

A Comprehensive Review on Magnesium: Preventive and Therapeutic Applications in various inflammatory disorders

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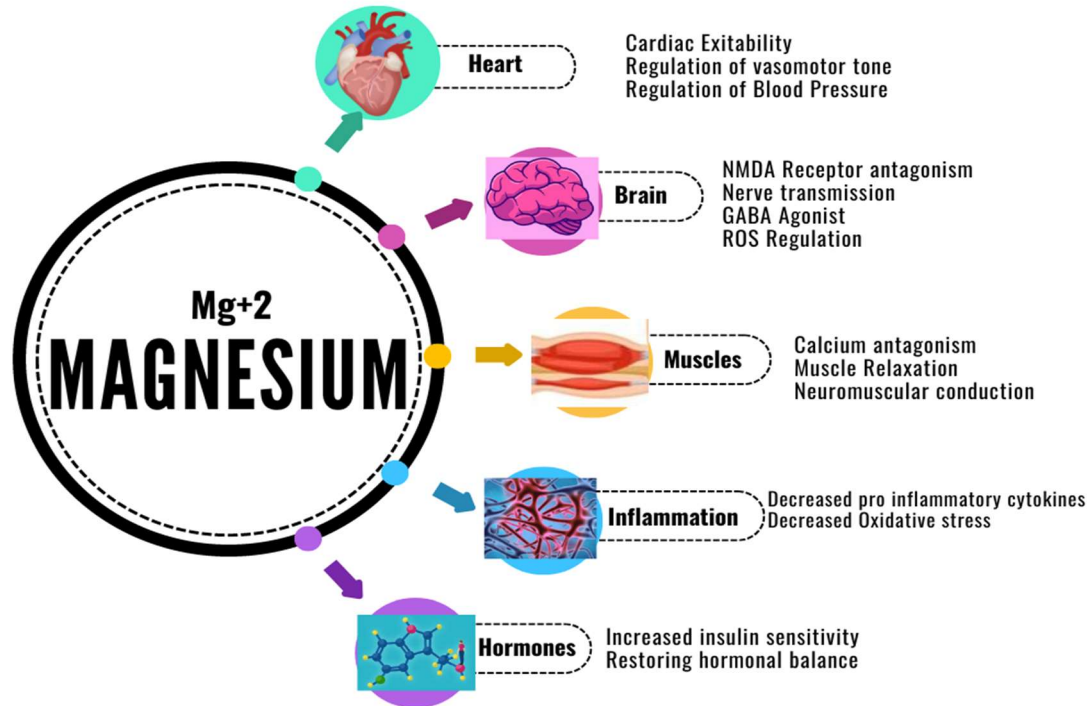
Abstract: Magnesium is an essential mineral crucial for numerous physiological processes, including enzymatic reactions, protein synthesis, cellular energy production, and nerve transmission. This comprehensive review examines magnesium's preventive and therapeutic roles in various inflammatory disorders. Magnesium deficiency has been linked to metabolic disorders such as obesity, insulin resistance, hypertension, and inflammation, while adequate magnesium intake or supplementation offers protective effects by improving metabolic parameters and reducing inflammation. In rheumatoid arthritis, magnesium alleviates joint pain and improves physical function by modulating oxidative stress and cytokine production. It inhibits cartilage degradation and enhances joint function in osteoarthritis. Magnesium's bronchodilatory properties benefit asthma and COPD patients by relaxing airway smooth muscles and reducing pro-inflammatory mediators. For polycystic ovarian syndrome, magnesium improves insulin sensitivity and hormonal balance. Inflammatory bowel diseases see benefits from magnesium's anti-inflammatory properties and its role in maintaining intestinal health. Type 2 diabetes management is enhanced through magnesium's involvement in glucose metabolism and insulin sensitivity. Magnesium also supports thyroid hormone metabolism, vascular health by regulating blood pressure and endothelial function, and liver health by reducing inflammation and supporting hepatic function. Furthermore, magnesium aids in managing gouty arthritis by regulating uric acid metabolism and alleviating symptoms. Despite the promise shown by magnesium supplementation in mitigating various inflammatory conditions, more large-scale, high-quality studies are required to fully elucidate its therapeutic potential and establish optimal supplementation strategies. This review underscores the need for increased awareness and promotion of magnesium supplementation within both medical and lay communities for its significant health benefits.

