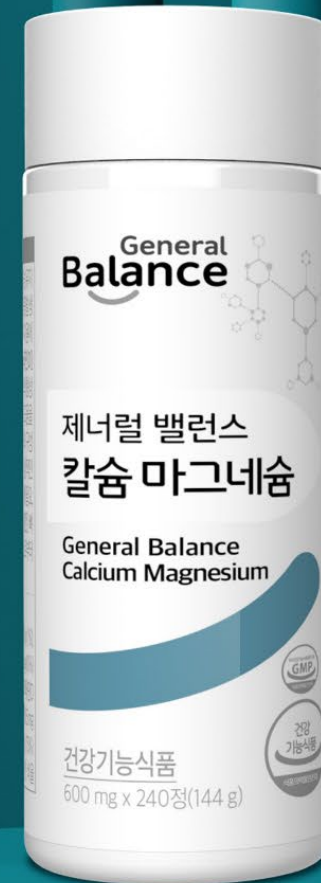
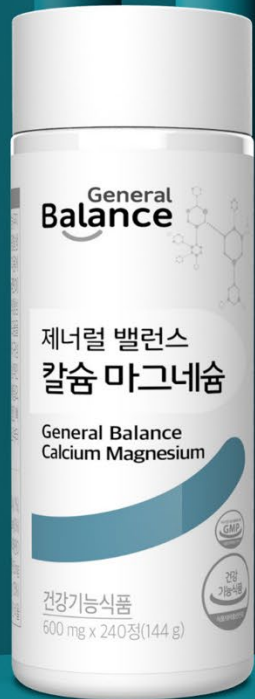




## General Balance Calcium Magnesium





## General Balance Calcium Magnesium

1. Key Points
2. Product Introduction
3. Product Features
4. Recommended for
5. Synergetic Supplements
6. General Information
7. FAQ

# General Balance Calcium Magnesium Key Points

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- 1 Double concentration ! , +4 vitamin/minerals!, Triple complex calcium formula**
- 2 7-in-1 Deal  
Original 3: calcium, magnesium, vitamin D. 4 New: vitamin K, zinc, copper, manganese**
- 3 Ideal 2:1 calcium-magnesium ratio for better absorption**
- 4 6 hand-picked quality supplementary ingredients**
- 5 Smaller tablets for easier intake**
- 6 No additives**

## Product Introduction

- + Product Name : **General Balance Calcium Magnesium**
- + Product Type : **Dietary Supplement**
- + Net Wt. : **600mg x 240 tablets (144g)**
- + Ingredients : **Algae Calcium, Magnesium Oxide, Calcium Citrate, Whey Calcium, Dried Yeast (Vitamin D2), Zinc Oxide, Manganese Sulfate, Copper Gluconate, Vitamin K Blend Powder (Gum Arabic, Vitamin K1, Sucrose), Lactose Powder (Lactose, Dextrin), Corn Starch, Rapeseed Oil Powder, Corn Protein Extract Powder, Glycerin, Shark Cartilage Extract, Safflower Seed Extract, Milk Protein Hydrolysate, Ginseng Fermented Extract Powder<Contains Milk>**
- + Suggested Use : **Take two tablets twice a day with water.**

### Precautions

- Please take as directed and check the expiration date before consuming.
- If you have a medication or are taking medication, consult a healthcare professional before use.
- If you are taking anticoagulants, consult a healthcare professional before use.
- If you experience any adverse events, discontinue use and consult a healthcare professional.
- If you have hypercalcemia or take medication, consult a healthcare professional.
- For individuals with allergies, please check all ingredients before use.
- Do not consume silica gel (desiccant) in the container.

\* Tablet does not contain chemical excipients and may break easily. Product is safe to consume.



# Product Features

---

1. Calcium
2. Calcium & Magnesium
3. Vitamin D
4. Vitamin K, Zinc, Copper, Manganese)
5. General Balance Calcium Magnesium Upgrade
6. 7-in-1 Efficiency
7. 6 hand-picked, quality sub-ingredients
8. No additives



# Product Features

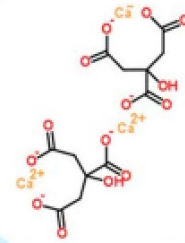
## 1. Calcium

General Bio's newly formulated Triple Complex Calcium formula is a blend of three calcium (algae, whey, and calcium citrate) in optimal proportions, "designed for all body types for even greater absorption and utilization by the body."

Algae Calcium



+



Triple Complex Formula

Whey Calcium

Calcium Citrate





# Product Features

## 2. Calcium & Magnesium

Calcium and magnesium need each other at the perfect amount for calcium to be efficiently absorbed within the body so it is important to "consume calcium and magnesium in the ideal ratio" to promote calcium absorption and maintain mineral balance.



체내 이용율을 높이기 위한  
이상적인 배합 비율!

**2:1**

Calcium 450mg    Magnesium 225mg

Ideal 2:1 ratio for maximum absorption



## Product Features

### 3. Vitamin D

It is recommended to take vitamin D in combination with calcium and magnesium as it “aids in the absorption of calcium from the small intestine and increases the body’s utilization of calcium.” Vitamin D also “prevents osteoporosis by reabsorbing calcium and preventing it from being excreted when the body’s calcium level is low.”



Vitamin D promotes calcium absorption and reabsorption by the small intestine and maintains bone calcium entry into the blood stream.





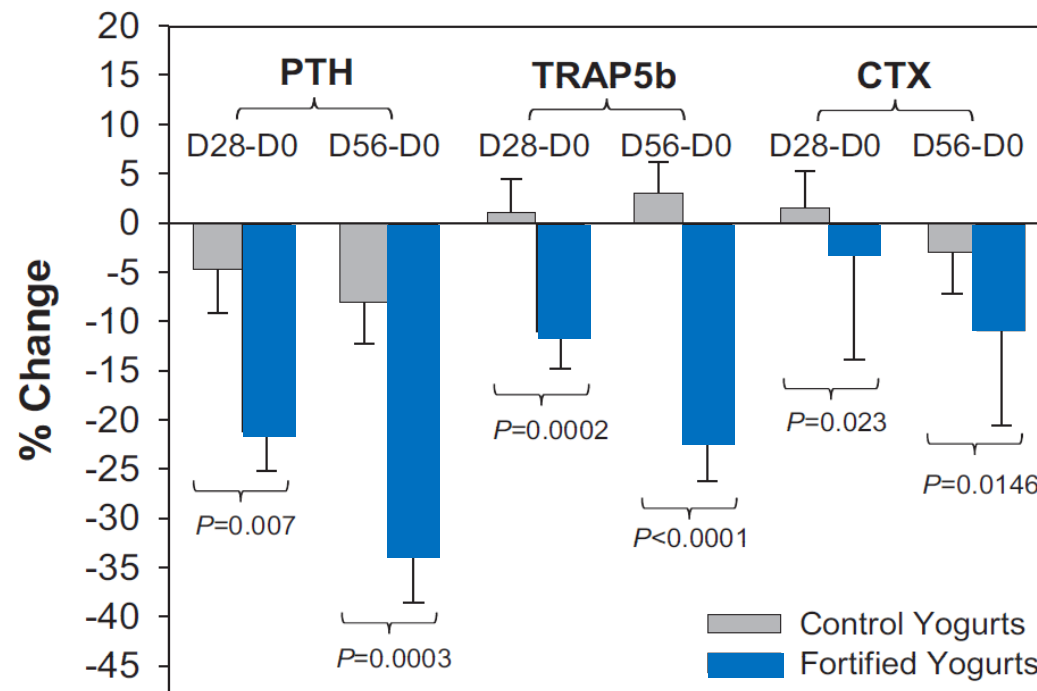
# Product Features

## 3. Vitamin D

### Combined Intake of Calcium and Vitamin D Slows Bone Loss



The Journal of Clinical  
Endocrinology &  
Metabolism  
98(7):2915-2921, 2013



The lower blood levels of PTH, TRAP5b, and CTX in the calcium plus vitamin D group compared to the control group suggests that taking calcium and vitamin D together not only improves the absorption of calcium, but also keeps blood calcium at a constant level for normal metabolism in the body.

\* PTH(Tarathyroid hormone):

Moves calcium from the bones into the blood when blood calcium levels are low.

\* TRAP5b(Tartrate-resistant acid phosphatase isoform-5b), CTX(Collagen type-1 C-

telopeptide): A bone reabsorption marker that measures the concentration of bone-destroying cells.

## Product Features

### 4. Vitamin K

Vitamin K is necessary for “blood to properly clot” and “to activate the Gla protein, which is needed to prevent cardiovascular disease, osteoporosis, diabetes, and cancer.”

Vitamin K1 or phylloquinone is found in green, leafy vegetables.

### Benefits of Vitamin K

1. Hemostasis
2. Reduces neonatal bleeding
3. Prevention and treatment of osteoporosis
4. Effective against ischemic heart disease (CHD)
5. Prevents bone loss from liver disease
6. Anti-inflammatory agent in geriatric diabetes mellitus

Source: Korean Pharmaceutical Information Center



정상적인 혈액응고 및  
뼈 구성 필요한 비타민K

### Blood Clotting

Vitamin K is necessary for the synthesis of prothrombin, a blood clotting agent. Platelets and potassium ions interact to form thrombin, which in turn acts on fibrinogen to form fibrin, which causes blood to clot.

### Bone Health

Vitamin K is also essential for bone health, but is often overlooked.

Source: Korea Food and Drug Safety, Functional Ingredients, Food and Drug Safety

# Product Features

## 5. Zinc



### 정상적인 면역기능·세포분열에 필요한 아연

Zinc is an essential nutrient that is a component of more than 200 compounds in the body and is involved in many of the body's major biological reactions.

Zinc is a trace element present in almost all tissues of the body, especially those with rapid cell turnover such as the nervous system.

It is an essential nutrient involved in the synthesis of nucleic acids such as DNA and RNA and this is required for normal cell division.

