

# Chelated Minerals Research

Please note these are research articles. See references  
on each slide.

**Article Title:** Invited review: Mineral absorption mechanisms, mineral interactions that affect acid-base and antioxidant status, and diet considerations to improve mineral status.

**Date & Journal:** J Dairy Sci. 2018 Apr

- Several minerals are required for life to exist. In animals, 7 elements (Ca, P, Mg, Na, K, Cl, and S) are required to be present in the diet in fairly large amounts (grams to tens of grams each day for the dairy cow) and are termed macrominerals. Several other elements are termed microminerals or trace minerals because they are required in much smaller amounts (milligrams to micrograms each day). In most cases the mineral in the diet must be absorbed across the gastrointestinal mucosa and enter the blood if it is to be of value to the animal. The bulk of this review discusses the paracellular and transcellular mechanisms used by the gastrointestinal tract to absorb each of the various minerals needed. Unfortunately, particularly in ruminants, interactions between minerals and other substances within the diet can occur within the digestive tract that impair mineral absorption. The attributes of organic or chelated minerals that might permit diet minerals to circumvent factors that inhibit absorption of more traditional inorganic forms of these minerals are discussed. Once absorbed, minerals are used in many ways. One focus of this review is the effect macrominerals have on the acid-base status of the animal. Manipulation of dietary cation and anion content is commonly used as a tool in the dry period and during lactation to improve performance. A section on how the strong ion theory can be used to understand these effects is included. Many microminerals play a role in the body as cofactors of enzymes involved in controlling free radicals within the body and are vital to antioxidant capabilities. Those same minerals, when consumed in excess, can become pro-oxidants in the body, generating destructive free radicals. Complex interactions between minerals can compromise the effectiveness of a diet in promoting health and productivity of the cow. The objective of this review is to provide insight into some of these mechanisms.

**Article Title:** Magnesium and malic acid supplement for fibromyalgia.

**Date & Journal:** Medwave. 2019 May 28

- **INTRODUCTION:** Fibromyalgia is characterized by myalgia and a combination of different symptoms including pain, fatigue, insomnia, morning rigidity, depression and a reduction in every-day functioning. Its aetiology is not clear, but it has been suggested that deficiency in certain minerals such as magnesium may play a role both in the physiopathology and in contributing to the symptoms.
- **METHODS:** We searched in Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others. We extracted data from the systematic reviews, reanalyzed data of primary studies, conducted a meta-analysis and generated a summary of findings table using the GRADE approach.
- **RESULTS AND CONCLUSIONS:** We identified seven systematic reviews which included 11 primary studies of which one was a randomized trial. Our conclusion is that the use of magnesium and malic acid in patients with fibromyalgia makes little or no difference on pain and on depressive symptoms.