Keywords: Magnesium, Inflammation, Metabolic disorders, Rheumatic diseases, Respiratory diseases, Endocrine disorders, Gastrointestinal diseases, Cardiovascular diseases, Uric acid metabolism

Introduction:

Magnesium is an essential mineral that plays a crucial role in various physiological processes within the human body. It acts as a cofactor in numerous enzymatic reactions, including protein synthesis, cellular energy production and storage, reproduction, DNA and RNA synthesis, and stabilizing mitochondrial membranes. Moreover, magnesium is vital for nerve transmission, cardiac excitability, neuromuscular conduction, muscular

contraction, vasomotor tone, blood pressure regulation, and glucose and insulin metabolism(1). Given its multifaceted functions, magnesium has been the subject of extensive research investigating its potential



therapeutic applications, particularly in the context of inflammatory diseases. This review aims to provide a comprehensive analysis of the current understanding of the therapeutic potential of magnesium in the management of inflammatory conditions.

Fig 1: Role of Magnesium in various physiological processes.

Magnesium deficiency is linked to various metabolic disorders including obesity, insulin resistance, hypertension, and inflammation, while adequate dietary intake or supplementation of magnesium appears to offer protective effects against these conditions by improving metabolic parameters and attenuating inflammatory processes. In the context of inflammatory diseases, magnesium has demonstrated the ability to modulate the immune system and exert anti-inflammatory effect(Pelczyńska et al., 2022). For instance, magnesium has been shown to inhibit the production of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF- α) and interleukin-6, and promote the release of anti-inflammatory mediators, like interleukin-10(3,4). Furthermore, magnesium has been found to suppress the activation of Nuclear Factor- κ B, a key transcription factor that regulates the expression of genes involved in inflammatory response(3,4).

In recent years, there has been considerable interest in the therapeutic potential of magnesium in inflammatory disorders. Notwithstanding the intricate nature of inflammatory processes and the diverse functions of magnesium in cellular physiology, scholarly investigations have yielded knowledge regarding the possible advantages of magnesium supplementation in conjunction with therapy. This segment will examine the extant body of evidence concerning the therapeutic capabilities of magnesium in diverse inflammatory disorders like Rheumatoid Arthritis, Osteoarthritis, Asthma, COPD emphasizing both the encouraging discoveries and the obstacles that must be surmounted in order to implement it in a clinical setting that is truly effective.

Role of magnesium in the management of Rheumatoid arthritis: Rheumatoid Arthritis (RA) is an autoimmune disease characterized by chronic inflammation of the joints, leading to synovial hypertrophy, cartilage destruction, and bone erosion. Several studies have investigated the relationship between magnesium status and the severity of rheumatoid arthritis symptoms(5,6). Magnesium deficiency has been associated with increased oxidative stress, elevated levels of pro-inflammatory cytokines, and enhanced expression of adhesion molecules, all of which contribute to the pathogenesis of rheumatoid arthritis(7). Magnesium supplementation has been shown to alleviate joint pain, improve physical function, and reduce the need for anti-inflammatory medications in patients with rheumatoid arthritis(5). Despite the confirmed importance of magnesium in health maintenance, simple and cost-effective magnesium supplementation remains under recognized and underutilized, indicating a need for greater awareness and promotion within medical and lay communities(8).