Source: Korea Food and Drug Safety, Functional Ingredients, Food and Drug Safety



# Product Features

## 6. Copper



유해산소로부터 세포 보호 및  
철에 흡수 이동을 돕는 구리

- Used to protect cells from free radicals
- Required for the transport and utilization of iron

Copper is a mineral found primarily in bones, muscle, and blood. It is used as a catalyst for enzymatic reactions in the body, and aids in the absorption and transportation of iron. It is also used to protect cells from free radicals.

Source: Korea Food and Drug Safety, Functional Ingredients, Food and Drug Safety





# Product Features

## 7. Manganese



유해 산소로부터 세포 보호 및  
골격 형성, 에너지 이용에 필요한 망간

- Protects cells from free radicals
- Necessary for energy utilization
- Necessary for bone formation

Manganese is an essential nutrient for skeletal development and the metabolism of sugars, fats, amino acids, cholesterol, and carbohydrates. It is also used to protect cells from free radicals.

Source: Korea Food and Drug Safety, Functional Ingredients, Food and Drug Safety

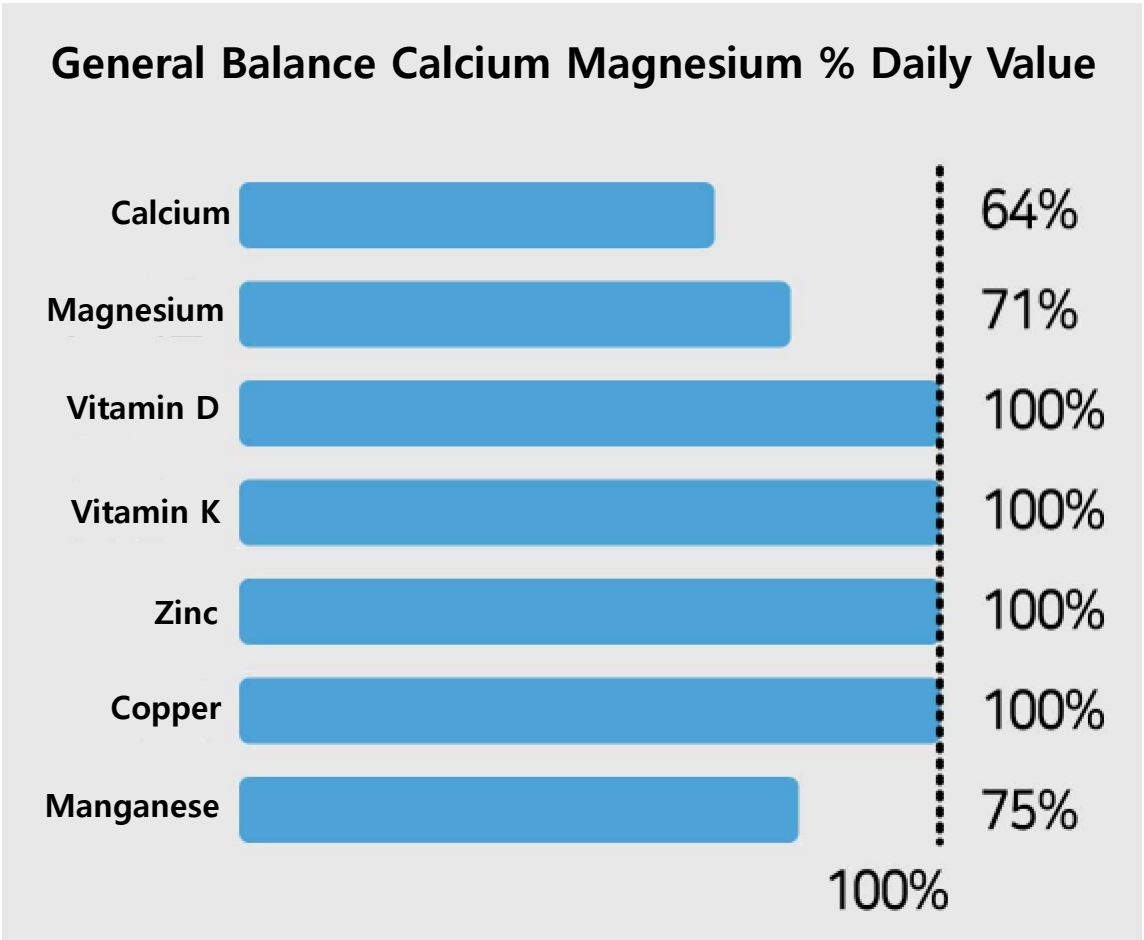
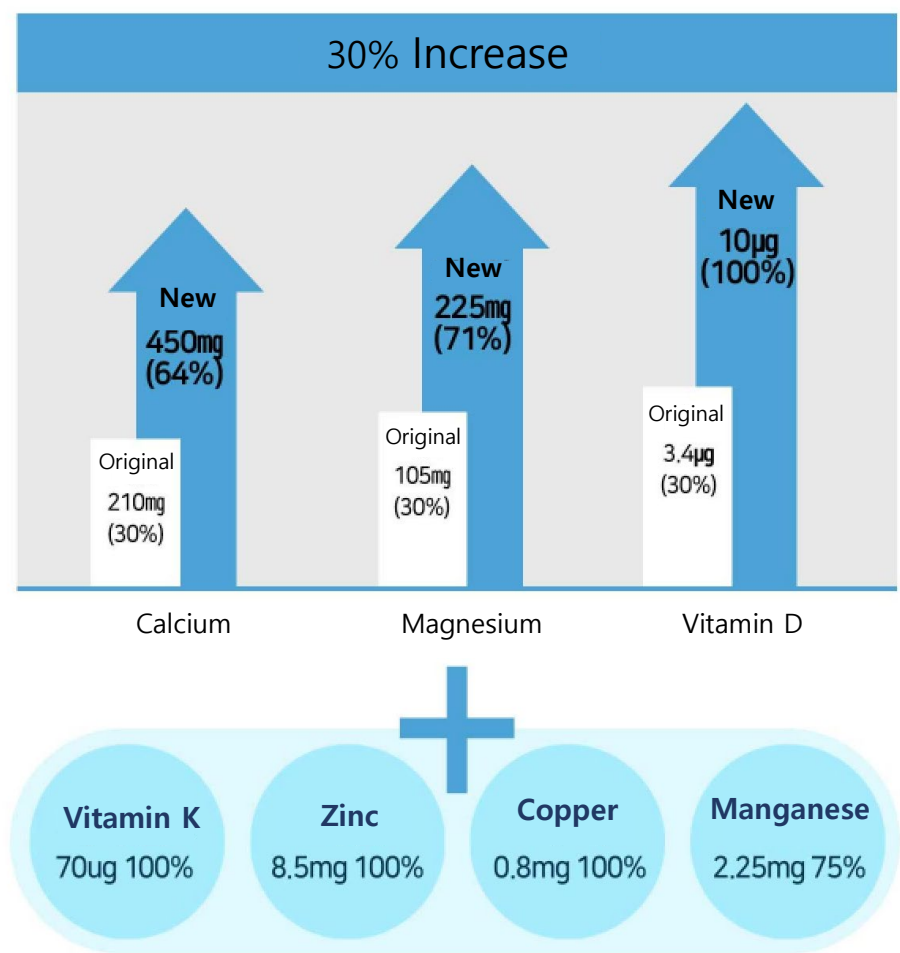




# Product Features

## 8. General Balance Calcium Magnesium Upgraded

The new General Balance Calcium Magnesium more than doubles the amount of calcium from 210 mg (30%) to 450 mg (64%), magnesium from 105 mg (30%) to 225 mg (71%), and vitamin D from 3.4 ug (30%) to 10 ug (100%), and four additional ingredients (vitamin K, zinc, copper, and manganese).



# Product Features

## 9. 7-in-1 Efficiency

**“General Balance Magnesium (Calcium, Magnesium, Vitamin D) + 4 New Ingredients (Vitamin K, Zinc, Copper, Manganese)”**

|                  |  |
|------------------|--|
| <b>Ca</b>        | Calcium <b>450mg (65%)</b> <ul style="list-style-type: none"><li>• Necessary for bone and teeth formation</li><li>• Necessary for proper blood clotting</li><li>• Necessary to maintain muscle and nerve function</li><li>• Helps prevent osteoporosis</li></ul> |
| <b>Mg</b>        | Magnesium <b>225mg (71%)</b> <ul style="list-style-type: none"><li>• Necessary for energy utilization</li><li>• Necessary to maintain muscle and nerve function</li></ul>  |
| <b>Vitamin D</b> | Vitamin D <b>10 ug (100%)</b> <ul style="list-style-type: none"><li>• Necessary for bone formation and maintenance</li><li>• Helps absorption and utilization of calcium</li><li>• Helps prevent osteoporosis</li></ul>  |



|                  |   |
|------------------|---|
| <b>Vitamin K</b> | Vitamin K <b>70 ug (100%)</b> <ul style="list-style-type: none"><li>• Necessary for bone and teeth formation</li><li>• Necessary for proper blood clotting</li><li>• Necessary to maintain muscle and nerve function</li><li>• Helps prevent osteoporosis</li></ul> |
| <b>Zn</b>        | Zinc <b>8.5 mg (100%)</b> <ul style="list-style-type: none"><li>• Necessary for immune system function</li><li>• Necessary for cell division</li></ul>  |
| <b>Cu</b>        | Copper <b>0.8 mg (100%)</b> <ul style="list-style-type: none"><li>• Necessary for transportation and utilization of iron</li><li>• Used to protect cells against free radicals</li></ul>  |
| <b>Mn</b>        | Manganese <b>2.25 mg (75%)</b> <ul style="list-style-type: none"><li>• Necessary for bone formation</li><li>• Necessary for energy utilization</li><li>• Used to protect cells against free radicals</li></ul>  |

# Product Features

## 10. 16 Quality Sub-Ingredients



Corn is a good source of antioxidants that contains nutrients like dietary fiber, vitamin A, vitamin E, niacin linoleic acid, and calcium beta-sitosterol.



