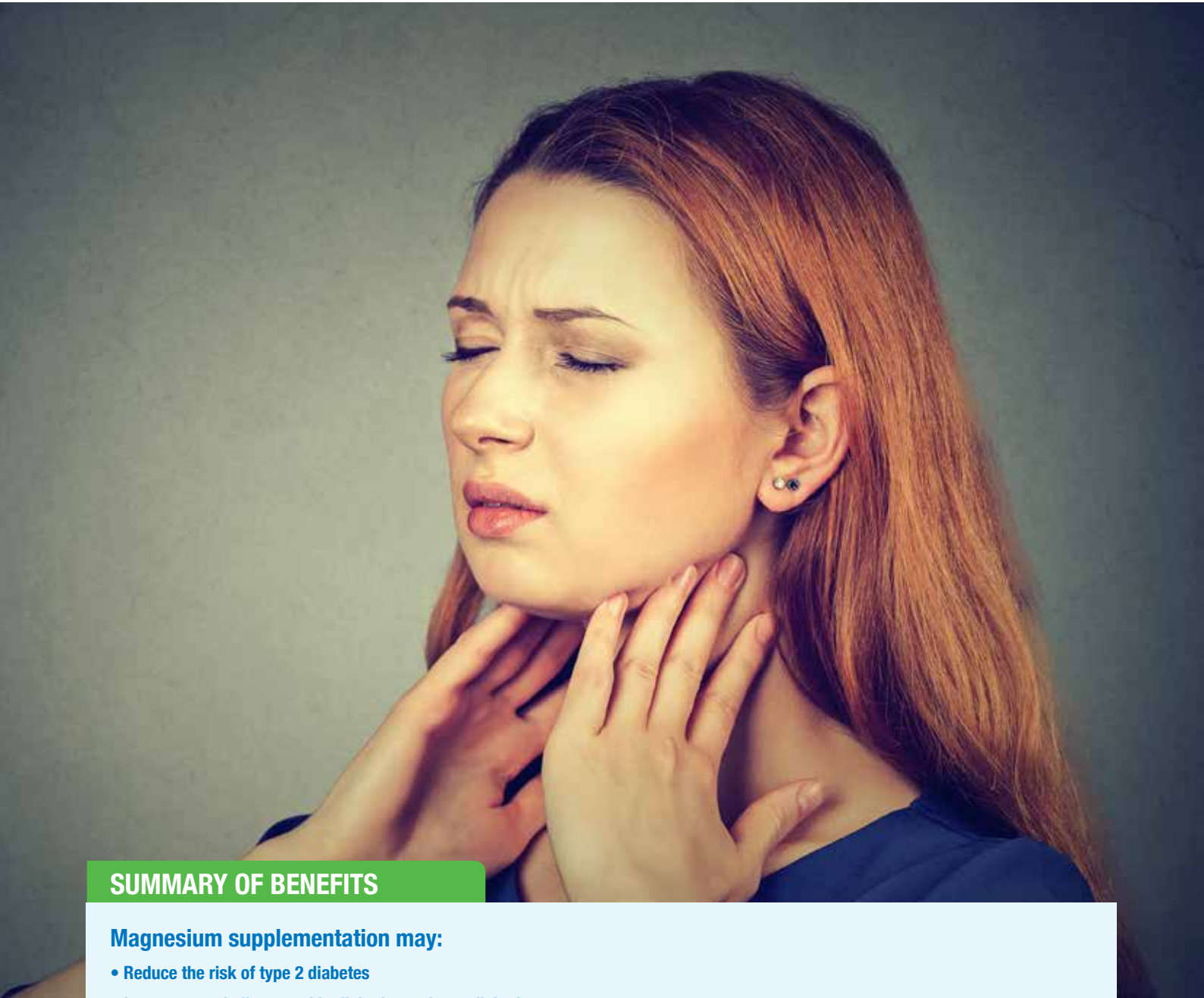
CONDITION	INDICATION	EVIDENCE		
		CLINICAL TRIALS*	SYSTEMATIC REVIEW/META-ANALYSIS*	EXPERIMENTAL TRIALS*
<b>Insomnia</b>	Improvements in insomnia severity index, sleep time, sleep efficiency, sleep onset latency, serum cortisol concentration, serum renin, and melatonin Improved sleep measures during alcohol detoxification Optimal magnesium levels are needed for normal sleep regulation	●		●
<b>Kidney disease</b>	Kidney disease disturbs magnesium homeostasis, with low magnesium levels observed in dialysis Improved phosphate absorption and vascular calcification in CKD	●		
<b>Menopause symptoms</b>	Climacteric symptom relief and an increase in the serum magnesium levels Significant reduction in hot flushes in women on tamoxifen or aromatase inhibitors for breast cancer	●		
<b>Migraines/Headaches</b>	Migraine sufferers often have low serum magnesium Migraine frequency, duration and intensity reduction	●		●
<b>Muscle and physical performance</b>	Improved muscle and physical performance in the elderly. Supplementation may be useful in athletes by supporting glucose utilisation and ATP production	●	●	
<b>Muscle cramps</b>	Muscle cramp reduction in pregnant and nonpregnant individuals	●		●
<b>Neuropathic pain</b>	Pain relief	●	●	
<b>Ocular disorders</b>	Risk reduction in glaucoma and cataracts			●
<b>Osteoporosis and bone health</b>	Low bone density has been linked to low serum magnesium Higher BMD Suppression of bone turnover Fracture reduction	●	●	●
<b>Parkinson's disease</b>	Low magnesium levels in PD brains			●
<b>PMS</b>	Decreased symptoms of PMD and dysmenorrhoea, including diminished pain and less mood changes	●		
<b>Pregnancy</b>	Magnesium deficiency is common in pregnancy Healthy pregnancy outcomes and infant health Lower frequency of preterm births Fewer low birth weight infants Higher birth weight infants Fewer small for gestational age newborns Lower blood pressure in mothers Preeclampsia rate reduction Reduction in pregnancy-related muscle cramps in the calf Beneficial effects on metabolic status and pregnancy outcomes in gestational diabetes Reduced risk of hospitalisation and intensity of premature labour Protection against eclampsia-like seizures	●	●	●
<b>Restless leg syndrome</b>	Reductions in periodic leg movements during sleep	●		
<b>Schizophrenia</b>	Clinical and symptom improvement	●		●
<b>Seizures</b>	Hypomagnesaemia is linked to non-neurological seizures May reduce drug-resistant seizures when used as an adjuvant Protection against eclampsia-like seizures	●		●
<b>Smoking cessation</b>	Reduction in the number of cigarettes smoked	●		
<b>Stress</b>	Stress induced magnesium deficiency	●		●
<b>Thyroid</b>	Severely low magnesium levels are associated with positive anti-thyroglobulin antibodies and hypothyroidism	●		

\* Evidence is found on one or more of the indications within each condition subgroup from all magnesium types and delivery systems

**COPD** = chronic obstructive pulmonary disease; **CVD** = cardiovascular disease; **AD** = atopic dermatitis; **PD** = Parkinson's disease;  
**ADHD** = attention deficit hyperactivity disorder; **CKD** = chronic kidney disease; **CAD** = coronary artery disease; **LDL** = low density lipoprotein; **HDL** = high density lipoprotein;  
**QoL** = quality of life; **BMD** = bone mass density; **RBC** = red blood cell

The following section covers study highlights showing how multiple conditions are adversely affected by magnesium deficiency or benefit with magnesium supplementation.

# ENDOCRINE SYSTEM



## SUMMARY OF BENEFITS

### **Magnesium supplementation may:**

- Reduce the risk of type 2 diabetes
- Improve metabolic control in diabetics and non-diabetics
- Decrease fasting glucose and HbA1c levels
- Improve insulin sensitivity in insulin resistance
- Reduce the insulin resistance marker (HOMA-IR) in diabetics, prediabetics and gestational diabetes
- Reduce the risk and improve diabetic neuropathy outcomes
- Improve lipid profiles in diabetics and non-diabetics
- Improve aspects of metabolic syndrome
- Decrease C-reactive protein levels in prediabetes with hypomagnesaemia
- Help with depression in elderly diabetics
- Improve diabetic mitochondrial function
- Protect thyroid function <sup>1-11</sup>

## Type 2 diabetes and blood sugar management

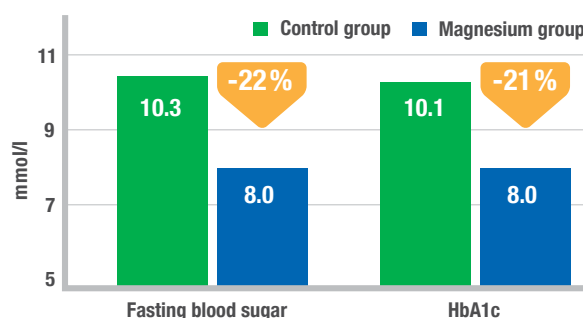
Magnesium is an essential enzyme cofactor in carbohydrate metabolism, and sensitises and regulates insulin receptor activity. Magnesium deficiency is linked to an increased incidence of diabetes and diabetic neuropathy, increased decline of kidney function, and poor lipid management. Supplementation may improve glycaemic and metabolic control, lipid profile management, and mood in diabetic and non-diabetic individuals.<sup>1-7</sup>

**According to a meta-analysis 'It was estimated that 100mg/ day of magnesium reduces the risk of type 2 diabetes by 15%.'**

### Magnesium supplementation improves metabolic control in diabetics

In a randomised, double-blind placebo-controlled trial, magnesium supplementation, at the dose of 650 mg for 16 weeks, significantly decreased fasting blood sugar and HbA1c by 22% and 21%, respectively, compared to placebo.