Magnesium and Osteoarthritis: Osteoarthritis is a degenerative joint disease characterized by the gradual breakdown of articular cartilage, leading to pain, stiffness, and reduced mobility. Emerging evidence suggests that magnesium may play a crucial role in the prevention and management of osteoarthritis(5). Magnesium has been found to inhibit the activity of matrix metalloproteinases, which are enzymes responsible for the degradation of cartilage extracellular matrix. Furthermore, magnesium intake has been linked to an increase in Foxp3 T regulatory cells and IL-10 levels, suggesting an immunomodulatory effect that could help suppress inflammation and reduce arthritis severity(9). A growing number of studies have demonstrated that magnesium supplementation may alleviate osteoarthritis symptoms, improve joint function, and slow the progression of the disease.

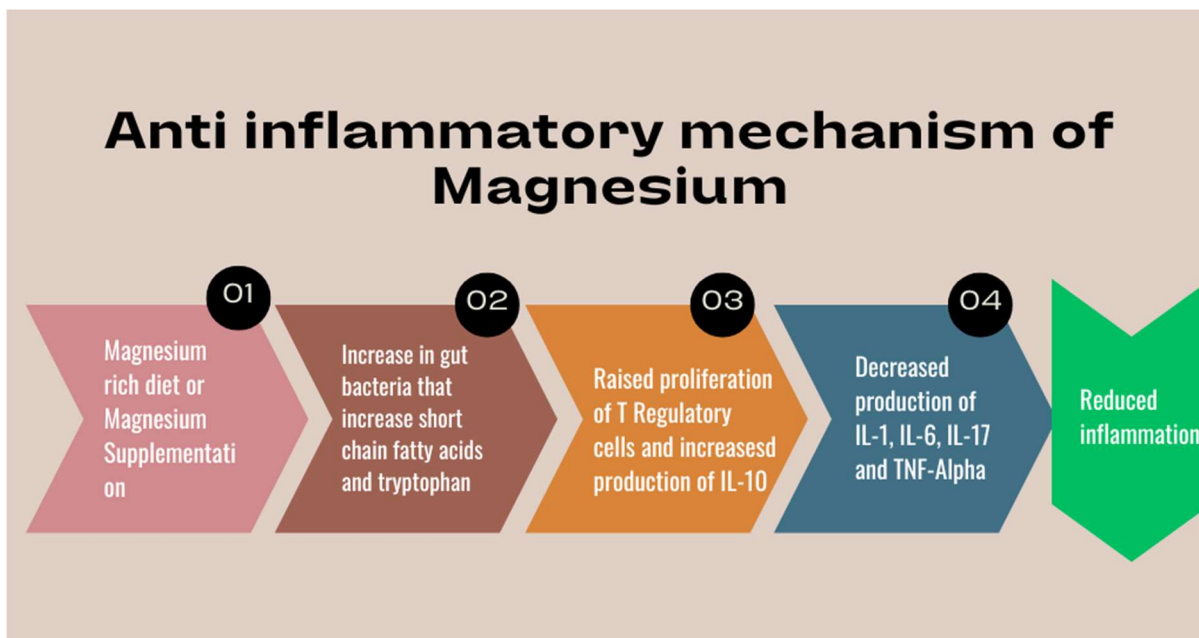


Fig 2: Magnesium’s mechanism in reducing inflammation

Magnesium and Respiratory Diseases: In addition to its benefits in the management of joint-related inflammatory conditions, magnesium has also emerged as a potential therapeutic agent in respiratory diseases characterized by inflammation, such as asthma and chronic obstructive pulmonary disease (COPD). Magnesium has been shown to possess bronchodilatory properties, which can help relax airway smooth muscle and improve lung function in patients with asthma and chronic obstructive pulmonary disease(10). Furthermore, magnesium has been found to suppress the release of pro-inflammatory mediators, such as histamine and leukotrienes, which

play a crucial role in the pathogenesis of these respiratory disorders(11). Several clinical studies have reported that intravenous or oral magnesium supplementation can effectively reduce the severity of asthma exacerbations, improve lung function, and decrease the need for rescue medications(12). The efficacy of nebulized magnesium in reducing hospitalization rates remains inconclusive. Some studies report small improvements in asthma severity scores but do not show a significant reduction in hospital admissions. However, nebulized magnesium may have a greater clinical effect in children with more severe exacerbations, highlighting the need for further research in this area(13,14).