Rapeseed is rich in beta-carotene, an antioxidant that helps boost the immune system. It also contains vitamin A and vitamin C which are beneficial for eye and skin health.



Ginseng extract can help boost the immune system, enhance memory, relieve stress, improve alcohol induced liver conditions, and prevent osteoporosis, eczema, and wrinkles.

[Source] 7 Benefits of 'Ginseng', a Timeless Medicine

[Source] Korea Policy Briefing



# Product Features

## 7. 16 Quality Sub-Ingredients



유단백가수  
분해물

Whey protein extract from milk helps prevent osteoporosis and strengthens weakened bones.



홍화씨  
추출물분말

Safflower seeds are rich in calcium and magnesium. They also contain an element called organophosphorus, which is effective in increasing bone density and may help prevent bone aging.



상어연골  
추출물분말

Shark cartilage contains high levels of chondroitin, which stimulates chondrocytes to repair tissue and maintain its function, which can help with the management of bone and cartilage problems such as arthritis and disks.





## Product Features

### 7. 16 Quality Sub-Ingredients

#### 10 Ingredient Blend



Blueberry



Oats



Green Tea



Spinach



Tomato



Walnut



Salmon



Grape



Garlic



Broccoli

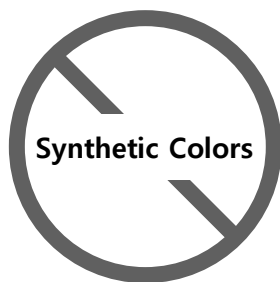
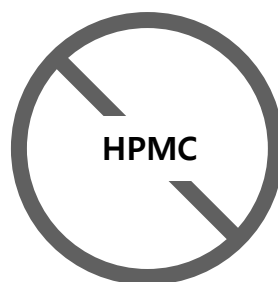
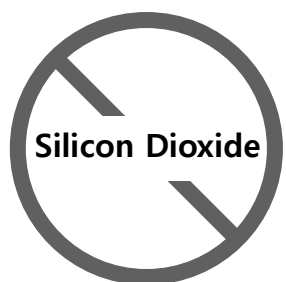




# Product Features

## No Additives

Made without chemical excipients (silicon dioxide, magnesium stearate, hydroxypropyl methylcellulose (HPMC)) used for production efficiency or product stabilization, and synthetic additives for flavor, color, or taste (synthetic flavors, colors, and sweeteners).



## Recommended for



Those who want to lower  
the risk of osteoporosis



Those with reduced  
calcium absorption



Those who need  
calcium supplements



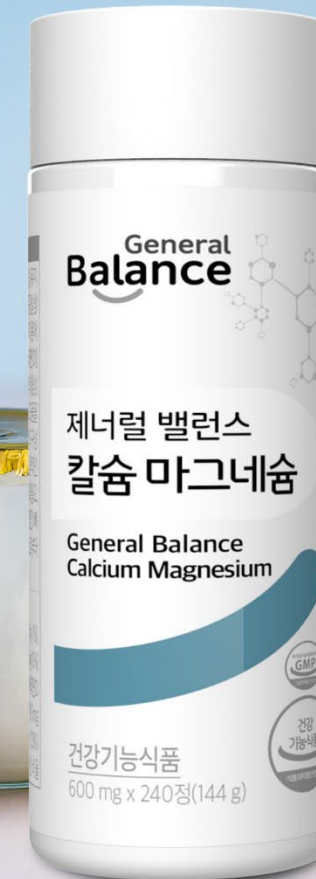
Those who want to stay active



Those seeking a  
healthy supplement



Those seeking a  
dietary supplement



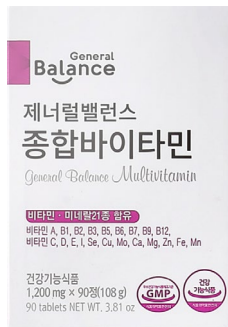
# Synergetic Supplements



**General Balance  
Plant-Based MSM**



**General Balance  
Mega Vitamin C**



**General Balance  
Multivitamin**



**Active DS  
Pro Whey / Veggie**

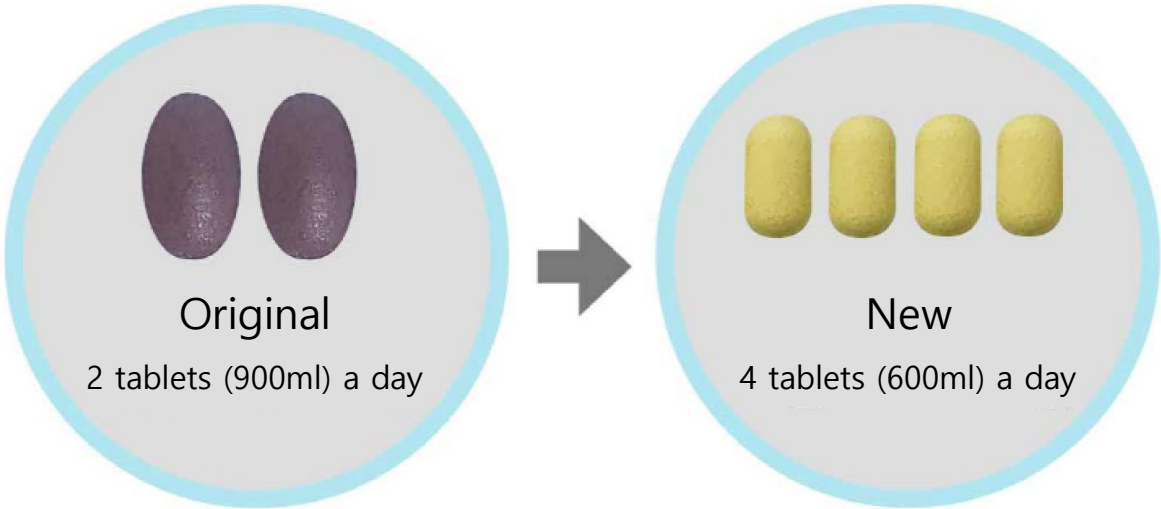


**General Balance Energy**



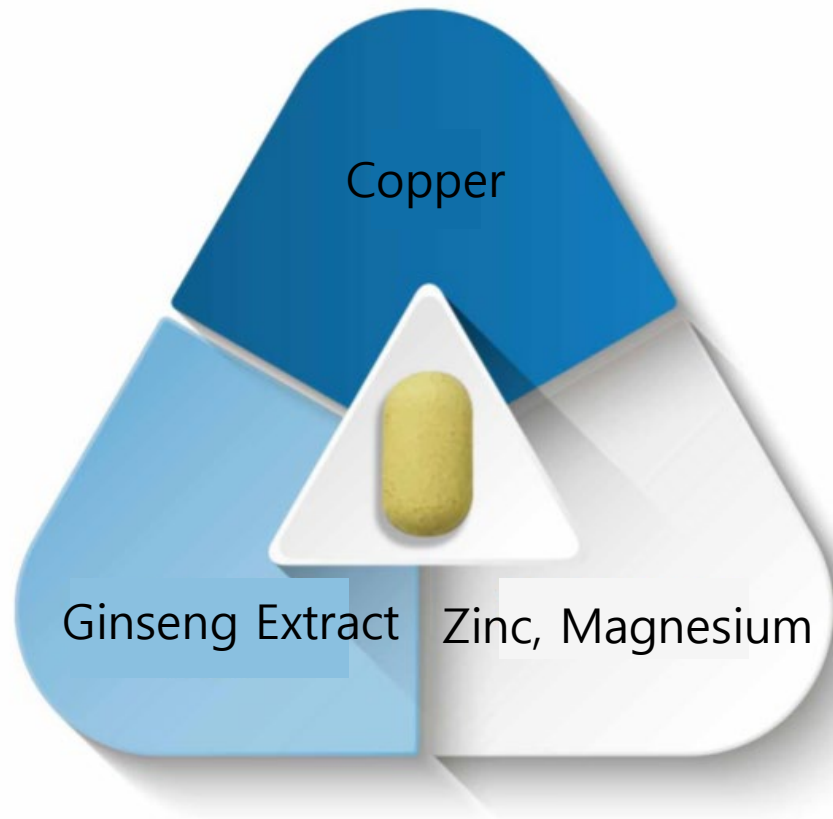


# General Information



# General Information

## Tablet & Package Point



The tiny blue spots in the tablet are copper, the brown spots are ginseng extract, and the white spots are zinc and magnesium.