## ANTIOXIDANT VITAMIN AND MINERAL SUPPLEMENTS FOR SLOWING THE PROGRESSION OF AGE-RELATED MACULAR DEGENERATION.

### MAIN RESULTS:

We included 19 studies conducted in USA, Europe, China, and Australia. We judged the trials that contributed data to the review to be at low or unclear risk of bias. Nine studies compared multivitamins with placebo (7 studies) or no treatment (2 studies) in people with early and moderate AMD. The duration of supplementation and follow-up ranged from nine months to six years; one trial followed up beyond two years. Most evidence came from the Age-Related Eye Disease Study (AREDS) in the USA. People taking antioxidant vitamins were less likely to progress to late AMD (odds ratio (OR) 0.72, 95% confidence interval (CI) 0.58 to 0.90; 2445 participants; 3 RCTs; moderate-certainty evidence). In people with very early signs of AMD, who are at low risk of progression, this would mean that there would be approximately 4 fewer cases of progression to late AMD for every 1000 people taking vitamins (1 fewer to 6 fewer cases). In people at high risk of progression (i.e. people with moderate AMD) this would correspond to approximately 8 fewer cases of progression for every 100 people taking vitamins (3 fewer to 13 fewer). In one study of 1206 people, there was a lower risk of progression for both neovascular AMD (OR 0.62, 95% CI 0.47 to 0.82; moderate-certainty evidence) and geographic atrophy (OR 0.75, 95% CI 0.51 to 1.10; moderate-certainty evidence) and a lower risk of losing 3 or more lines of visual acuity (OR 0.77, 95% CI 0.62 to 0.96; 1791 participants; moderate-certainty evidence). Low-certainty evidence from one study of 110 people suggested higher quality of life scores (National Eye Institute Visual Function Questionnaire) in treated compared with the non-treated people after 24 months (mean difference (MD) 12.30, 95% CI 4.24 to 20.36). Six studies compared lutein (with or without zeaxanthin) with placebo. The duration of supplementation and follow-up ranged from six months to five years. Most evidence came from the AREDS2 study in the USA. People taking lutein or zeaxanthin may have similar or slightly reduced risk of progression to late AMD (RR 0.94, 95% CI 0.87 to 1.01; 6891 eyes; low-certainty evidence), neovascular AMD (RR 0.92, 95% CI 0.84 to 1.02; 6891 eyes; low-certainty evidence), and geographic atrophy (RR 0.92, 95% CI 0.80 to 1.05; 6891 eyes; low-certainty evidence). A similar risk of progression to visual loss of 15 or more letters was seen in the lutein and control groups (RR 0.98, 95% CI 0.91 to 1.05; 6656 eyes; low-certainty evidence). Quality of life (measured with Visual Function Questionnaire) was similar between groups in one study of 108 participants (MD 1.48, 95% -5.53 to 8.49, moderate-certainty evidence). One study, conducted in Australia, compared vitamin E with placebo. This study randomised 1204 people to vitamin E or placebo, and followed up for four years. Participants were enrolled from the general population; 19% had AMD. The number of late AMD events was low (N = 7) and the estimate of effect was uncertain (RR 1.36, 95% CI 0.31 to 6.05, very low-certainty evidence). There were no data on neovascular AMD or geographic atrophy. There was no evidence of any effect of treatment on visual loss (RR 1.04, 95% CI 0.74 to 1.47, low-certainty evidence). There were no data on quality of life. Five studies compared zinc with placebo. The duration of supplementation and follow-up ranged from six months to seven years. People taking zinc supplements may be less likely to progress to late AMD (OR 0.83, 95% CI 0.70 to 0.98; 3790 participants; 3 RCTs; low-certainty evidence), neovascular AMD (OR 0.76, 95% CI 0.62 to 0.93; 2442 participants; 1 RCT; moderate-certainty evidence), geographic atrophy (OR 0.84, 95% CI 0.64 to 1.10; 2442 participants; 1 RCT; moderate-certainty evidence), or visual loss (OR 0.87, 95% CI 0.75 to 1.00; 3791 participants; 2 RCTs; moderate-certainty evidence). There were no data reported on quality of life. Very low-certainty evidence was available on adverse effects because the included studies were underpowered and adverse effects inconsistently reported.

[Nutrients](#). 2017 Aug 9;9(8). pii: E849. doi: 10.3390/nu9080849.

## IMPACT OF FREQUENCY OF MULTI-VITAMIN/MULTI-MINERAL SUPPLEMENT INTAKE ON NUTRITIONAL ADEQUACY AND NUTRIENT DEFICIENCIES IN U.S. ADULTS.

Although >50% of U.S. adults use dietary supplements, little information is available on the impact of supplement use frequency on nutrient intakes and deficiencies. Based on nationally representative data in 10,698 adults from the National Health and Nutrition Examination Surveys (NHANES) 2009 to 2012, assessments were made of intakes from food alone versus food plus multi-vitamin/multi-mineral supplements (MVMS) of 17 nutrients with an Estimated Average Requirement (EAR) and a Tolerable Upper Intake Level (UL), and of the status of five nutrients with recognized biomarkers of deficiency. Compared to food alone, MVMS use at any frequency was associated with a lower prevalence of inadequacy ( $p < 0.01$ ) for 15/17 nutrients examined and an increased prevalence of intakes >UL for 7 nutrients, but the latter was  $\leq 4\%$  for any nutrient. Except for calcium, magnesium, and vitamin D, most frequent MVMS use ( $\geq 21$  days/30 days) virtually eliminated inadequacies of the nutrients examined, and was associated with significantly lower odds ratios of deficiency for the examined nutrient biomarkers except for iron. In conclusion, among U.S. adults, MVMS use is associated with decreased micronutrient inadequacies, intakes slightly exceeding the UL for a few nutrients, and a lower risk of nutrient deficiencies.

## HYPONATREMIA, BONE MINERAL DENSITY AND FALLS IN THE ELDERLY; RESULTS FROM AHAP STUDY.

**BACKGROUND:** Hyponatremia (HN) can be associated with osteoporosis, falls and bone fractures in the elderly. Recent researches demonstrated different results about the correlation of HN with bone mineral density and bone fractures.

**METHODS:** This analytic research came from the AHAP project in northern IRAN. All people aged 60 years and over were included in the study. Individuals with severe comorbidities and them who had concurrent conditions which could have impact on bone mineral densities (BMD) such as long-term use of steroids, calcium and/or vitamin D supplements, bisphosphonates, calcitonin, thiazides and hormonal medications were excluded.

**RESULTS:** One thousand and one hundred and thirteen older persons were entered in the study. More than 10 percent of the participants had HN (serum Na<sup>+</sup> level  $\leq$  137mEq/L). No significant difference has been observed between hyponatremic and nonhyponatremic individuals about their balance abilities; bone mineral density; incidence of falls and/or bone fracture during the previous 6 month; dependency in activities of daily living; and osteoporosis.