Rodriguez-Moran M et al. Oral magnesium supplementation improves insulin sensitivity and metabolic control in type 2 diabetic subjects. *Diabetes Care* 2003; 1147-52



## Magnesium citrate in glucose management of overweight individuals

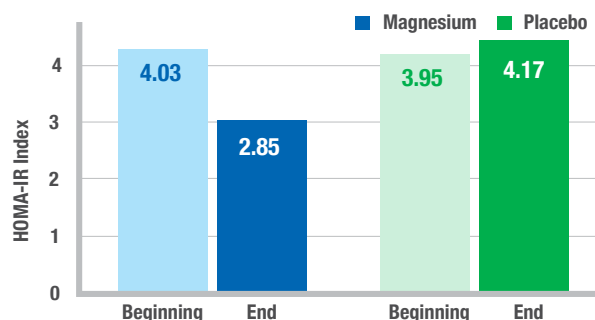
In a randomised crossover trial, 500mg of magnesium citrate per day for 4 weeks improved insulin and glucose homeostasis in overweight or obese individuals. Supplementation led to changes in gene expression and proteomic profiling consistent with favorable effects on several metabolic pathways.

Chacko SA, Sul J, Song Y, Li X, LeBlanc J, You Y, Butch A, Liu S. Magnesium supplementation, metabolic and inflammatory markers, and global genomic and proteomic profiling: a randomized, double-blind, controlled, crossover trial in overweight individuals. *The American journal of clinical nutrition*. 2010 Dec 15;93(2):463-73.

### Significant reduction in insulin resistance marker in prediabetes and hypomagnesaemia

In a randomised, double-blind, placebo-controlled trial 382mg of magnesium given daily to subjects with hypomagnesaemia and prediabetes, the HOMA-IR (insulin resistance marker) was significantly reduced, compared to the placebo.

Guerrero-Romero et al. Oral magnesium supplementation improves glycaemic status in subjects with prediabetes and hypomagnesaemia: A double-blind placebo-controlled randomized trial. *Diabetes & Metabolism* 41 (2015) 202–207



## Gestational diabetes

Oral magnesium supplementation (250 mg) for 6 weeks also resulted in a significant reduction of the HOMA IR (insulin resistance) index in gestational diabetes.

Asemi et al. Magnesium supplementation affects metabolic status and pregnancy outcomes in gestational diabetes: a randomized, double-blind, placebo-controlled trial. *Am J Clin Nutr*. 2015 Jul;102(1):222-9

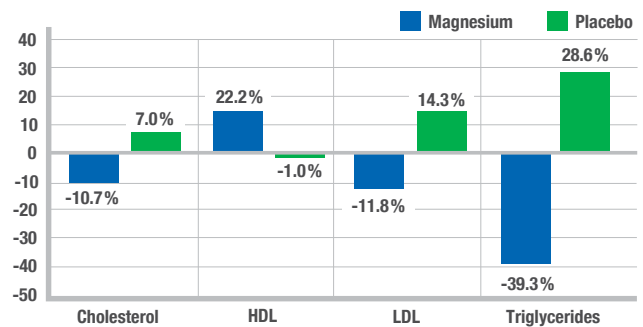
## Metabolic syndrome

Metabolic syndrome is a cluster of risk factors for CVD and type 2 diabetes, which includes dyslipidaemia, hyperglycaemia, obesity, and hypertension. Magnesium deficiency has been linked to all aspects of metabolic syndrome, with a meta-analysis showing magnesium supplementation can improve risk factors of metabolic syndrome in those with hypomagnesaemia.<sup>5</sup>

### Magnesium supplementation improves blood lipid profiles

In a 3 month randomised, double-blind placebo-controlled trial, 300mg of magnesium daily significantly improved blood lipid profiles of non-diabetic subjects with insulin resistance, compared to placebo. Magnesium influenced lipid biosynthesis.

Guerrero-Romero, F., Tamez-Perez, H.E., González-González, G.E., Salinas-Martinez, A.M., Montes-Villarreal, J., Trevino-Ortiz, J.H. and Rodriguez-Moran, M., 2004. Oral magnesium supplementation improves insulin sensitivity in non-diabetic subjects with insulin resistance. A double-blind placebo-controlled randomized trial. *Diabetes & metabolism*, 30(3), pp.253-258.



## Hypothyroidism

A range of trace minerals are required for thyroid function and health. There are few studies on thyroid and magnesium; however, a 2018 cross-sectional study showed that the risks of subclinical hypothyroidism and positive anti-thyroglobulin antibodies were highest in the lowest serum magnesium level group.



Wang K, Wei H, Zhang W, Li Z, Ding L, Yu T, Tan L, Liu Y, Liu T, Wang H, Fan Y. Severely low serum magnesium is associated with increased risks of positive anti-thyroglobulin antibody and hypothyroidism: A cross-sectional study. *Scientific reports*. 2018;8.

### According to research, magnesium supplementation may:

- Reduce the risk of type 2 diabetes
- Improve metabolic control in diabetics and non-diabetics
- Decrease fasting glucose and HbA1c levels
- Improve insulin sensitivity in insulin resistance
- Reduce the insulin resistance marker (HOMA-IR) in diabetics, prediabetics and gestational diabetes
- Reduce the risk and improve diabetic neuropathy outcomes
- Improve lipid profiles in diabetics and non-diabetics
- Improve aspects of metabolic syndrome
- Decrease C-reactive protein levels in prediabetes with hypomagnesaemia
- Help with depression in elderly diabetics
- Improve diabetic mitochondrial function
- Protect thyroid function<sup>1-11</sup>





# REPRODUCTIVE SYSTEM CONDITIONS & PREGNANCY



## SUMMARY OF BENEFITS

### CONDITIONS

#### **Magnesium supplementation may:**

- Reduce PMS and dysmenorrhoea symptoms
- Prevent and reduce frequency and intensity of premenstrual migraines
- Reduce peri- and postmenopausal symptoms
- Reduce hot flashes in breast cancer treatment<sup>1-9</sup>

### PREGNANCY

#### **Magnesium supplementation may:**

- Prevent the development of gestational hypertension
- Reduce the risk of preeclampsia/eclampsia
- Reduce insulin resistance in gestational diabetes
- Prevent the risk of premature labour
- Reduce the intensity and symptoms of premature labour
- Improve infant size, weight and health
- Reduce frequency and intensity of pregnancy-induced leg cramps<sup>1-9</sup>

# Magnesium and gynaecological conditions

Magnesium deficiency may play a role in premenstrual syndrome, dysmenorrhoea and postmenopausal-related symptoms, with supplementation showing benefits in all conditions.

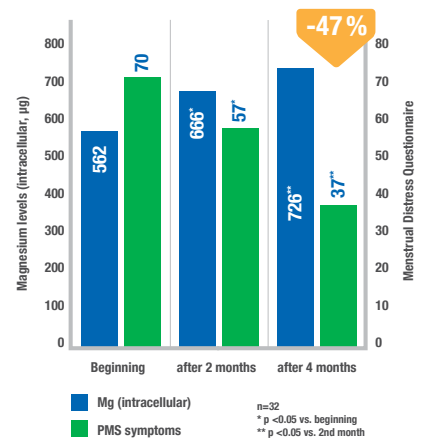
## Premenstrual syndrome (PMS)

PMS affects up to 80-90% of females of reproductive age and is characterised by luteal phase physical, mood and behavioural symptoms. PMS has a large impact on quality of life and daily activities. It is believed magnesium modulates hormonal levels, especially progesterone, to relieve symptoms of depression, irritability, tiredness, and anxiety.<sup>1</sup>

### Increased intracellular magnesium levels correlate with reduced PMS symptoms

In a randomised, double-blind, placebo-controlled trial, magnesium supplementation, at the dose of 360 mg given from the 15th day of the menstrual cycle until menstruation (2 cycles), significantly improved PMS symptoms, mood fluctuations and depression by 47%, compared to baseline. As the levels of intracellular magnesium increased the PMS symptomatology decreased.

Facchinetti F, Borella P, Sances G, et al. Oral magnesium successfully relieves premenstrual mood changes. *Obstet Gynecol.* 1991;78(2):177-81.



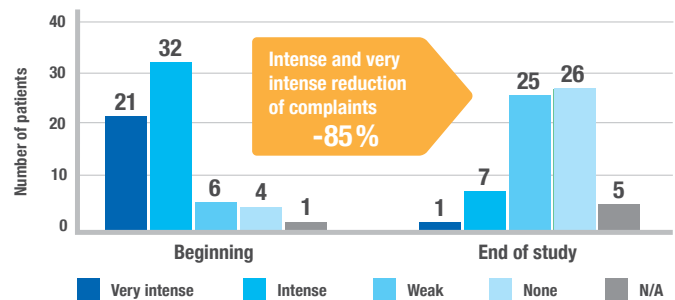
## Dysmenorrhoea

Dysmenorrhoea means painful uterine cramps that precede or accompany menstruation, due to myometrium hypercontractility and arteriolar vasoconstriction. The action of magnesium on dysmenorrhoea is through an inhibitory effect on prostaglandin (PGF2α) synthesis, resulting in muscular relaxation and vasodilation.<sup>1,2,3</sup>

### Magnesium citrate improves intense and very intense symptoms of dysmenorrhoea

In a clinical trial assessing the effects of 300mg of magnesium citrate per day, the results showed an 85% reduction in intense and very intense symptoms of dysmenorrhoea.

Wilmzig C, Pannewig K. High-dose oral magnesium therapy in pregnancy. *Der Allgemeinarzt (General Practitioner).* 1994;18:1466-71.