\*Tablet contains no excipients, may break easily

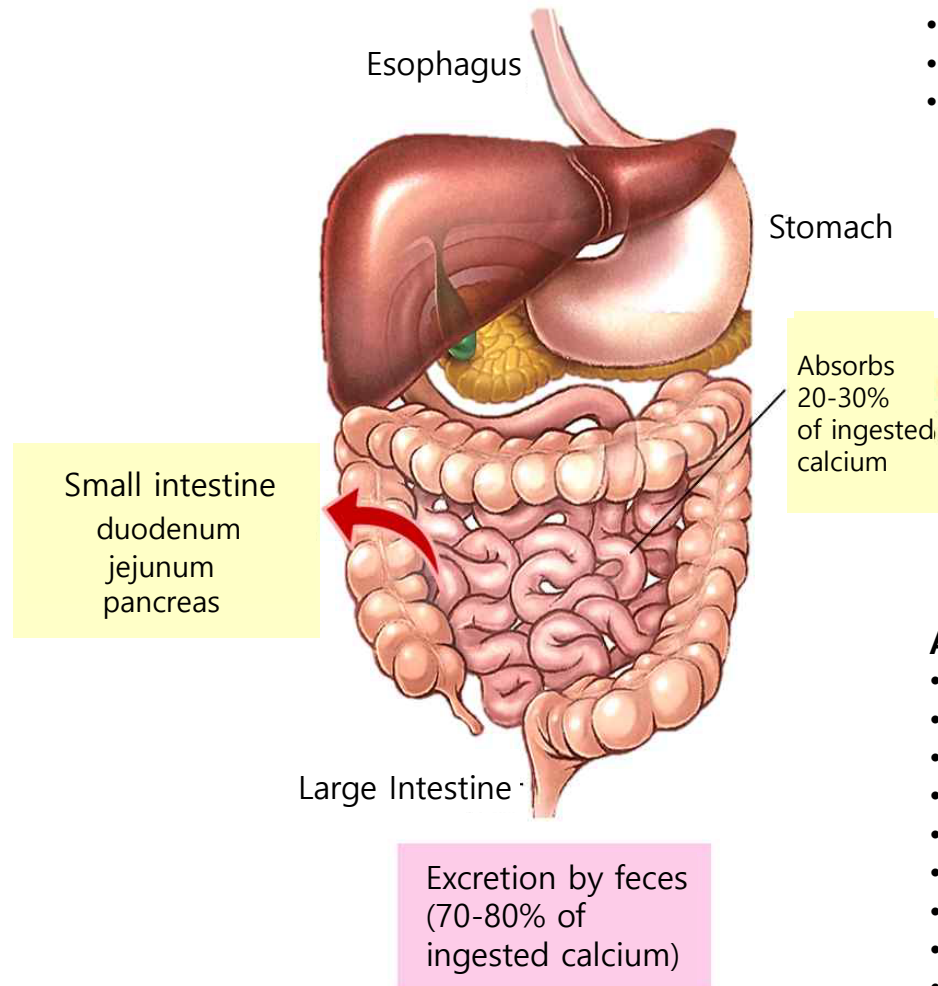




# General Information

## Calcium Metabolism

### Intake & Digestion



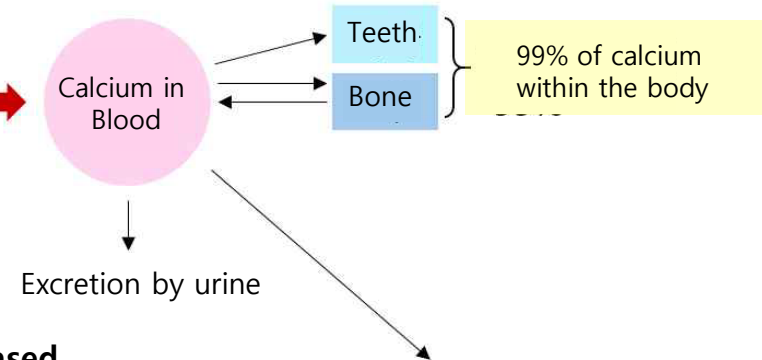
### Absorption increased

- Needed within the body
- Vitamin D is readily available
- Protein
- Lactose
- Acidic conditions within the digestive system

Calcium is more easily absorbed in an acidic state, so absorption occurs in the duodenum and jejunum, which are highly acidic. The transporter that carries calcium into the bloodstream is regulated by vitamin D. Therefore, if vitamin D intake is low, calcium absorption in the small intestine is reduced.

### Absorption decreased

- Vitamin D is not available
- Ca-P imbalance
- Phytic acid
- Oxalic acid
- Dietary fiber
- Obesity
- High alkalinity
- Stress
- Lack of exercise



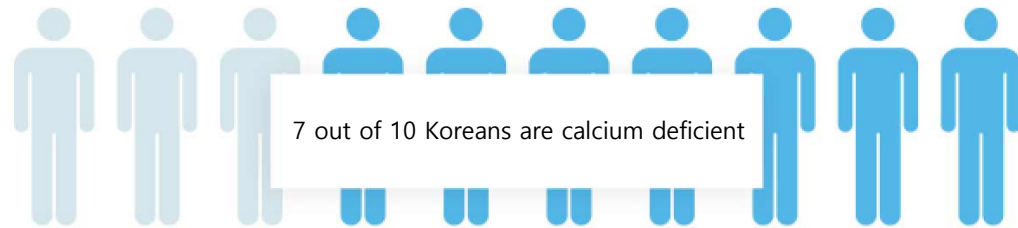
### 1% of calcium in the body

- Maintains excitability of muscles and nerves
- Regulates heartbeat
- Necessary for blood to clot
- Activates enzymes
- Increases permeability of cell membranes

## General Information

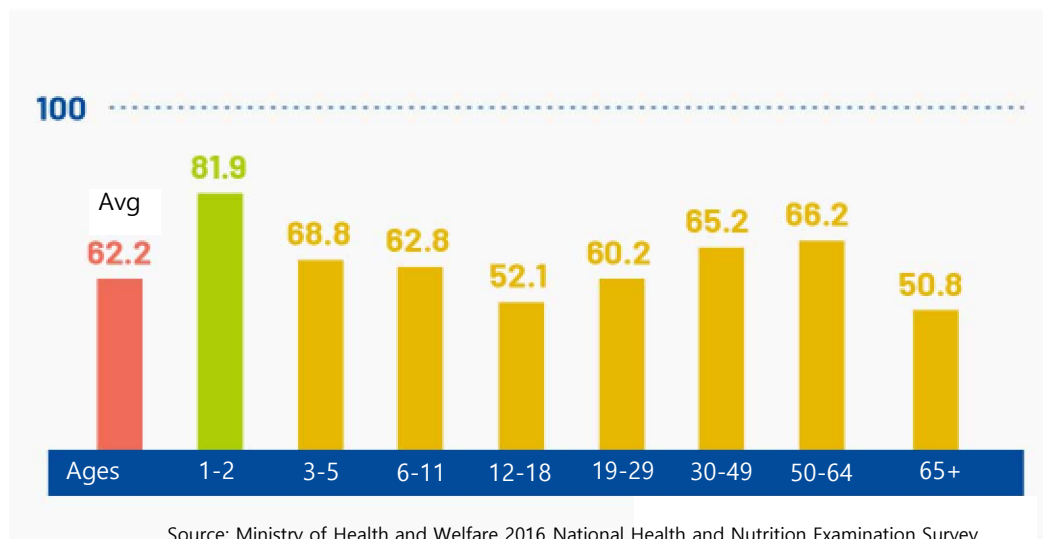
### The #1 Nutrient Koreans are Most Likely Deficient In

The #1 Nutrient Koreans are Most Likely Deficient In



Calcium Deficiency Across All Age Groups

Source: Ministry of Health and Welfare 2015 National Health and Nutrition Examination Survey



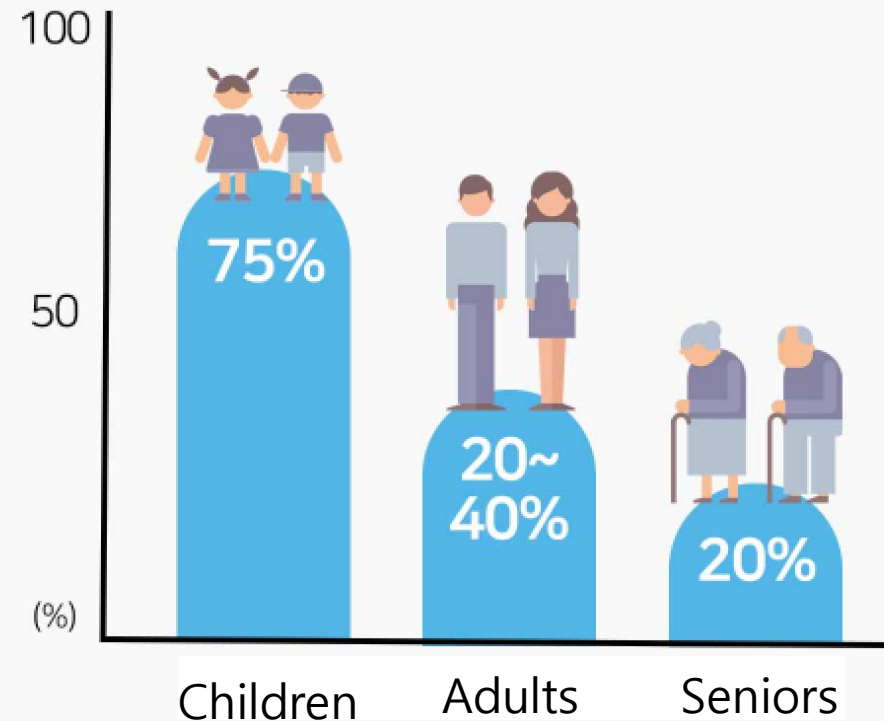
More than 7 out of 10 South Koreans consume less than the recommended amount of calcium, a nutrient important for bone and dental health. All but infants report a calcium deficiency, with more women than men, seniors over 65, and adolescents aged 13 to 19 consuming less than half the recommended daily amount.

## General Information

### Calcium Absorption Decreases with Age

According to medical experts, calcium absorption is naturally on the lower side compare the other nutrients and as we age, the body's ability to absorb calcium decreases. Adults are only able to absorb about 20-40% of the calcium they consume with the rest being excreted.