**CONCLUSION:** HN was not a prevalent problem in older adults who met the inclusion criteria of this research. No significant difference has been observed between HN and bone mineral density and falls in the elderly.

# TITLE: EFFECTS OF MAGNESIUM CITRATE, MAGNESIUM OXIDE AND MAGNESIUM SULFATE SUPPLEMENTATION ON ARTERIAL STIFFNESS IN HEALTHY OVERWEIGHT INDIVIDUALS: A STUDY PROTOCOL FOR A RANDOMIZED CONTROLLED TRIAL

## Abstract

Background: Arterial stiffness is closely related to the process of atherosclerosis, an independent cardiovascular risk factor, and predictive of future cardiovascular events and mortality. Recently, we showed that magnesium citrate supplementation results in a clinically relevant improvement of arterial stiffness. It remained unclear whether the observed effect was due to magnesium or citrate, and whether other magnesium compounds may have similar effects. Therefore, we aim to study the long-term effects of magnesium citrate, magnesium oxide and magnesium sulfate on arterial stiffness. In addition, we aim to investigate possible underlying mechanisms, including changes in blood pressure and changes in gut microbiota diversity.

Discussion: The present study is expected to provide evidence for the effects of different available magnesium formulations (organic and inorganic) on well-established cardiovascular risk markers, including arterial stiffness and blood pressure, as well as on the human gut microbiota. As such, the study may contribute to the primary prevention of cardiovascular disease in slightly obese, but otherwise healthy, individuals.

Schutten JC, Joris PJ, Mensink RP, et al. Effects of magnesium citrate, magnesium oxide and magnesium sulfate supplementation on arterial stiffness in healthy overweight individuals: a study protocol for a randomized controlled trial. *Trials*. 2019;20(1):295. Published 2019 May 28. doi:10.1186/s13063-019-3414-4

# TITLE: SELENIUM AND AUTOIMMUNE DISEASES: A REVIEW ARTICLE

## Abstract

**Background:** Selenium is an essential trace element with fundamental effects on human biology. Trace elements deficiency is not an uncommon finding in autoimmune diseases. This deficiency may be a consequence of autoimmune diseases or may contribute to their etiology. With regard to evidence showing the association between selenium deficiency and generation of reactive oxygen species and subsequent inflammation, reviewing the role of selenium in collagen vascular diseases could help researchers to devise strategies for managing these diseases.

**Objective:** The present study aimed to evaluate the role of selenium and autoimmune rheumatic diseases

**Study eligibility criteria:** All the studies on the use of selenium without any limitations in terms of the preparation method, administration route, or formulation process were included in the study. The exclusion criteria were: 1) Articles published in languages other than English, 2) Administration of chemical and hormonal drugs rather than selenium, 3) Investigation of the effects of selenium on the autoimmune problems in animal models, and 4) Insufficiency of the presented data or poor description of the applied methods. Furthermore, review articles, meta-analyses, expert opinions, editorial letters, case reports, consensus statements, and qualitative studies were excluded from the study.

Sahebari M, Rezaieyazdi Z, Khodashahi M. Selenium and Autoimmune Diseases: A Review Article. *Curr Rheumatol Rev.* 2019;15(2):123–134. doi: 10.2174/1573397114666181016112342

# TITLE: SELENOMETHIONINE RELIEVES INFLAMMATION IN THE CHICKEN TRACHEA CAUSED BY LPS THROUGH INHIBITING THE NF-KB PATHWAY

## Abstract

Selenomethionine is able to relieve the effect of inflammation in various tissues and organs. However, there are few studies about the influences of organic selenium resisting inflammation induced by LPS in chicken trachea. Therefore, the purpose of this experiment is to explore the organic selenium (selenomethionine) can raise immune function and relieve the LPS-induced inflammation of chicken trachea via inhibiting the NF- $\kappa$ B pathway. To investigate the mechanism of organic selenium on chicken trachea, the supplement of selenomethionine and/or LPS-induced chicken models were established. One hundred 46-week-old isa chickens were randomly divided into four groups (n = 25). The four groups were the control group, the selenomethionine group (Se group), the LPS-induced group (LPS group), and the Se and LPS interaction group (Se + LPS group). Then, the expressions of inflammatory factors (including induced nitric oxide synthase (iNOS), nuclear factor-kappa B(NF- $\kappa$ B), tumor necrosis factor (TNF- $\alpha$ ), cyclooxygenase-2 (COX-2), and prostaglandin E (PTGEs) synthase), inflammation-related cytokines (including interleukin (IL-2, IL-6, IL-8, IL-17) and immunoglobulin (IgA, IgM, IgY)), the marker of immune function (avian  $\beta$ -defensins (AvBD6, AvBD7)), heat shock proteins (including HSP60, HSP90), and selenoproteins (including Selo, Sels, Selm, Selh, Selu, Seli, SPS2, GPx1, GPx2, Dio1, Sepx1, Sep15, Sepp1, Txnrd1) were detected in our experiment. The above genes were significantly changed in different groups (p < 0.05). We can conclude that organic selenium can increase the function of immunity and the expression of selenoproteins, and mitigate the inflammation induced by LPS via suppression of the NF- $\kappa$ B pathway.