### Premenstrual migraines

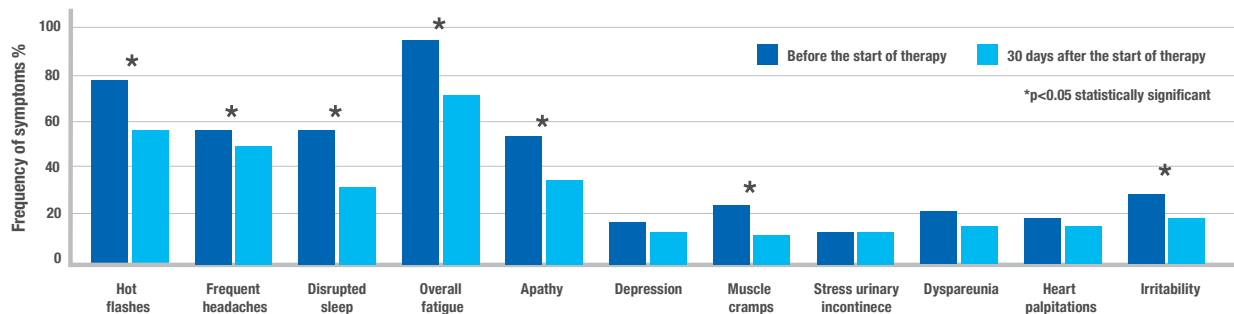
It is estimated 50% of reproductive age women have suffered a menstrual migraine, with the migraine threshold lowered in the premenstrual period. Low magnesium levels are associated with increased platelet aggregation, vasoconstriction, neural excitability, NMDA receptor activity and cortical depression spreading, as well as impairing serotonin receptor function and neurotransmitter production and release. Studies show magnesium supplementation is beneficial in reducing severity and frequency of migraines.<sup>1,5-7</sup>

### Menopause and climacteric symptoms

Mood disorders and hot flashes affect up to 90% of peri- and postmenopausal women. Women are more sensitive to low magnesium levels, with deficiency potentially linked to menopausal symptoms. Supplementation has been found beneficial in reducing hot flashes and other symptoms in menopause and in women taking medication for breast cancer.<sup>1,5,6</sup>

#### Magnesium citrate reduces multiple symptoms of menopause

In a clinical and laboratory study of 30 female patients aged from 47 to 57, magnesium citrate supplementation, at the dose of 300mg, significantly decreased multiple symptoms of menopause.



Khashukoeva A.Z., Agaeva Z.A., Agayeva M.I., Sukhova T.N., Moseshvili G.G., Nurbekova Zh.K. The role of magnesium in the treatment of symptoms climacteric syndrome. Meditsinsky Sovet. 2018; 21: 162-166.

### Magnesium supplementation in hot flashes with breast cancer treatment

A phase II trial tested magnesium on hot flush frequency at the dose of 400mg (and escalated to 800mg if needed) per day in breast cancer patients taking tamoxifen, aromatase inhibitors or antidepressants. A 41.4% reduction was seen in hot flush frequency per week and the hot flush score was reduced by 50.4%. Fatigue, sweating and distress were also significantly reduced.



Park H, Parker GL, Boardman CH, Morris MM, Smith TJ. A pilot phase II trial of magnesium supplements to reduce menopausal hot flashes in breast cancer patients. Supportive Care in Cancer. 2011 Jun 1;19(6):859-63.

#### According to research, magnesium supplementation may:

- Reduce PMS and dysmenorrhoea symptoms
- Prevent and reduce frequency and intensity of premenstrual migraines
- Reduce peri- and postmenopausal symptoms
- Reduce hot flashes in breast cancer treatment<sup>1-9</sup>



# Magnesium and pregnancy related indications

Magnesium deficiency is common in pregnancy with evidence that it can affect pregnancy outcomes and offspring health. Magnesium supplementation has been shown beneficial in pregnancy hypertension, pregnancy outcomes, gestational diabetes and preeclampsia/eclampsia.<sup>1</sup>

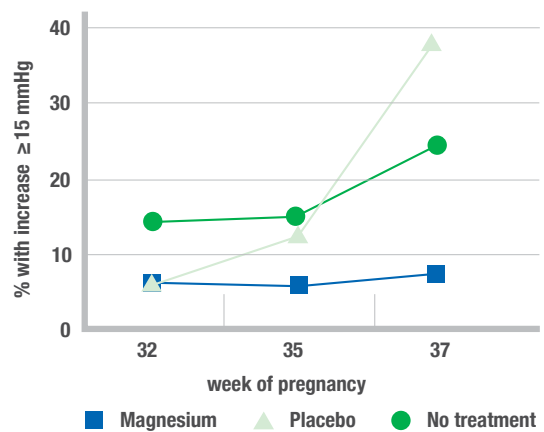
## Pregnancy hypertension

Pregnancy induced or gestational hypertension ( $\geq 140/90$ ) is common, affecting up to 10% of all pregnancies, with mineral deficiencies, such as magnesium, one of the risk factors. Magnesium is involved with BP regulation, with urinary magnesium excretion in early pregnancy positively correlated with a rise in blood pressure in late pregnancy. An increase in diastolic blood pressure by  $\geq 15$ mmHg is a risk factor for preeclampsia.<sup>2,3</sup>

### Magnesium citrate significantly reduces gestational blood pressure risk

In a randomised, placebo-controlled trial, 61 pregnant women were given 300mg of magnesium citrate per day from week 25 until delivery. Increases in diastolic blood pressure by  $\geq 15$ mmHg at weeks 35 and 37 were significantly reduced in the magnesium group, compared to the placebo and no treatment groups.

Bullarbo M, Ödman N, Nestler A, Nielsen T, Kolisek M, Vormann J, Rylander R. Magnesium supplementation to prevent high blood pressure in pregnancy: a randomised placebo control trial. Archives of gynecology and obstetrics. 2013 Dec 1;288(6):1269-74.



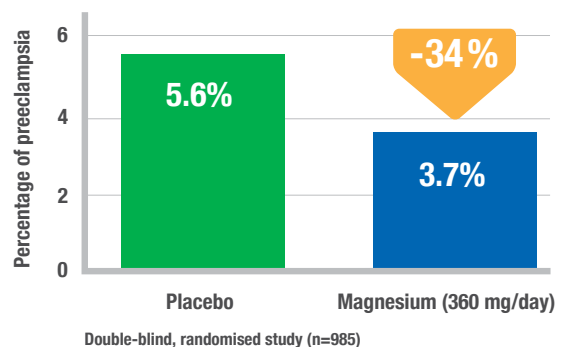
## Preeclampsia/eclampsia

Pregnancy hypertension combined with protein in the urine (0.3gm/day) is defined as preeclampsia (PE), and if left untreated can result in convulsions, called eclampsia. These conditions are life threatening. Research showed that 16% of women with PE have significantly lower magnesium levels than those with a normal pregnancy.<sup>2,3</sup>

### Magnesium supplementation reduces preeclampsia risk by 34%

In a randomised, double-blind, placebo-controlled trial, 360mg of magnesium given to pregnant women every day reduced the risk of preeclampsia by 34%, compared to placebo.

Kovac L, Molnar BG, Huhn E, Bodis L. Magnesium substitution in pregnancy – randomized double blind study. Geburtshilfe Frauenheilkd 1988; 48(8): 595-600.



## Pregnancy-related calf muscular cramps

Calf muscle cramps in pregnancy has been reduced by 80% in one clinical study with the intake of 360mg of magnesium in 73 pregnant women. In another study, 300mg significantly reduced frequency and intensity of calf cramps in pregnancy, compared to placebo.<sup>4,5</sup>

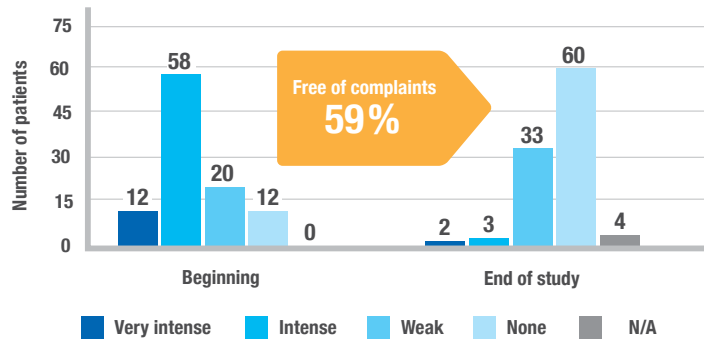
## Premature labour

Preterm infants are at greater risk of adverse health outcomes; therefore, premature labour prevention is critical. Magnesium deficiency can lead to muscle cramps and uterine hyperactivity, which can increase cervical dilatation and premature onset of labour. In women with low magnesium levels, supplementation may prevent preterm labour.<sup>6</sup>

### Magnesium supplementation reduces symptoms and intensity of premature labour pains

In a clinical trial assessing the effects of 300mg of magnesium citrate every day for 15 weeks, the symptoms in patients with premature labour pains were significantly reduced, with 59% complaint-free after supplementation. This potentially reduces the risk of hospitalisations.

Wilmzig C, Pannewig K. High-dose oral magnesium therapy in pregnancy. *Der Allgemeinarzt (General Practitioner)*. 1994;18:1466-71.



## Offspring outcomes

Magnesium supplementation given before the 25th week of gestation is associated with:

- Less preterm births
- Fewer low birth weight babies
- Less smaller for gestational age newborns
- Fewer days in neonatal intensive care<sup>1</sup>

Preliminary evidence suggests that foetal hypomagnesaemia is associated with later-life metabolic syndrome.<sup>1</sup>

### Gestational diabetes

Oral magnesium supplementation (250 mg) for 6 weeks reduces insulin resistance in gestational diabetes.