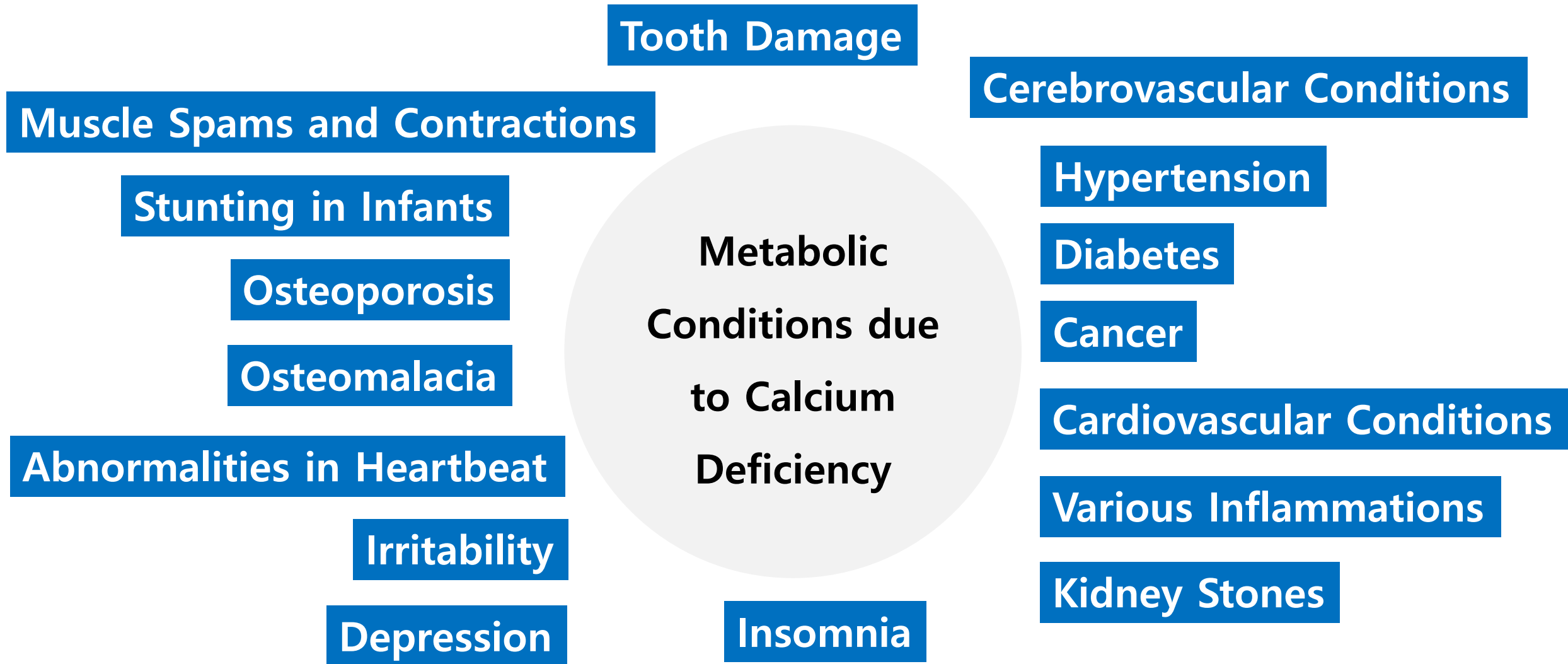
Change in Calcium Absorption Rate by Age



## General Information

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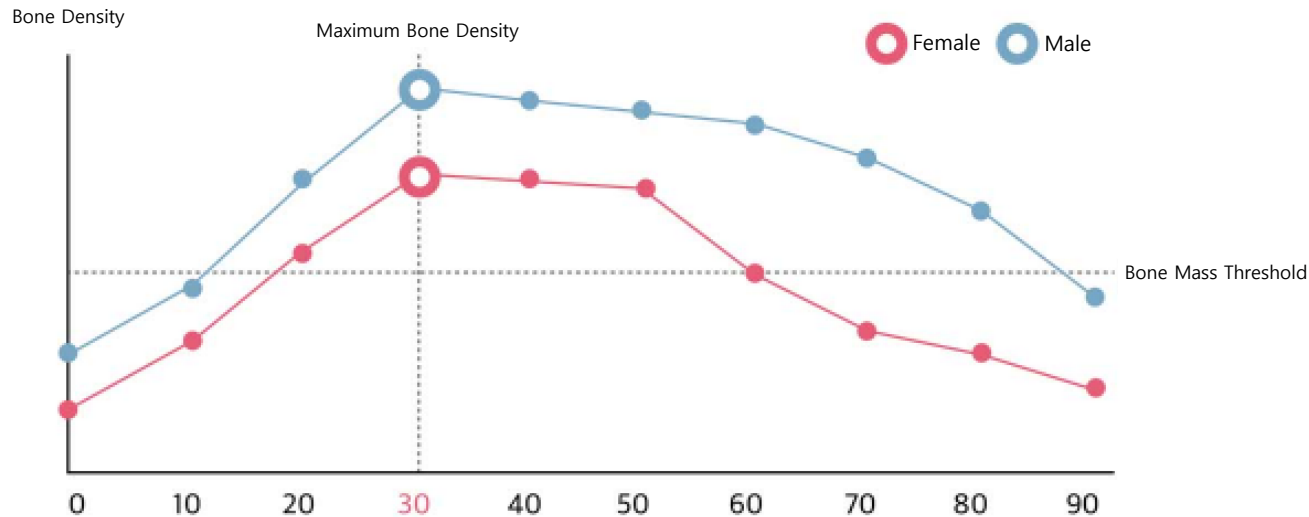
### Possible Conditions Due to Calcium Deficiency



# General Information

## Bone Density Declines when Calcium is Deficient

Bone Density Decline Starts at 30

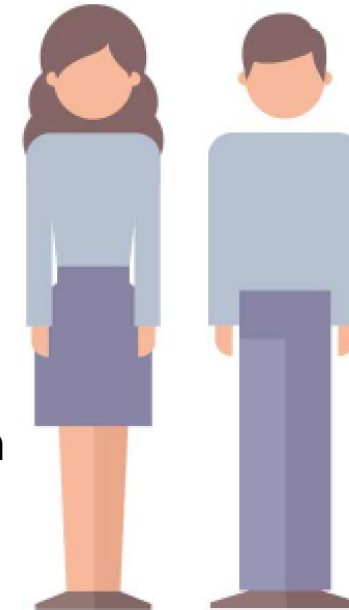


Prevalence of Osteoporosis in Females 35%

Prevalence of Osteopenia in Females 80%

Prevalence of Osteoporosis in Males 10%

Prevalence of Osteopenia in Males 50%



Bone density steadily increases until 30  
At 30 bone density starts declining

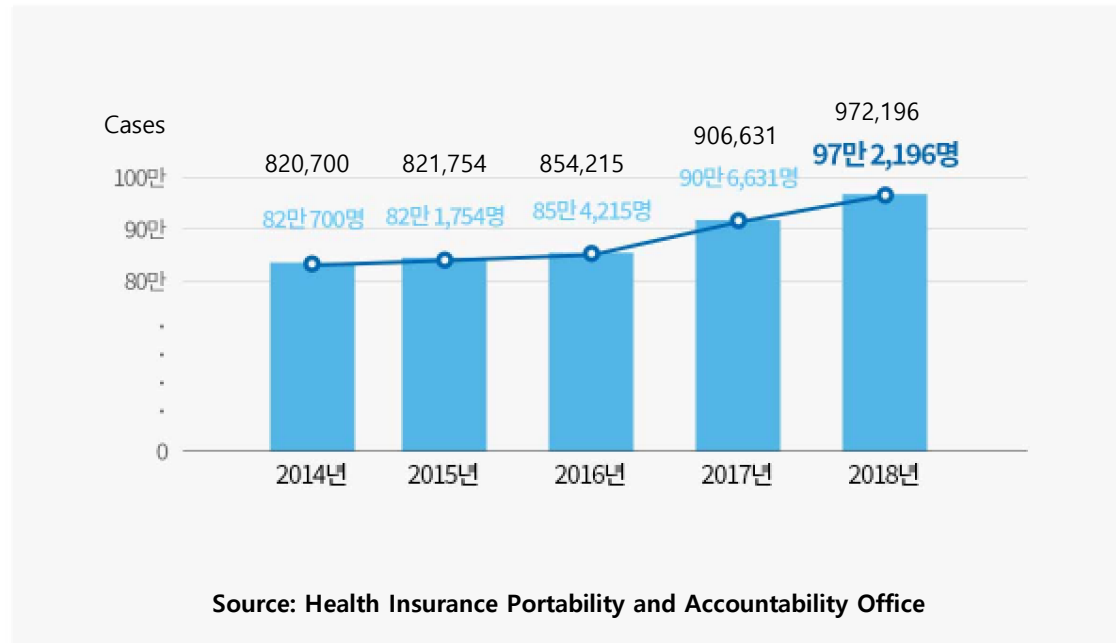
Source: Korean Society of Endocrinology / 2014 Korean Osteoporosis FACT