Role of magnesium in the management of Polycystic ovarian syndrome: Polycystic ovarian syndrome (PCOS) is a complex endocrine disorder characterized by chronic low-grade inflammation, insulin resistance, and hormonal imbalances. Magnesium deficiency has been associated with increased inflammation, oxidative stress, and metabolic abnormalities in women with PCOS. Emerging evidence suggests that magnesium supplementation may have a beneficial impact on the management of PCOS by improving insulin sensitivity, reducing inflammation, and restoring hormonal balance(11). Magnesium supplementation can improve insulin sensitivity in women with PCOS. Magnesium acts as a cofactor for enzymes involved in insulin signaling, potentially explaining this effect. Improved insulin sensitivity can lead to better blood sugar control and potentially alleviate other PCOS symptoms(15). Some studies suggest magnesium could positively impact other PCOS-related issues, such as irregular menstrual cycles, hirsutism (excess hair growth), and acne. However, more research is needed to confirm these findings(16).

Magnesium and inflammatory bowel disease: Inflammatory bowel diseases, such as Crohn's disease and ulcerative colitis, are complex, chronic conditions characterized by persistent inflammation of the gastrointestinal tract. Emerging research has highlighted the potential therapeutic role of magnesium in the management of these inflammatory bowel diseases. Magnesium deficiency is commonly observed in individuals with inflammatory bowel diseases, likely due to malabsorption and increased intestinal losses. Magnesium has been shown to possess anti-inflammatory properties, with the ability to modulate pro-inflammatory cytokine production and reduce oxidative stress(2,7). Several studies have reported that magnesium supplementation may offer potential benefits in the treatment of inflammatory bowel diseases, including the ability to aid in reducing disease activity, improving intestinal barrier function, and alleviating symptoms in affected individuals. The underlying mechanisms by which magnesium may exert these beneficial effects on inflammatory bowel diseases are not fully elucidated, but may involve its role in regulating inflammatory pathways and supporting overall intestinal health. As such, further research is warranted to explore the therapeutic potential of magnesium as a complementary approach in the management of these complex gastrointestinal conditions.

Magnesium and type 2 diabetes mellitus: Type 2 diabetes mellitus is a chronic metabolic disorder characterized by insulin resistance and impaired glucose homeostasis. Emerging evidence suggests that magnesium plays a crucial role in the management of this condition(17). Magnesium deficiency is commonly observed in individuals with type 2 diabetes, and low magnesium levels have been associated with an increased risk of developing the disease. Magnesium is involved in insulin sensitivity, glucose metabolism, and the regulation of blood pressure(2). Both hyperglycemia and hyperinsulinemia may increase urinary magnesium excretion, and urinary magnesium excretion and fasting blood glucose have been found to be inversely related to serum magnesium levels. Thus, hyperglycemia decreases magnesium tubular reabsorption(18). One potential connection between magnesium deficiency and impaired insulin sensitivity is the presence of oxidative stress and inflammation, as elevated free radical levels are commonly seen in conditions like type 2 diabetes, hypertension, metabolic syndrome, and aging, all of which are also linked to magnesium imbalances(7). Some studies have reported that magnesium supplementation may improve glycemic control, enhance insulin sensitivity, and potentially reduce the risk of diabetic complications in individuals with type 2 diabetes(15).

Additionally, dietary and supplemental magnesium have been shown to improve insulin sensitivity and glycemic control, and may potentially reduce the risk of developing type 2 diabetes(19). However, the results from randomized controlled trials on the benefits of magnesium supplementation for glycemic control have been mixed, with some studies showing no significant effects(20).