Asemi et al. Magnesium supplementation affects metabolic status and pregnancy outcomes in gestational diabetes: a randomized, double-blind, placebo-controlled trial. *Am J Clin Nutr*. 2015 Jul;102(1):222-9

### According to research, magnesium supplementation may:

- Prevent the development of gestational hypertension
- Reduce the risk of preeclampsia/eclampsia
- Reduce insulin resistance in gestational diabetes
- Prevent the risk of premature labour
- Reduce the intensity and symptoms of premature labour
- Improve infant size, weight and health
- Reduce frequency and intensity of pregnancy-induced leg cramps<sup>1-9</sup>



# MUSCULOSKELETAL SYSTEM



## SUMMARY OF BENEFITS

### **Magnesium supplementation may:**

- Reduce the frequency and intensity of calf muscle cramps
- Improve muscle performance in the elderly
- Reduce the symptoms of fibromyalgia
- Improve bone metabolism biomarkers in osteoporosis
- Reduce the risk of fractures
- Help increase bone density mass <sup>1-11</sup>

## Muscle cramps

Chronic persistent leg cramps are common with increased frequency in pregnancy and the older population. Magnesium deficiency leads to a loss of calcium antagonism, which increases neuro-muscular hyperexcitability, resulting in muscular cramping. Magnesium is at its lowest level at night; therefore, leg cramps are felt more at this time, with around 60 percent of adults reporting nocturnal leg cramps during their lifetime. Magnesium supplementation reduces the frequency and intensity of muscle cramps.<sup>1,2,3,4</sup>

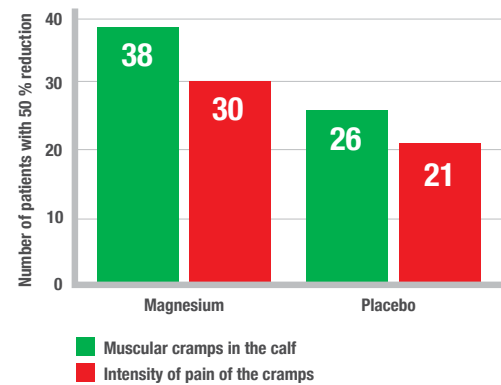
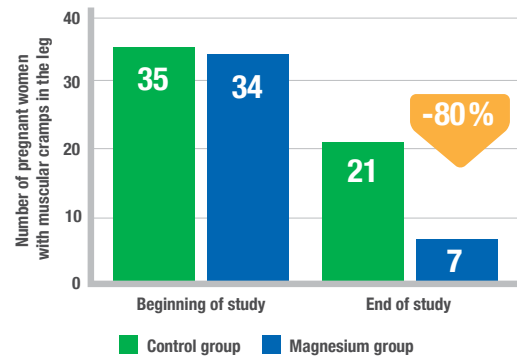
### Magnesium supplementation reduces pregnancy-related muscular cramps

In a randomised, double-blind placebo-controlled trial, magnesium supplementation, at the dose of 360 mg for 3 weeks from week 29 of pregnancy, significantly reduced calf cramps by 80%.

Dahle LO, Berg G, Hammar M, Hurtig M, Larsson L. The effect of oral magnesium substitution on pregnancy-induced leg cramps. *American journal of obstetrics and gynecology*. 1995 Jul 1;173(1):175-80.

In another randomised, double-blind, placebo-controlled study the researchers tested if supplementation of 300mg magnesium reduced the frequency and intensity of muscle cramps 50% of the time. The magnesium group had significantly more incidences of cramp reduction by 50% in both frequency and intensity than the placebo group.

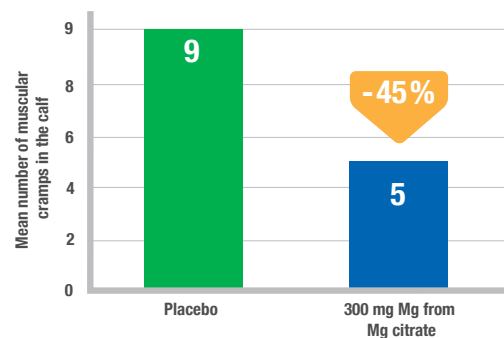
Supakatisant C, Phupong V. Oral magnesium for relief in pregnancy-induced leg cramps: a randomised controlled trial. *Maternal & child nutrition*. 2015 Apr;11(2):139-45.



### Leg cramps in the elderly reduced by 45% with magnesium citrate

In a 4-week randomised, double-blind study, adults aged around 68 years old received 300mg of magnesium citrate daily. The magnesium group experienced 45% less muscular calf cramps than the placebo group.

Rofle C, Shills S, Crome P, Jones P. Randomised, cross-over, placebo controlled trial of magnesium citrate in the treatment of chronic persistent leg cramps. *Medical Science Monitor*. 2002 May 15;8(5):CR326-30.



## Muscle performance in the elderly

In the elderly, serum magnesium concentration is positively correlated with muscle performance, including:

- Grip strength
- Lower leg muscle power
- Knee extension torque
- Ankle extension isometric strength

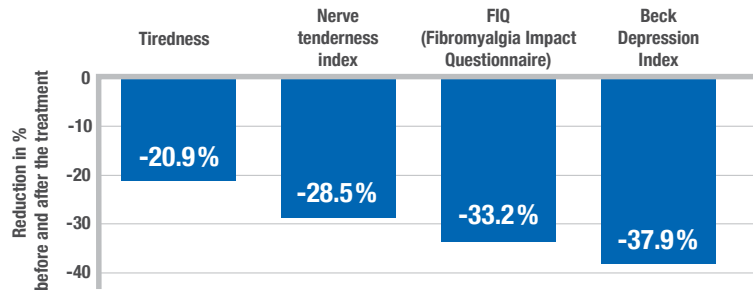
Magnesium supplementation improves physical performance in the elderly.<sup>5</sup>

## Fibromyalgia

Fibromyalgia is a chronic disease characterised by chronic widespread pain and tenderness over certain body points (called tender points). Sufferers may also encounter fatigue, sleep disorders, bowel dysfunction and headaches.<sup>6</sup>

### Magnesium citrate significantly reduces fibromyalgia symptoms

Pain intensity, pain threshold, the number of tender points, the tender point index, the fibromyalgia impact questionnaire (FIQ), the Beck depression and Beck anxiety scores, and patient symptoms were evaluated in women with fibromyalgia before and after an 8 week daily dose of magnesium citrate. The results showed significant reductions in fibromyalgia symptoms in the magnesium group.



Bagis S, Karabiber M, As I, Tamer L, Erdogan C, Atalay A. Is magnesium citrate treatment effective on pain, clinical parameters and functional status in patients with fibromyalgia?. *Rheumatology international*. 2013 Jan 1;33(1):167-72.

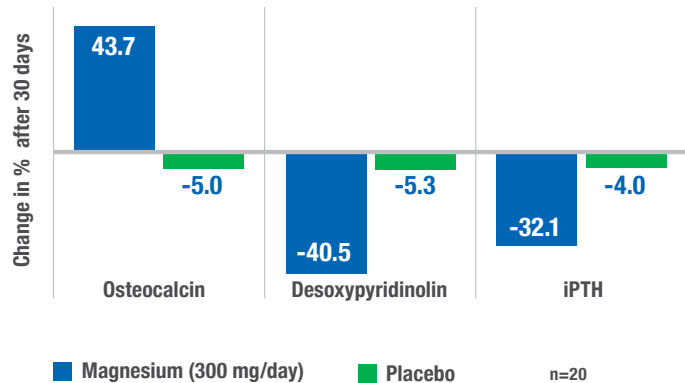
## Osteoporosis

About 60% of total magnesium is stored in the bone, providing structural flexibility, with hypomagnesaemia resulting in higher bone fragility and osteoporosis promotion. Magnesium is also readily exchangeable from bone at times of increased blood pH, to reduce acidity. Ongoing loss of magnesium from the bone may increase the risk of osteoporosis. Magnesium is crucial for vitamin D activation into its active form, which supports calcium absorption and metabolism, and parathyroid hormone function. Higher bone mass density has been associated with higher magnesium intake, with supplementation shown to suppress bone turnover in postmenopausal women and young adult males.<sup>5</sup>

### Magnesium citrate reduces markers of bone loss in only 30 days

In postmenopausal women with osteoporosis, supplementation with magnesium citrate (300mg/day) resulted in a reduction of markers of bone loss after 30 days.

Aydin H, Deyneli O, Yavuz D, Gözü H, Mutlu N, Kaygusuz I, Akalin S. Short-term oral magnesium supplementation suppresses bone turnover in postmenopausal osteoporotic women. *Biological trace element research*. 2010 Feb 1;133(2):136-43.