# General Information

## Increase in the Number of Patients with Osteoporosis

Approximately 18% increase in patients with osteoporosis over 5 years

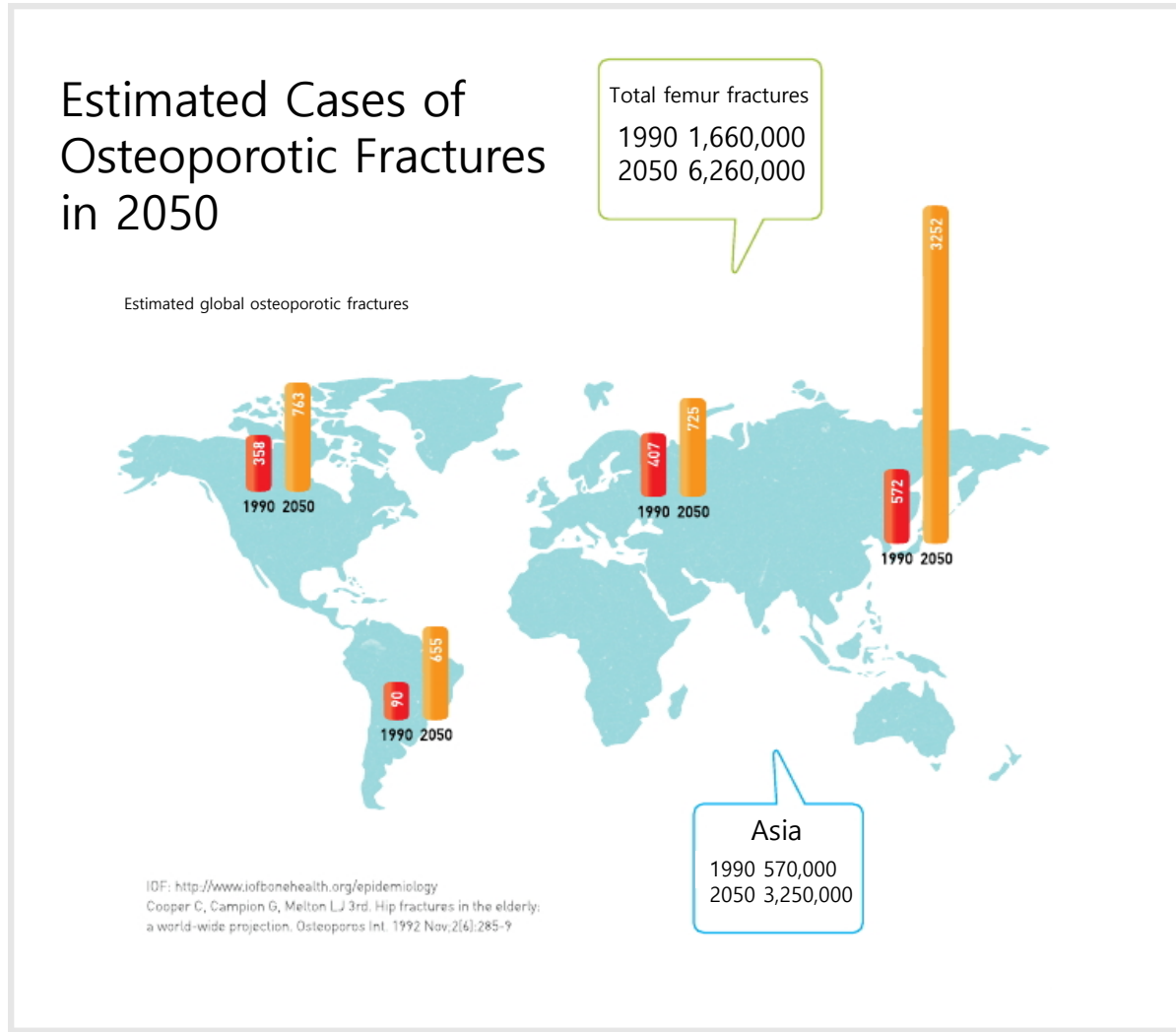


According to the Health Insurance Portability and Accountability Office, the number of people with osteoporosis has increased by 18.4% over the past five years, with more women than men suffering from the disease as of 2017. Women over 50 had the most cases.



# General Information

## Global Osteoporosis and Osteoporotic Fracture Incidents projected to Rise

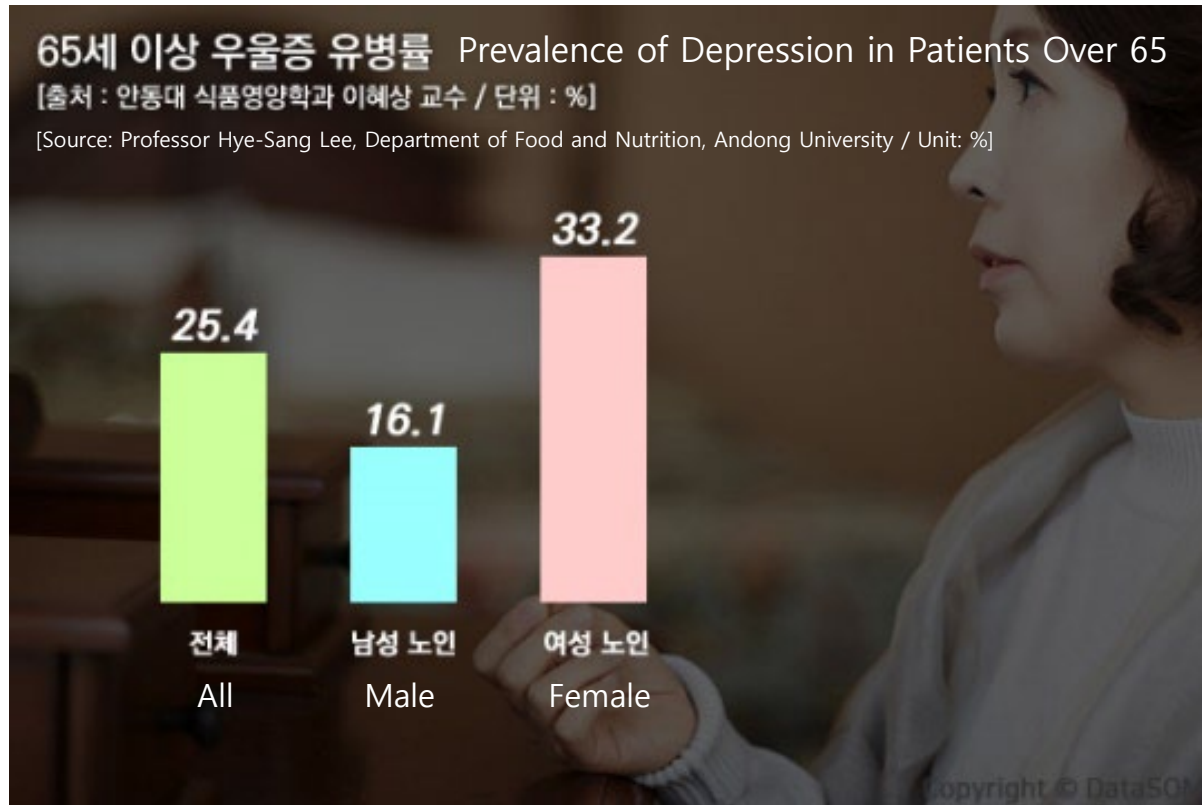


The International Osteoporosis Foundation (IOF) has projected that the global incidence of osteoporotic fractures will increase by 2050.

The IOF states that "one in three women and one in five men over the age of 50 will experience an osteoporotic fracture." IOF estimates that the global incidence of osteoporotic fractures in 2050 will increase globally with differences depending on the region.

## General Information

### Low Calcium Intake in Older Adults Increases Risk of Depression

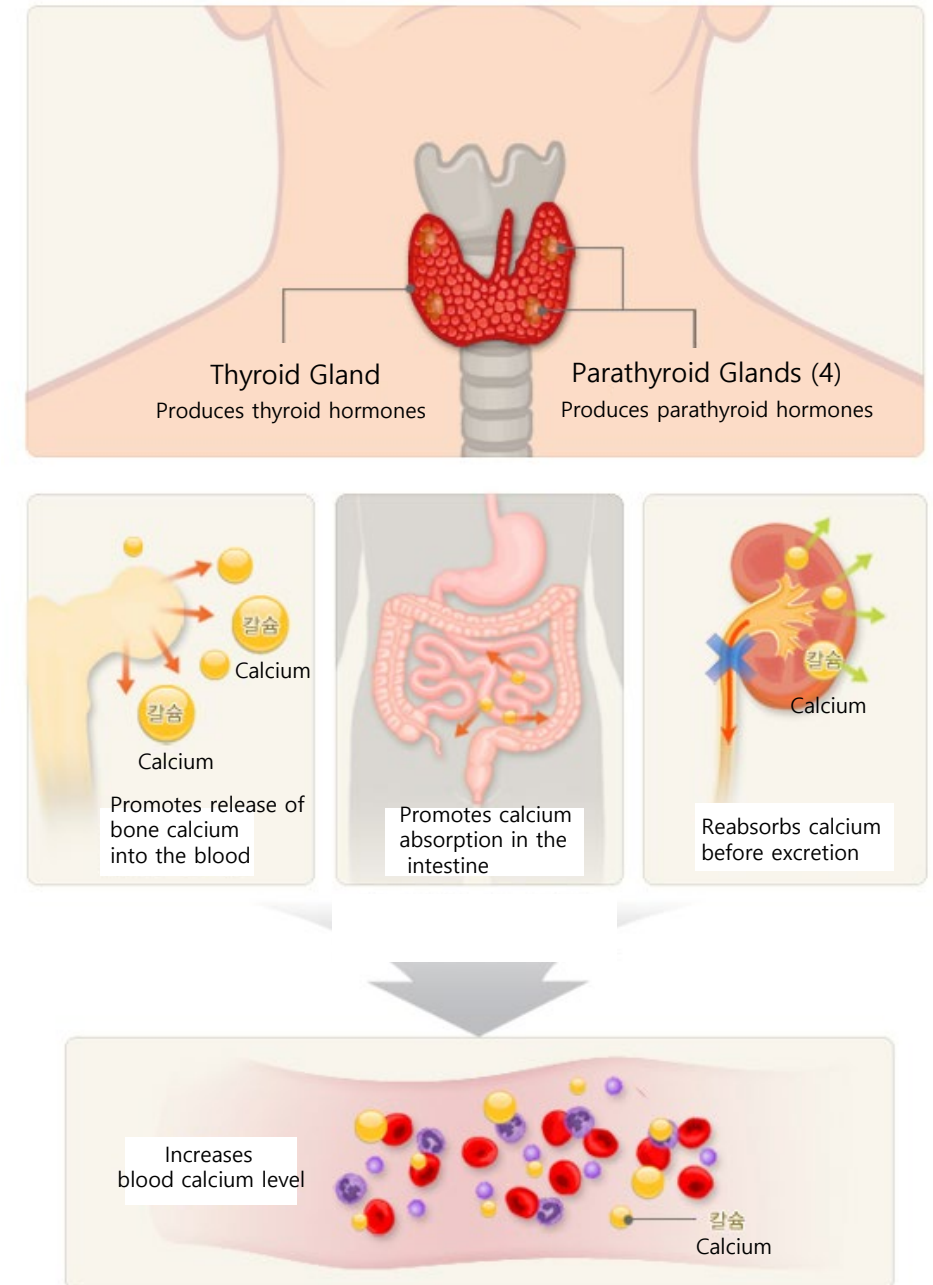


The prevalence of depression in the elderly aged 65 years and older was 25.4%. One in four seniors suffer from depression, and the prevalence of the disorder in female seniors (33.2%) was more than twice as high as in male seniors (16.1%). The nutrient associated with depression in the elderly is calcium, which is the most deficient mineral in the Korean diet. The risk of depression among seniors with inadequate calcium intake was 1.7 times that of seniors with adequate calcium intake.