Shi X, Wang W, Zheng S, Zhang Q, Xu S. Selenomethionine relieves inflammation in the chicken trachea caused by LPS through inhibiting the NF- $\kappa$ B pathway. *Biol Trace Elem Res.* 2020;194(2):525–535. doi:10.1007/s12011-019-01789-1

# TITLE: SELENOMETHIONINE SUPPLEMENTATION REDUCES LESION BURDEN, IMPROVES VESSEL FUNCTION AND MODULATES THE INFLAMMATORY RESPONSE WITHIN THE SETTING OF ATHEROSCLEROSIS

## Abstract

Atherosclerosis is a chronic inflammatory disease of the vasculature characterised by the infiltration of activated neutrophils and macrophages at sites of damage within the vessel wall, which contributes to lesion formation and plaque progression. Selenomethionine (SeMet) is an organic form of selenium (Se), an essential trace element that functions in the regulation of the immune response by both bolstering the endogenous thioredoxin and glutathione antioxidant defence systems and by directly scavenging damaging oxidant species. This study evaluated the effect of dietary SeMet supplementation within a high fat diet fed apolipoprotein E deficient (ApoE<sup>-/-</sup>) mouse model of atherosclerosis. Dietary supplementation with SeMet (2 mg/kg) increased the tissue concentration of Se, and the expression and activity of glutathione peroxidase, compared to non-supplemented controls. Supplementation with SeMet significantly reduced atherosclerotic plaque formation in mouse aortae, resulted in a more stable lesion phenotype and improved vessel function. Concurrent with these results, SeMet supplementation decreased lesion accumulation of M1 inflammatory type macrophages, and decreased the extent of extracellular trap release from phorbol myristate acetate (PMA)-stimulated mouse bone marrow-derived cells. Importantly, these latter results were replicated within ex-vivo experiments on cultured neutrophils isolated from acute coronary syndrome patients, indicating the ability of SeMet to alter the acute inflammatory response within a clinically-relevant setting. Together, these data highlight the potential beneficial effect of SeMet supplementation as a therapeutic strategy for atherosclerosis.

Zhang Y, Cartland SP, Henriquez R, et al. Selenomethionine supplementation reduces lesion burden, improves vessel function and modulates the inflammatory response within the setting of atherosclerosis. *Redox Biol.* 2020;29:101409. doi:10.1016/j.redox.2019.101409

**ARTICLE TITLE: INVITED REVIEW: MINERAL ABSORPTION MECHANISMS, MINERAL INTERACTIONS THAT AFFECT ACID-BASE AND ANTIOXIDANT STATUS, AND DIET CONSIDERATIONS TO IMPROVE MINERAL STATUS.**

**DATE & JOURNAL: J DAIRY SCI. 2018 APR**

- ▶ Several minerals are required for life to exist. In animals, 7 elements (Ca, P, Mg, Na, K, Cl, and S) are required to be present in the diet in fairly large amounts (grams to tens of grams each day for the dairy cow) and are termed macrominerals. Several other elements are termed microminerals or trace minerals because they are required in much smaller amounts (milligrams to micrograms each day). In most cases the mineral in the diet must be absorbed across the gastrointestinal mucosa and enter the blood if it is to be of value to the animal. The bulk of this review discusses the paracellular and transcellular mechanisms used by the gastrointestinal tract to absorb each of the various minerals needed. Unfortunately, particularly in ruminants, interactions between minerals and other substances within the diet can occur within the digestive tract that impair mineral absorption. The attributes of organic or chelated minerals that might permit diet minerals to circumvent factors that inhibit absorption of more traditional inorganic forms of these minerals are discussed. Once absorbed, minerals are used in many ways. One focus of this review is the effect macrominerals have on the acid-base status of the animal. Manipulation of dietary cation and anion content is commonly used as a tool in the dry period and during lactation to improve performance. A section on how the strong ion theory can be used to understand these effects is included. Many microminerals play a role in the body as cofactors of enzymes involved in controlling free radicals within the body and are vital to antioxidant capabilities. Those same minerals, when consumed in excess, can become pro-oxidants in the body, generating destructive free radicals. Complex interactions between minerals can compromise the effectiveness of a diet in promoting health and productivity of the cow. The objective of this review is to provide insight into some of these mechanisms.