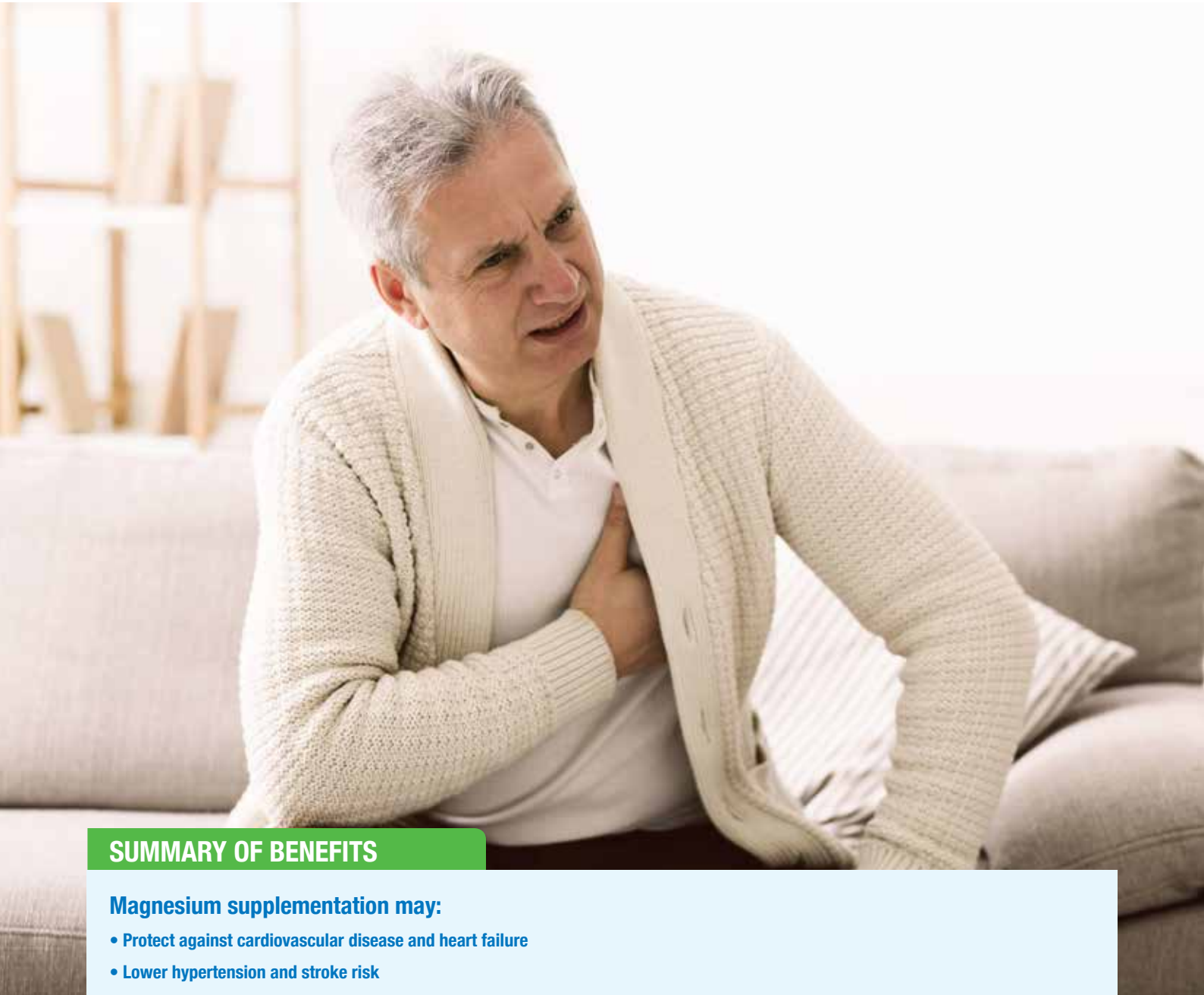
### According to research, magnesium supplementation may:

- Reduce the frequency and intensity of calf muscle cramps
- Improve muscle performance in the elderly
- Reduce the symptoms of fibromyalgia
- Improve bone metabolism biomarkers in osteoporosis
- Reduce the risk of fractures
- Help increase bone density mass<sup>1-11</sup>





# CARDIOVASCULAR SYSTEM



## SUMMARY OF BENEFITS

### **Magnesium supplementation may:**

- **Protect against cardiovascular disease and heart failure**
- **Lower hypertension and stroke risk**
- **Improve lipid profiles**
- **Reduce the risk of arrhythmias**
- **Prevent the development of gestational hypertension<sup>1-9</sup>**

# Magnesium and CVD

Magnesium plays an important role in many facets of cardiovascular prevention and disease reduction, with hypomagnesaemia associated in a number of cardiac events. The following table highlights the effects of adequate magnesium levels on the CV system.<sup>1</sup>

## MAGNESIUM EFFECTS ON THE CARDIOVASCULAR SYSTEM

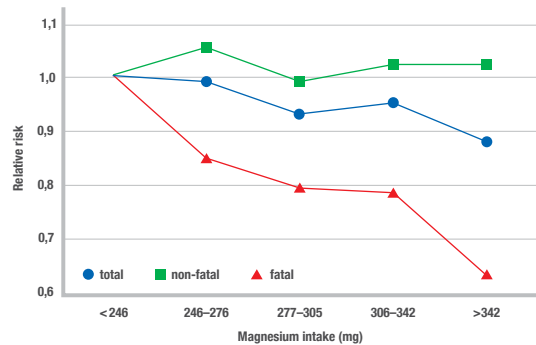
- ✓ Improvement in endothelial function
- ✓ Induction of direct and indirect vasodilation
- ✓ Improvement in blood pressure
- ✓ Beneficial effects on arrhythmias, inflammatory reactions, and platelet aggregation
- ✓ Potential effect in improving exercise tolerance in patients with stable coronary artery disease
- ✓ Improvement of insulin homeostasis and lipid metabolism
- ✓ Reduces platelet activation and thrombosis
- ✓ Reduces cellular ischemic injury by reducing calcium overload in coronary arteries

Epidemiological studies show an inverse correlation with magnesium intake and the risk of coronary heart disease, myocardial infarction and sudden cardiac death.<sup>2-4</sup>

### Relative risk reduction of CHD with magnesium intake

This study examined the association between dietary and plasma magnesium and risk of coronary heart disease (CHD) among middle-aged and older women. A higher intake (246 to >342mg) of magnesium significantly reduced the relative risk of CHD, especially fatal CHD.

Chiuve SE, Sun Q, Curhan GC, Taylor EN, Spiegelman D, Willett WC, Manson JE, Rexrode KM, Albert CM. Dietary and plasma magnesium and risk of coronary heart disease among women. Journal of the American Heart Association. 2013 Mar 18;2(2):e000114.



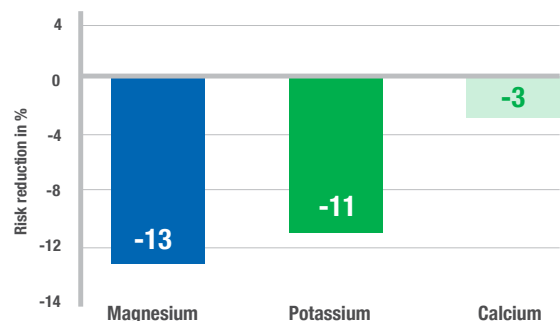
## Stroke

Magnesium may lower hypertension, the principal modifiable stroke risk factor. Prospective studies show an 8% risk reduction in stroke with every increase of magnesium by 100mg per day.<sup>5,6</sup>

### Magnesium and potassium lower stroke risk, but not calcium

In the Nurses Health Study I and II, there was a significant correlation between a high intake of magnesium and potassium, but not of calcium, and the reduction of stroke risk.

Adebamowo S et al. Association between intakes of magnesium, potassium, and calcium and risk of stroke: 2 cohorts of US women and updated meta-analyses 2015. Am J Clin Nutr; 1-9



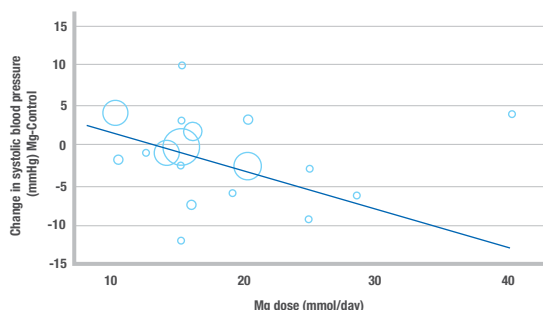
Data from the controlled Nurse Health Studies I and II (n=180'324) (Difference of quintiles 1 – 5 of the NHS I and II studies)

## Hypertension

Magnesium enhances the vasodilatory effect of nitric oxide (NO) and antagonises the substances with vasoconstricting effects, including calcium, to reduce vascular tone and resistance. As an antioxidant, magnesium also protects the vascular endothelium.<sup>1</sup>

### Magnesium reduces blood pressure – results of a meta-analysis

In a meta-analysis using magnesium for blood pressure reduction, the analysis of the randomised controlled trials showed magnesium intake caused dose-dependent blood pressure reductions. They found reductions of 4.3 mmHg in systolic blood pressure and 2.3 mmHg in diastolic blood pressure for each 10 mmol/day increase in magnesium dose. This chart shows the effect of magnesium on systolic blood pressure, with each circle representing a study.



Jee SH, Miller ER, Guallar E, Singh VK, Appel LJ, Klag MJ. The effect of magnesium supplementation on blood pressure: a meta-analysis of randomized clinical trials. *American journal of hypertension*. 2002 Aug 1;15(8):691-6.