# General Information

## Calcium Deficiency and Hypertension

Calcium is contained in a ratio of 100 million parts in bone, 10,000 parts in blood, and 1 part in cells. Calcium levels in the blood are maintained at 8.6-10.4 mg/dL and when the level drops below 8.6 mg/dL, parathyroid hormone is released, dissolving bone and releasing calcium into the blood. The loss of calcium from the bones not only leads to osteoporosis, but the dissolved calcium from the bones enters the blood, deposits in the blood vessels, and narrows the walls of the blood vessels, causing numerous diseases such as hypertension, atherosclerosis, cerebrovascular disorders, myocardial infarction, senile dementia, diabetes, and cancer.





# General Information

## Vitamin D Deficiency

Vitamin D deficient patients have increased 10-fold in 4 years



2010-2014 National Health Insurance Service Health Insurance and Medical Benefits Review Data

## Vitamin D Intake Recommendation

| Category                              | RDA (daily)    | Recommended by  |
|---------------------------------------|----------------|---|
| Children, Teens                       | 400 IU         | American Academy of Pediatrics (2008)   |
| Adults & Pregnant Women               | 800 IU         | Korea Women's Health and Osteoporosis Foundation<br>Korean Osteoporosis Society<br>Korean Society of Obstetrics, Gynecology and Endocrinology<br>Join Enactment Recommendation (2011) |
| Adults 50+ & Menopausal Women         | 800-1,000 IU   | Korean Society of Bone Metabolism<br>International Osteoporosis Foundation (2014)   |
| Limited Sunlight Exposure             | 2,000 IU       | International Osteoporosis Foundation (2010)  |
| Vitamin D Deficient (30mg/ml or less) | 1,000-1,500 IU | Endocrine Society   |

According to various societies, 800-1000 IU of vitamin D per day is recommended for the general adult population, but up to 2,000 IU per day is recommended for those who have limited exposure to sunlight due to increased indoor activity and sunscreen use, or those who have a vitamin D deficiency of 30mg/ml or less.



## "Immunomodulatory effect"

Seminars in Cell & Developmental Biology 17 (2006) 654–666

### Review

## TRPM channels, calcium and redox sensors during innate immune responses

Pam Massullo<sup>a,b</sup>, Adriana Sumoza-Toledo<sup>a</sup>,  
Harivadan Bhagat<sup>a</sup>, Santiago Partida-Sánchez<sup>a,\*</sup>

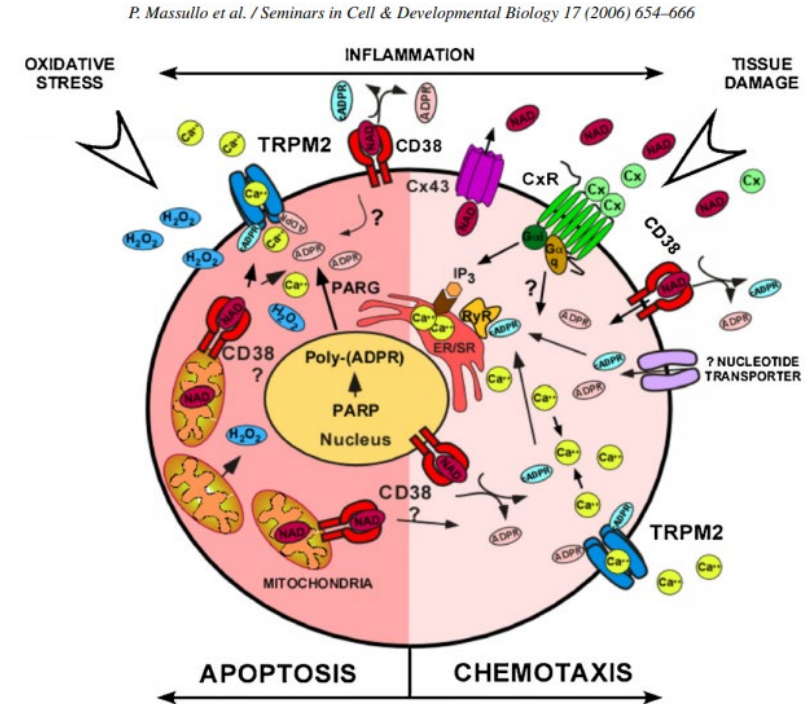
<sup>a</sup> Columbus Children's Research Institute, Center for Microbial Pathogenesis, The Ohio State University,  
700 Children's Drive, W512, Columbus, OH 43205, United States

<sup>b</sup> Molecular, Cellular, and Developmental Biology Program, The Ohio State University, Columbus, OH 43210, United States

Available online 21 November 2006

seminars in  
CELL & DEVELOPMENTAL  
BIOLOGY

www.elsevier.com/locate/semcdb



- Utilized the role of calcium in immune cells reactions to confirm anti-inflammation and the immune system.
- Mitigated oxidative stress by activating TRPM2-related immune factors.
- Regulated calcium levels through the ADPR/TRPM2 ion channel to terminate oxidation-induced cells.

[Source: Cell & Developmental biology (2006), June 17, 654-666. TRPM channels, calcium and redox sensors during innate immune responses. Pam Massullo, Adriana Sumoza-Toledo, Harivadan Bhagat, Santiago Partida-Sanchez.]

“Immunomodulatory effect”

JOURNAL OF THE AMERICAN COLLEGE OF NUTRITION  
https://doi.org/10.1080/07315724.2020.1785971



Check for updates

Combating COVID-19 and Building Immune Resilience: A Potential Role for Magnesium Nutrition?

Taylor C. Wallace<sup>a,b,c</sup>

<sup>a</sup>Think Healthy Group, Washington, DC, USA; <sup>b</sup>Department of Nutrition and Food Studies, George Mason University, Fairfax, Virginia, USA; <sup>c</sup>Center for Magnesium Education & Research, Pahoehoe, Hawaii, USA

ABSTRACT

**Background:** In December 2019, the viral pandemic of respiratory illness caused by COVID-19 began sweeping its way across the globe. Several aspects of this infectious disease mimic metabolic events shown to occur during latent subclinical magnesium deficiency. Hypomagnesemia is a relatively common clinical occurrence that often goes unrecognized since magnesium levels are rarely monitored in the clinical setting. Magnesium is the second most abundant intracellular cation after potassium. It is involved in >600 enzymatic reactions in the body, including those contributing to the exaggerated immune and inflammatory responses exhibited by COVID-19 patients. **Methods:** A summary of experimental findings and knowledge of the biochemical role magnesium may play in the pathogenesis of COVID-19 is presented in this perspective. The National Academy of Medicine's Standards for Systematic Reviews were independently employed to identify clinical and prospective cohort studies assessing the relationship of magnesium with interleukin-6, a prominent drug target for treating COVID-19. **Results:** Clinical recommendations are given for prevention and treatment of COVID-19. Constant monitoring of ionized magnesium status with subsequent repletion, when appropriate, may be an effective strategy to influence disease contraction and progression. The peer-reviewed literature supports that several aspects of magnesium nutrition warrant clinical consideration. Mechanisms include its "calcium-channel blocking" effects that lead to downstream suppression of nuclear factor-κB, interleukin-6, c-reactive protein, and other related endocrine disruptors; its role in regulating renal potassium loss; and its ability to activate and enhance the functionality of vitamin D, among others. **Conclusion:** As the world awaits an effective vaccine, nutrition plays an important and safe role in helping mitigate patient morbidity and mortality. Our group is working with the Academy of Nutrition and Dietetics to collect patient-level data from intensive care units across the United States to better understand nutrition care practices that lead to better outcomes.

ARTICLE HISTORY

Received 13 May 2020  
Accepted 16 June 2020

KEYWORDS

Magnesium; COVID-19; coronavirus; COVID-19; nutrition; potassium; vitamin D; hypokalemia; hypomagnesemia; inflammation; cytokine

Table 2. Intravenous dosing of potassium and magnesium in patients with normal renal function.

| Dosing of potassium chloride  |             |  |
|-------------------------------|-------------|--|
| Serum K (mEq/L)               | Dose (mEq)  | Laboratory Work  |
| 3.5 – 3.9 <sup>a</sup>        | 40 (x 1)    | Assess basal metabolic profile and check magnesium status next morning.  |
| 3.0 – 3.4                     | 40 (x 2)    | Assess basal metabolic profile and check magnesium status next morning; may wish to assess potassium status 2-hours after second 40 mEq bolus, especially if losses are suspected to be high. Reassess |
| 2.0 – 2.9                     | 40 (x 3+)   | Assess potassium status 2-hours after second 40 mEq infusion and reassess; may need 1 – 2 additional boluses; repeat. Check magnesium status. Reassess.  |
| Dosing of Magnesium Gluconate |             |  |
| Serum Mg (mg/dL)              | Dose (g/kg) |  |
| 1.6 – 1.8                     | 0.05        |  |
| 1.0 – 1.5                     | 0.1         |  |
| <1.0                          | 0.15        |  |

Adapted with permission from Dickerson 2001 (89).

<sup>a</sup>Some clinicians choose not to provide any potassium for a serum concentration of 3.5–3.9 mEq/L, depending on the clinical scenario.