Magnesium and thyroid disorders: Magnesium plays a crucial role in thyroid hormone metabolism and function. It is involved in the synthesis, secretion, and activation of thyroid hormones, as well as the regulation of the hypothalamic-pituitary-thyroid axis(21). Magnesium deficiency has been linked to an increased risk of thyroid disorders, including hypothyroidism and Hashimoto's thyroiditis. Conversely, magnesium supplementation has been reported to improve thyroid function and potentially alleviate symptoms in individuals with thyroid disorders(22). The mechanisms by which magnesium modulates thyroid function are not fully understood, but may involve its role in regulating oxidative stress, inflammation, and the enzyme activities involved in thyroid hormone metabolism. Further research is needed to clarify the therapeutic potential of magnesium in the management of various thyroid disorders.

Magnesium and vascular health: Magnesium plays a crucial role in regulating blood pressure and promoting vascular health through multiple mechanisms. Firstly, it modulates vascular tone by enhancing vasodilation and reducing vasoconstriction, thereby lowering peripheral vascular resistance. Secondly, magnesium maintains proper electrolyte balance by blocking sodium attachment to vascular smooth muscle cells, supporting normal vascular function. Additionally, it increases the production of vasodilating prostaglandin E and boosts nitric oxide levels, promoting vasodilation and improving blood flow dynamics(23). Magnesium also plays a role in improving endothelial function, which is essential for effective vascular tone regulation. Furthermore, its antioxidant properties help reduce inflammation and oxidative stress in the vasculature, contributing to the maintenance of optimal vascular function and mitigating hypertension risk factors(24). Studies have demonstrated the potential of magnesium supplementation in lowering blood pressure, particularly in individuals with hypertension or prehypertension, and it may also offer protective benefits against the development of cardiovascular diseases.

Magnesium in liver diseases: Magnesium deficiency is commonly observed in individuals with liver diseases, including non-alcoholic fatty liver disease (NAFLD), alcoholic liver disease, and cirrhosis. This is primarily due to decreased intestinal absorption, increased urinary excretion, and impaired hepatic magnesium metabolism(25). Magnesium deficiency can exacerbate liver damage, promote inflammation, and contribute to the development of complications associated with liver diseases. Conversely, magnesium supplementation has been shown to have potential therapeutic benefits in liver diseases, including the ability to improve liver function, reduce inflammation, and mitigate the risk of complications(26). The mechanisms by which magnesium exerts its protective effects in liver diseases are multifaceted and may involve its role in regulating oxidative stress, modulating immune function, and supporting cellular energy metabolism(Kisters, 2015). Furthermore, magnesium may also help to maintain proper mitochondrial function, which is crucial for hepatocyte survival and liver regeneration(28). However, the available evidence is still limited, and more research is needed to fully elucidate the therapeutic potential of magnesium in the management of various liver disorders.

Magnesium and gouty arthritis: Magnesium plays a crucial role in the regulation of uric acid metabolism and the prevention of gouty arthritis. Magnesium deficiency has been associated with an increased risk of hyperuricemia, the underlying cause of gouty arthritis. Magnesium helps to maintain the solubility of uric acid and facilitates its excretion through the kidneys(29,30). Additionally, magnesium exhibits anti-inflammatory properties, which can help to alleviate the symptoms of acute gouty attacks. Studies have shown that magnesium supplementation may be effective in reducing serum uric acid levels, preventing the development of gouty

arthritis, and managing the symptoms of existing gouty arthritis. The mechanisms by which magnesium exerts its protective effects in gouty arthritis include its ability to inhibit the formation of monosodium urate crystals, reduce inflammation, and potentially enhance the effectiveness of uric acid-lowering medication(31).

Summary:In conclusion, the available evidence suggests that magnesium plays a crucial role in the prevention and management of various inflammatory diseases. Magnesium deficiency has been linked to the development of metabolic disorders, cardiovascular diseases, liver diseases, and gouty arthritis, all of which are characterized by underlying inflammatory processes. Magnesium supplementation has shown promise in improving glycemic control, vascular function, liver health, and reducing uric acid levels, thereby mitigating the risk and severity of these inflammatory conditions. However, more large-scale, high-quality studies are still needed to fully elucidate the therapeutic potential of magnesium and establish optimal supplementation strategies for the management of these inflammatory disorders.

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