### Research shows magnesium can also reduce the risk of gestational hypertension

Bullarbo M, Ödman N, Nestler A, Nielsen T, Kolisek M, Vormann J, Rylander R. Magnesium supplementation to prevent high blood pressure in pregnancy: a randomised placebo control trial. *Archives of gynecology and obstetrics*. 2013 Dec 1;288

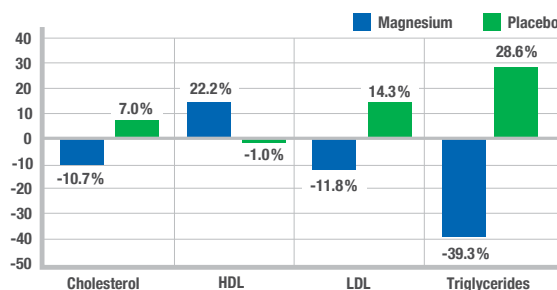
## Dyslipidaemia

Research shows magnesium levels affect blood lipid, lipoprotein and triglyceride levels, and magnesium supplementation may assist with the conversion of triglycerides to high-density lipoproteins.<sup>8</sup>

### Magnesium supplementation improves blood lipid profiles

In a 3 month randomised, double-blind, placebo-controlled trial, 300mg of magnesium daily significantly improved blood lipid profiles in subjects with insulin resistance.

Guerrero-Romero, F., Tamez-Perez, H.E., González-González, G.E., Salinas-Martinez, A.M., Montes-Villarreal, J., Trevino-Ortiz, J.H. and Rodriguez-Moran, M., 2004. Oral magnesium supplementation improves insulin sensitivity in non-diabetic subjects with insulin resistance. A double-blind placebo-controlled randomized trial. *Diabetes & metabolism*, 30(3), pp.253-258.

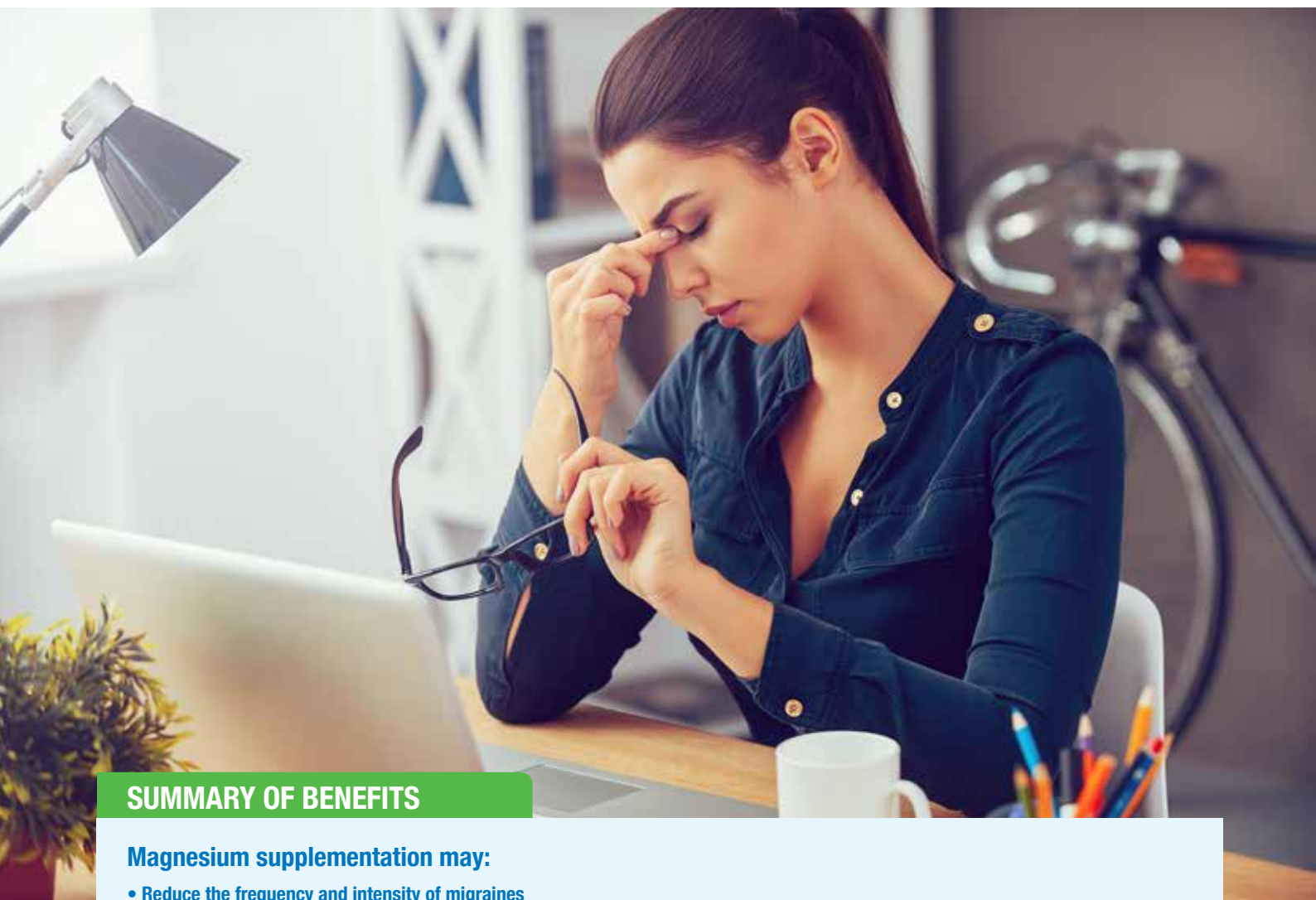


### According to research, magnesium supplementation may:

- Protect against cardiovascular disease and heart failure
- Lower hypertension and stroke risk
- Improve lipid profiles
- Reduce the risk of arrhythmias
- Prevent the development of gestational hypertension<sup>1-9</sup>



# NERVOUS SYSTEM



## SUMMARY OF BENEFITS

### **Magnesium supplementation may:**

- Reduce the frequency and intensity of migraines
- Improve sleep quality and reduce stress
- Reduce depression and anxiety symptoms
- Be an effective therapy for RLS
- Reduce hyperactivity and restore magnesium levels in ADHD
- Benefit neurodegenerative and other neurological conditions<sup>1-12</sup>

## Migraines

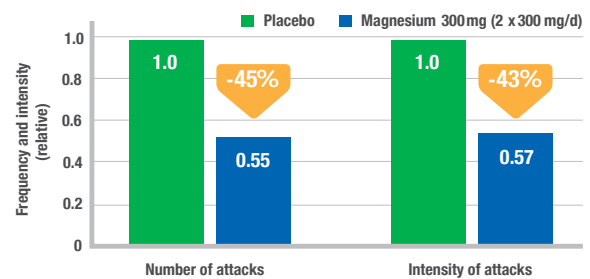
Magnesium deficiency has been reported in 50% of migraine sufferers. In migraines, low magnesium levels are associated with increased platelet aggregation, vasoconstriction, neural excitability, NMDA receptor activity and cortical depression spreading, as well as impaired serotonin receptor function and neurotransmitter production and release. Studies show magnesium supplementation is beneficial in reducing severity and frequency of migraines.<sup>1-6</sup>

**‘A Cochrane review grades Mg as one of the strongly recommended treatments for migraine headaches.’<sup>34</sup>**

### Magnesium citrate significantly reduces frequency and intensity of migraines

In this double-blind, randomised, 3-month study, the intake of 600mg of magnesium citrate per day lead to a significant reduction in frequency and intensity of migraine attacks without aura by 45% and 43%, respectively.

Köseoglu et al. The effects of magnesium prophylaxis in migraine with aura. Magnesium Research 2008; 21 (2): 101-8



In another double-blind, randomised clinical trial, 600mg of magnesium citrate per day for 3 months reduced the frequency and intensity of migraines by 41%, compared to 15.89% in the placebo group.

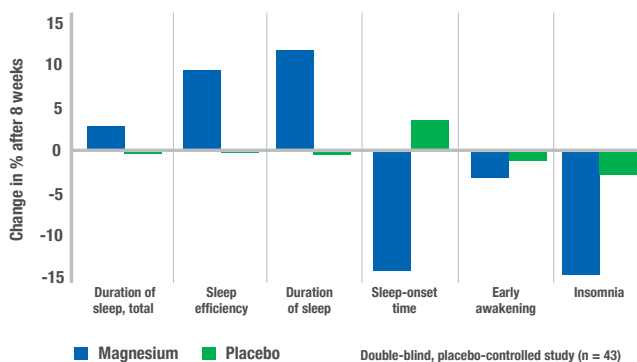
Peikert A, Wilimzig C, Köhne-Volland R. Prophylaxis of migraine with oral magnesium: results from a prospective, multi-center, placebo-controlled and double-blind randomized study. Cephalalgia. 1996 Jun;16(4):257-63.

## Insomnia

It is estimated that 50% of older adults suffer from insomnia. Magnesium has been associated with improving sleep phases as it is a natural NMDA receptor antagonist and a GABA agonist, which increases relaxation and facilitates sleep. Magnesium supplementation has been shown to increase renin and aldosterone levels, while reducing serum cortisol levels and improving sleep quality.<sup>7</sup>

### Magnesium improves sleep quality and modulates serum melatonin and cortisol levels in the elderly

In a double-blind, randomised trial, 500mg of magnesium per day improved subjective sleep measures, as well as increasing serum renin and melatonin and decreasing cortisol levels in the elderly.



	Magnesium	Placebo
<b>Magnesium</b>	4.2	-1.3
<b>Renin</b>	36.7	-5.9
<b>Melatonin</b>	35.0	-1.1
<b>Hydrocortisone</b>	-8.2	3.5

Difference vs. baseline in %

Abbasi B, Kimiagar M, Sadeghniai K, Shirazi MM, Hedayati M, Rashidkhani B. The effect of magnesium supplementation on primary insomnia in elderly: A double-blind placebo-controlled clinical trial. Journal of research in medical sciences. 2012 Dec;17(12):1161.