Note: These doses are based on “average sized” adults and should not be used for patients with renal impairment or adrenal insufficiency. Always examine magnesium status in any patient who is hypokalemic. Increase the amount of potassium in the IV/parental nutrition solutions if possible. Be sure to check arterial pH level to ascertain whether any aberrations in serum potassium are due to an abnormal pH.

- Identified the effects of IL-6 modulation and the reduction of cytokine-related genes in Covid-19 patients.
- Reduces the generation time of free radicals in the body.
- Inhibits potassium loss and activates vitamin function in the kidneys.

[Source: JOURNAL OF THE AMERICAN COLLEGE NUTRITION. 2020, June. Combating COVID-19 and Building immune Resilience: A potential Role foe Magnesium Nutrition? Taylor C. Wallace]

## “Detoxification of Heavy Metal”

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Review

### CADMIUM TOXICITY REVISITED: FOCUS ON OXIDATIVE STRESS INDUCTION AND INTERACTIONS WITH ZINC AND MAGNESIUM

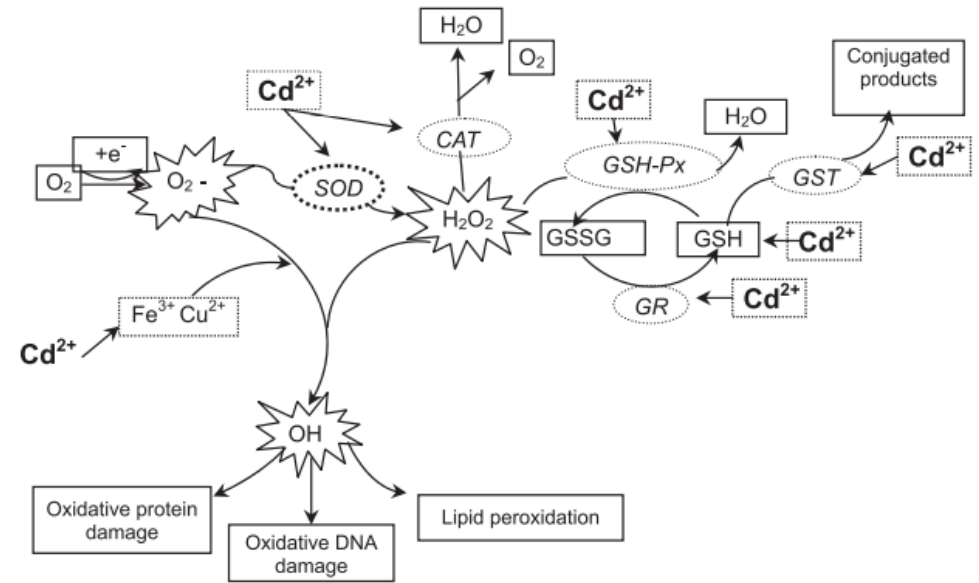
Vesna MATOVIĆ, Aleksandra BUHA, Zorica BULAT, and Danijela ĐUKIĆ-ĆOSIĆ

Department of Toxicology “Akademik Danilo Soldatović”, Faculty of Pharmacy, University of Belgrade,  
Belgrade, Serbia

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**Figure 1** Pathways of Cd-induced generation of reactive oxygen species (adapted from ref. 39 by Danijela Đukić-Ćosić). Cadmium impairs enzyme activity of antioxidative defence system (superoxide dismutase, SOD; catalase, CAT; glutathione peroxidase, GSH-Px; glutathione-S-transferase, GST; glutathione reductase, GR) and of the non-enzymatic component glutathione, GSSG and GSH. Cadmium also elevates the levels of Fenton metals ( $\text{Fe}^{3+}$ ,  $\text{Cu}^{2+}$ ), which can break down hydrogen peroxide,  $\text{H}_2\text{O}_2$  to a reactive hydroxyl radical, OH.

- Confirmed the role of magnesium and zinc in cadmium toxin excretion.
- ROS generation due to cadmium induces oxidative stress and liver inflammatory responses.
- Magnesium supplement (40mg/kg/day) reduced said responses and increased DNA and RNA structural repair.



# General Information

## “Immunomodulatory effect”

Journal of Autoimmunity 85 (2017) 78–97



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### Modulation of inflammatory and immune responses by vitamin D

Francesco Colotta <sup>a,\*</sup>, Birger Jansson <sup>a</sup>, Fabrizio Bonelli <sup>b</sup>

<sup>a</sup> DiaSorin SpA, Saluggia, VC, Italy

<sup>b</sup> DiaSorin Inc, Stillwater, MN, USA



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#### ABSTRACT

Vitamin D (VitD) is a prohormone most noted for the regulation of calcium and phosphate levels in circulation, and thus of bone metabolism. Inflammatory and immune cells not only convert inactive VitD metabolites into calcitriol, the active form of VitD, but also express the nuclear receptor of VitD that modulates differentiation, activation and proliferation of these cells. In vitro, calcitriol upregulates different anti-inflammatory pathways and downregulates molecules that activate immune and inflammatory cells. Administration of VitD has beneficial effects in a number of experimental models of autoimmune disease. Epidemiologic studies have indicated that VitD insufficiency is frequently associated with immune disorders and infectious diseases, exacerbated by increasing evidence of suboptimal VitD status in populations worldwide. To date, however, most interventional studies in human inflammatory and immune diseases with VitD supplementation have proven to be inconclusive. One of the reasons could be that the main VitD metabolite measured in these studies was the 25-hydroxyVitD (25OHD) rather than its active form calcitriol. Although our knowledge of calcitriol as modulator of immune and inflammatory reactions has dramatically increased in the past decades, further in vivo and clinical studies are needed to confirm the potential benefits of VitD in the control of immune and inflammatory conditions.

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**Table 1**  
Summary table on effects of calcitriol on immune and inflammatory cells.

| Target cells               | Effects   |  | References               |
|----------------------------|---|--|--------------------------|
|                            | Suppression   | Induction  |                          |
| Dendritic Cells.           | Pro-inflammatory cytokines.<br>Class II MHC and costimulatory molecules (CD40, CD80, CD86).   | Anti-inflammatory cytokine IL-10.<br>Tolerogenicity.   | [78–80,82–84]            |
| Monocytes and macrophages. | Pro-inflammatory cytokines IL-1 $\beta$ , IL-6, TNF $\alpha$ , RANKL and COX-2.   | Anti-inflammatory cytokine IL-10.<br>Cathelicidin (anti-microbial).  | [72,88]                  |
| B-cells.                   | Proliferation, immunoglobulin class switching & production.<br>CD 86 and CD74 (reduced T-cells stimulation and MHC-II assembly).<br>B-cells to plasma cells.  | Apoptosis.<br>Anti-inflammatory cytokine IL-10.  | [94–96,98–101]           |
| CD4 <sup>+</sup> T cells.  | IFN $\gamma$ and IL-2 in Th1 cells.<br>Th17 differentiation and activation by the inhibition of IL-17A, IL-17F, RORC, and CCR6.<br>IL-4 in naïve CD62 ligand + CD4 <sup>+</sup> T cells during in vitro polarization. | IL-4 and GATA3 in cultures driven by Ag, anti-CD3 and CD28.<br>FoxP3 and Tregs differentiation in vitro and in vivo in mice. | [74,107,108,111–116,121] |
| CD8 <sup>+</sup> T cells.  | IFN $\gamma$ and TNF $\alpha$ .   |  | [126]                    |
| Unconventional T Cells.    | IFN- $\gamma$ .   | Invariant NKT cells (iNKT).  | [104,128]                |
| Innate Lymphoid Cells.     | NK development.   | Cytolytic killing capacity.  | [130,131]                |

- Identified the effects of active vitamin D in immune inflammatory cells.
  - Confirmed that calcitriol (active vitamin D) decreases the production of type 1 pro-inflammatory cytokines IL-12, IFN-g, IL-6, IL-8, TNF- $\alpha$ , IL-17, and IL9.
  - Increased the production of the type 2 anti-inflammatory cytokines IL-4, IL-5, and IL-10.
  - Exhibits anti-inflammatory effects through cytokine modulation and inhibition of NF-KB p65 activity..

[Source: Journal of Autoimmunity, 2017,(85) 78-97, Modulation of inflammatory and immune responses by vitamin D Francesco Colotta, Birger Jansson, Fabrizio Bonelli]

# FAQ

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## 1. What are the benefits and when do I take it?

Calcium is the most important element for the growth of a fetus. A lack of calcium can lead to rickets, osteomalacia, osteoporosis, and other diseases such as high blood pressure, arteriosclerosis, and diabetes. Magnesium helps support bone health and reduce the risk of osteoporosis, is necessary for maintaining nerve and muscle function, and supports normal blood clotting. For other functions, see the Nutrition Facts. Calcium is best absorbed when taken between or after meals, as food stimulates the secretion of stomach acid, which facilitates the absorption of calcium.

## 2. Why take calcium, magnesium, and vitamin D together?

Vitamin D is known to help the absorption of calcium from the mucosal cells of the small intestine and to promote the reutilization of calcium in the body. In addition, taking calcium and vitamin D at the same time has been shown to delay bone loss. Therefore, adequate intake of vitamin D is important to support the absorption of calcium and magnesium.

## 3. Why are there spots or crack on the tablet?

The blue spots are gluconic acid copper, brown spots are ginseng fermented extract powder, and white spots are zinc and magnesium. The product may be slightly cracked because it does not contain chemical excipients. The product is safe to consume.

## 4. Can pregnant/nursing women take it?

According to the Korean Ministry of Food and Drug Safety, the recommended calcium intake for pregnant women is 1,200 to 1,500 mg. There is no specific timing for pregnant women to take calcium, but it is generally recommended to take it throughout pregnancy, starting at 20 weeks. It is recommended that prenatal calcium be continued until three months after delivery.

## 5. Who should not take calcium?

If you are taking anticoagulants, have hypercalcemia or kidney stone, it is highly recommended you consult a healthcare professional before use.