## Restless leg syndrome

Research shows that magnesium deficiency, due to its antagonistic effect on calcium, may be implicated in the cause of restless leg syndrome (RLS). In a small open-label trial, magnesium was reported as being an effective therapy for RLS.<sup>4</sup>

## Stress

Magnesium regulates the HPA axis, and stress of any kind—physical, environmental, psychological and nutritional—increases the need for magnesium. When subjected to stress the body releases catecholamine and corticosteroid, which also induces a shift of magnesium from the intracellular space to the extracellular space increasing its potential for excretion in urine. Magnesium supplementation has been shown to reduce serum cortisol levels.<sup>4,7-9</sup>

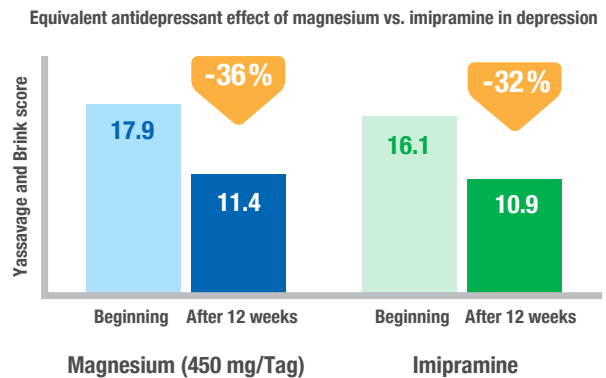
## Depression and anxiety

Studies show a relationship between low magnesium levels and depression and anxiety. Magnesium is a natural NMDA receptor antagonist and GABA agonist, which has an antidepressant effect. Magnesium is also required for the conversion of tryptophan into the mood modulating neurotransmitter, serotonin. Magnesium supplementation has been shown to decrease depression and anxiety scores.<sup>4</sup>

### Research show the effectiveness of magnesium in depression and anxiety

In a randomised equivalent trial, researchers tested 450mg of magnesium a day compared to the antidepressant imipramine in an elderly population with type 2 diabetes, for 12 weeks. The results showed an equivalent effect of depression reduction in both magnesium and antidepressant groups (36% and 32% reduction, respectively) with the magnesium groups having significant decreases in depression (PHQ-9) and anxiety (GAD) scores.

Barragán-Rodríguez L, Rodríguez-Morán M, Guerrero-Romero F. Efficacy and safety of oral magnesium supplementation in the treatment of depression in the elderly with type 2 diabetes: a randomized, equivalent trial. *Magnesium research*. 2008 Dec 1;21(4):218-23.



	N	PHQ-9			GAD-7		
		Change	95% CI	P	Change	95% CI	P
<b>Magnesium</b>	<b>112</b>	<b>-4.9</b>	<b>-6.0, -3.9</b>	<b>&lt;0.001</b>	<b>-3.6</b>	<b>-4.9 - 2.3</b>	<b>&lt;0.001</b>
<b>Control</b>	<b>112</b>	<b>+1.1</b>	<b>-0.1, +2.3</b>	<b>0.08</b>	<b>+0.9</b>	<b>-0.4 + 2.1</b>	<b>0.17</b>

PHQ-9 = Patient Health Questionnaire-9; GAD-7 = Generalised Anxiety Disorder-7; CI = confidence interval; P = probability value.

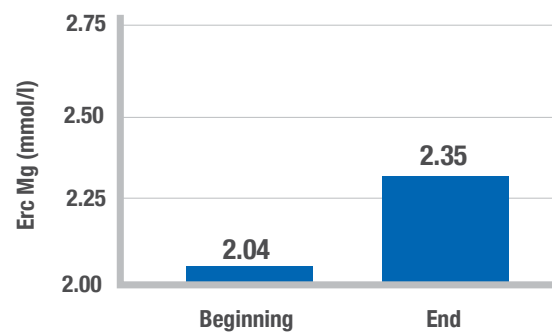
## ADHD

Magnesium deficiency appears to be a common nutritional deficiency in those with ADHD. Supplementation has shown improvements in magnesium levels, and attention and hyperactivity behaviours.<sup>4</sup>

### Correction of magnesium erythrocyte levels in ADHD

According to an open study, children were hyperexcitable with low erythrocyte magnesium levels. After supplementation, for 3 to 24 weeks, the erythrocyte levels were restored, with improved behaviour.

Mousain-Bosc M, Roche M, Rapin J, Bali JP. Magnesium VitB6 intake reduces central nervous system hyperexcitability in children. *Journal of the American College of Nutrition*. 2004 Oct 1;23(5):545S-8S.



## Neurodegenerative/other neurological conditions

Magnesium deficiency & supplementation have been associated with effects on the following neurodegenerative & neurological conditions:

- **Multiple sclerosis**
- **Dementia**
- **Schizophrenia**
- **Parkinson's disease**
- **Alzheimer's disease**<sup>4,10</sup>

### According to research, magnesium supplementation may:

- Reduce the frequency and intensity of migraines
- Improve sleep quality and reduce stress
- Reduce depression and anxiety symptoms
- Be an effective therapy for RLS
- Reduce hyperactivity and restore magnesium levels in ADHD
- Benefit neurodegenerative and other neurological conditions<sup>1-12</sup>



# RESPIRATORY / INTEGUMENTARY / DIGESTIVE SYSTEMS



## SUMMARY OF BENEFITS

### **Magnesium supplementation may:**

- Reduce asthma frequency and use of inhaled medications, when used as an adjuvant
- Benefit the severity of COPD
- Reduce the symptoms and inflammation of atopic dermatitis
- Reduce GIT inflammation and improve gut health<sup>1-5</sup>



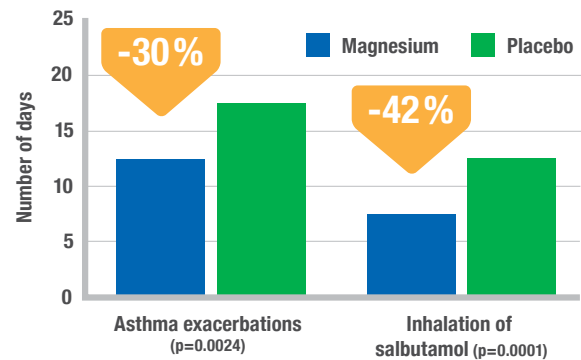
## Asthma

Adjuvant magnesium therapy in children can significantly reduce both the number of asthma attacks and the use of inhalable medicines. The effect of magnesium is based on the vasodilatation of bronchial muscles, inhibition of inflammation by a down-regulation of the cholinergic transmitter system, stimulation of nitric oxide (NO) and prostacyclin synthesis, and stabilisation of mast cells and T-lymphocytes.<sup>1</sup>

### Magnesium significantly reduces asthma attacks and use of inhalation medication after two months

In a double-blind, placebo-controlled, parallel study, 300mg magnesium, given as an adjuvant therapy daily, reduced asthma exacerbations by 30% and the need for inhaled medication by 42%.

Gontijo-Amaral C, Ribeiro MA, Gontijo LS, Condino-Neto A, Ribeiro JD. Oral magnesium supplementation in asthmatic children: a double-blind randomized placebo-controlled trial. *European journal of clinical nutrition*. 2007 Jan;61(1):54.



## COPD

Magnesium deficiency may also be associated with the severity of disease and length of hospital stay in advanced chronic obstructive pulmonary disease (COPD).<sup>2</sup>

### Atopic dermatitis

Magnesium serum levels have been shown to be lower in atopic dermatitis sufferers. Magnesium may reduce inflammation, enhance skin hydration and dermal permeability and repair, and assist epithelial proliferation and differentiation.<sup>3</sup>

## Intestinal health

Magnesium deficiency has been shown to contribute to GIT inflammation, with potential negative effects on bifidobacteria levels, and increased risk for colon cancer and constipation.<sup>4,5</sup>

### According to research, magnesium supplementation may:

- Reduce asthma frequency and use of inhaled medications, when used as an adjuvant
- Benefit the severity of COPD
- Reduce the symptoms and inflammation of atopic dermatitis
- Reduce GIT inflammation and improve gut health<sup>1-5</sup>



# RENAL SYSTEM AND AGEING



## Kidney health and magnesium - the interrelationship

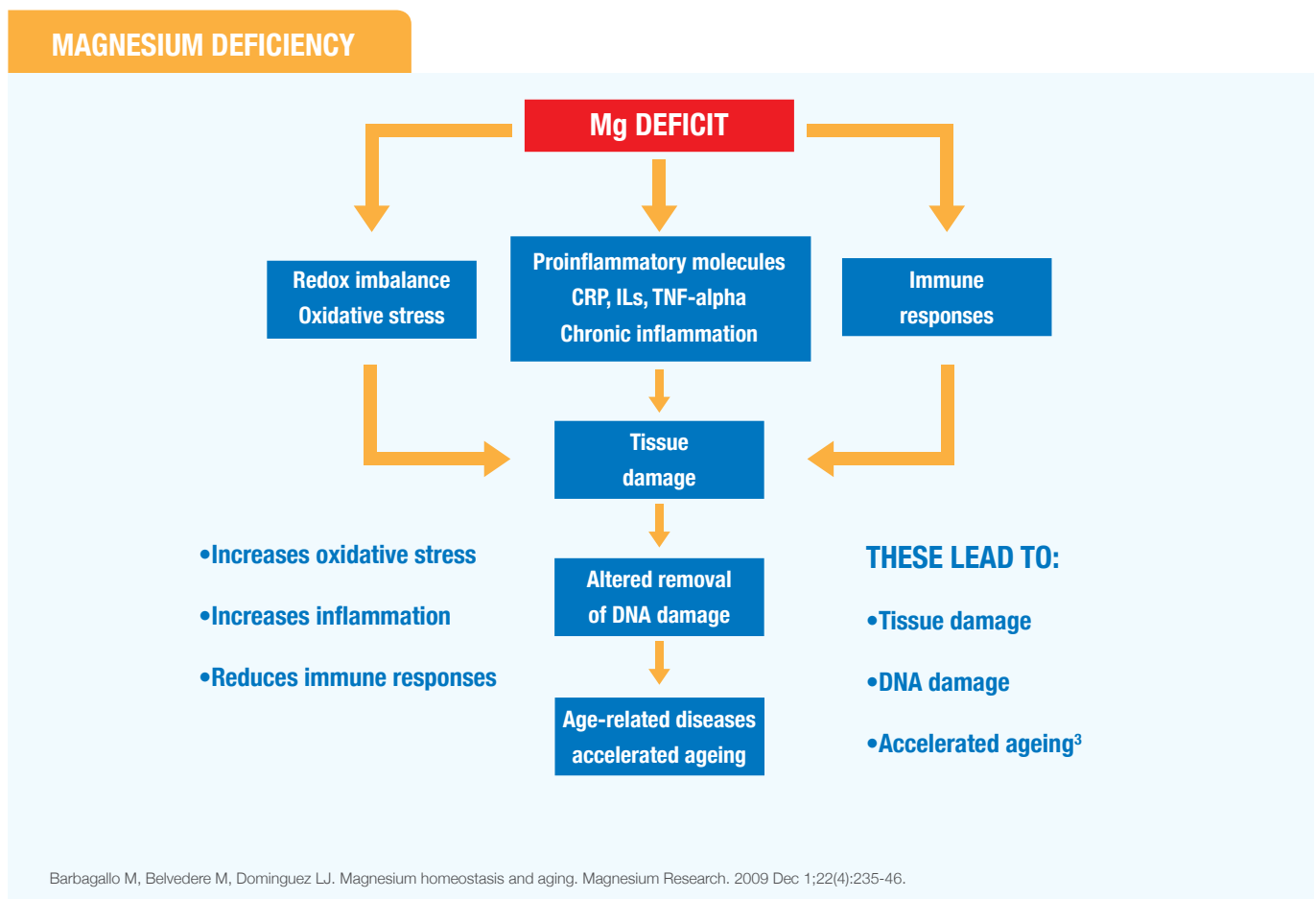
The kidneys are important for magnesium homeostasis, with mild to moderate impairment increasing magnesium excretion to compensate for glomerular filtration loss.<sup>1</sup> Magnesium citrate is an important alkalisating mineral used by the body as buffering against excess acidity. Excess acidity, often due to an overly acidogenic diet, is excreted by the kidneys; however, over time kidney function is affected adversely through ageing and the excess acid. Magnesium is drawn from tissues, muscles and bones at times of acidosis to balance the pH (acid-alkaline) level of the blood. The constant removal of alkalisating minerals, such as magnesium, from the bone, muscles and tissues can have a detrimental health effect. Alkaline minerals supplements taken regularly, including magnesium citrate, may prevent the damaging effects of excess acid on the kidneys.

### Kidney stones

Magnesium is well known as an oxalate binder in the intestines, which reduces the absorption of oxalate and potential formation of calcium oxalate kidney stones. Magnesium citrate, with potassium citrate, has been found to reduce calcium oxalate kidney stone formation by 85% over 3 years.<sup>2</sup>

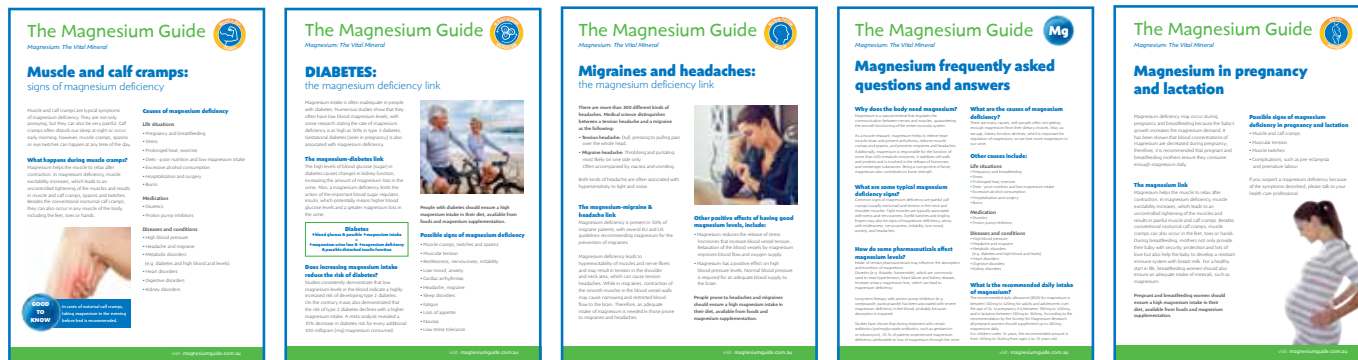
## Ageing and magnesium deficiency

Magnesium protects DNA against damage, inhibits many neurodegenerative processes caused by calcium, such as oxidative stress, dysfunctional energy production, excitotoxicity and membrane plasticity, and is a necessary alkalisating mineral to buffer excess acids and prevent kidney damage. All of these factors affect the ageing process; however, like kidney function, total magnesium body levels are diminished with age.<sup>3</sup>



# Patient brochures

The magnesium patient brochure series provides you with extra support in educating your clients on various topics, including the role of magnesium in managing muscle cramps, diabetes, migraines and headaches. The magnesium FAQ brochure covers the different types of magnesium, deficiency symptoms and signs, why we need magnesium and the daily recommended dose. While the magnesium in pregnancy and lactation brochure outlines the importance of magnesium supplementation for expectant mothers and their baby.



## Order a PDF version of the brochures from:

**bWellness Practitioner Assistance**  
 (AU) 1300 551 077 (NZ) +64 9 845 1245  
 or your Territory Manager

# Educational animations

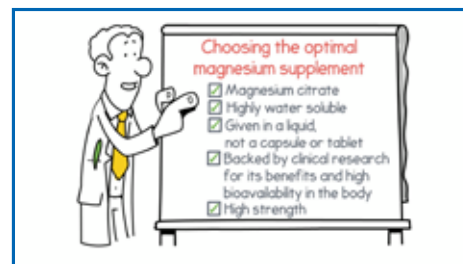
Animations provide your clients with a visual understanding of everything magnesium, including symptoms of deficiency, the different types of magnesium and the importance of correct supplementation.

These short and concise videos are ideally used during the consultation, within your reception area, or for patient follow-up.

Additionally, for more videos and educational posts visit or direct your patients to the Magnesium Guide Facebook page at:



[www.facebook.com/MagnesiumGuide/](http://www.facebook.com/MagnesiumGuide/)



Learn more about magnesium on

# the Magnesium Guide website

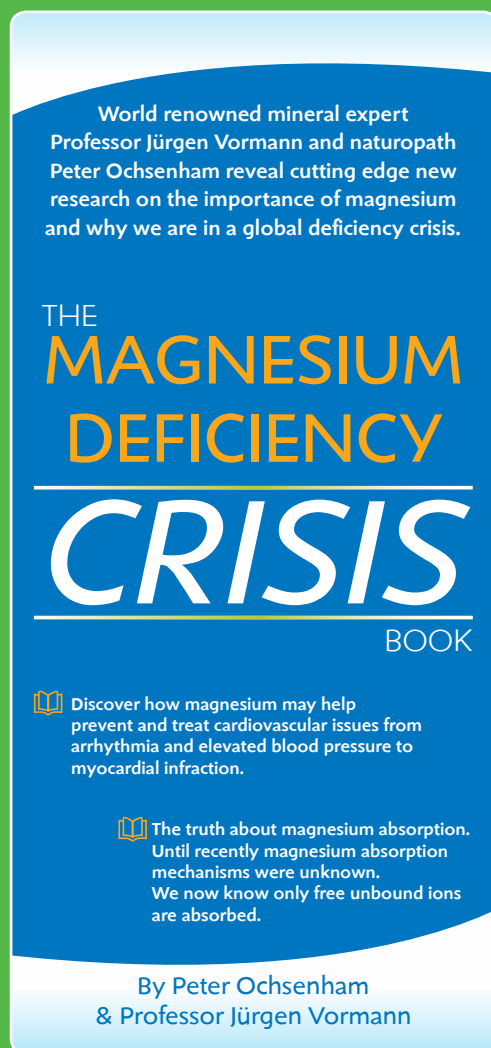
The Magnesium Guide is an evidence-based website designed to help you gather information about the need for and use of magnesium as part of a healthy lifestyle.

## Featuring:

- The magnesium minute survey
- Magnesium deficiency signs and symptoms
- An explanation of the four types of deficiencies
- Factors that impede or promote absorption
- Population groups that require more magnesium
- How to choose a magnesium supplement
- Magnesium research in multiple conditions
- Practitioner Directory

For more information visit:  
[www.magnesiumguide.com.au](http://www.magnesiumguide.com.au)

## DISCOVER MORE



## Key highlights and important new research from The Magnesium Deficiency Crisis Book:

- Why every pregnancy can be aided by magnesium supplementation.
- Why every person on heart medication should use magnesium.
- Magnesium and the prevention and treatment of insulin resistance.
- Magnesium benefits in chronic fatigue syndrome and fibromyalgia.
- The use of magnesium in depression, anxiety and muscular cramps.
- Cutting edge research on why magnesium status is so important in the prevention of type II diabetes.
- Our shocking magnesium consumption statistics and why supplementation should be widespread.

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