OptiMSM®

SULFUR:
THE FORGOTTEN NUTRIENT

Bergstrom® Nutrition

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When an element plays multiple supportive roles, it can often get lost behind some of its better-known constituents, no matter how critical it is. Such is the case with sulfur—the often forgotten nutrient. Perhaps this is because sulfur has historically been considered for its importance in soil and plant health, rather than for its importance in human health.

In human nutrition, sulfur is often only thought of as a constituent of well-known compounds like Methionine and Glutathione. This narrow view overlooks the multitude of physiological pathways in which sulfur plays a critical metabolic or structural role. Sulfur is an essential nutrient for the human body, and overlooking its role may come at the expense of health and wellness.

This summary brings sulfur to the front stage, giving it the recognition, it deserves as an essential nutrient, allowing us to remember the link sulfur has with so many other critical nutrients and pathways.

SULFUR

Sulfur is a major inorganic element with biological importance across species because of its integration into many molecules, including amino acids, proteins, enzymes, vitamins, and more[1]. Following calcium and phosphorus, sulfur is the third most abundant mineral in the human body, representing ~0.3% of total body mass. The fact that sulfur is the third most abundant mineral on its own, should not be overlooked. Third most abundant for a reason, and one that we can support with targeted nutrition. The majority of dietary sulfur is provided by the sulfur-containing amino acids (SAAs) methionine and cysteine, with an estimated requirement for young men of ~14 mg/day per kg body weight[2]. Dietary sulfur comes from proteins, and yet only 2 of the 20 amino acids normally present in proteins contain sulfur. One of these amino acids, methionine, cannot be synthesized by our bodies and must, therefore, be supplied by the diet. Cysteine, another sulfur-containing amino acid, and an important part of a large number of key metabolic intermediates essential for life can be synthesized by the human body, but the process requires a steady supply of sulfur[2].

Sulfur is found in a variety of foods, but dietary intakes have declined due to modern agricultural practices, thereby increasing interest in supplemental sources[3]. However, the majority of the research regarding sulfur intake refers to the sulfur-containing amino acids (SAAs) methionine, cysteine, and taurine as the primary dietary sources rather than sulfur itself[3]. This is because the amino acids methionine and cysteine provide most of the sulfur to meet the body's need, and methionine is most abundant in animal sources[3]. Additionally, glutathione (a natural intracellular antioxidant) provides a source of dietary sulfur and is found in fruits and vegetable[4].

Speculation has recently surfaced about methionine meeting dietary needs, causing us to wonder if sulfur needs are also being met through diet[5]. While most Western diets are adequate in methionine, in many parts of the world, including the U.S., the sulfur content of the soil is inadequate, affecting other sources, namely glutathione and methionine[6]. In addition to decreased levels in soils, diets that are predominantly vegan or vegetarian may also be low in methionine and therefore sulfur.

This is critical because of the role that the SAAs play in multiple physiological pathways. For example, they provide sulfates for glycosaminoglycans (GAG) and glutathione (GSH), which in turn play a key role in collagen and cartilage health. It should be noted that intake does not have to be deficient to create physiological concerns. It has been suggested that even when intake is marginally sufficient, the sulfur is directed towards the synthesis of proteins and other key metabolic intermediates that have critical roles in brain and organ function like GSH and S-Adenosyl Methionine (SAM) [5]. For all of these reasons above, we believe that the importance of sulfur in the human diet is being overlooked.

SULFUR AND HUMAN HEALTH

Sulfur has many functions in human health. It has a long history of use for dermatologic issues (for example; acne and overall skin appearance), wound healing and acute exposure to radioactive material[4]. Additional functions of sulfur include metal transport, free radical scavenging, regulation of gene expression, protein stabilization and synthesis, tissue integrity protection, enzyme functionality, DNA methylation and repair, remodeling of extracellular matrix components, lipid metabolism, and detoxification of xenobiotics/signaling molecules in plants and animals[7].

Two of the most critical roles sulfur plays in the body lie in connective tissue and the liver. Connective tissue like skin, tendons, and ligaments rely on sulfur for proper cross-linking and extracellular matrix proteins like GAGs and hyaluronic acids (HA). Disulfide bonds are key to the strong, yet flexible characteristics of connective tissue. ECM proteins, which are highly sulfonated, provide strength, cushion, and retain moisture (sulfonated means contains sulfur or semblance thereof). In the liver, sulfur plays two key roles. As a significant component of glutathione, the most prevalent antioxidant made by the body, sulfur helps the body react to oxidative stress and regain homeostasis. Sulfur is also a major component of Phase 2 detoxification in the liver. This process attaches sulfur to various toxic molecules, to neutralize these toxins and allow them to be excreted.

Does sulfur's involvement in so many aspects of health and well-being seem too good to be true? Considering how many pathways and metabolites it is part of, sulfur's multiple roles are well supported. For example, sulfur is part of many metabolites and pathways like glutathione, which in turn is part of antioxidant and other functions. Some of the additional metabolic and health roles sulfur has a hand in include: the n-3 and n-6 polyunsaturated fatty acids, minerals such as selenium, zinc, copper, magnesium, vitamins E and C, antioxidants such as the proanthocyanidins and lipoic acid, many of which are involved in the synthesis of prostaglandins and in the antioxidant cascade[5]. Even how the body responds to stress is impacted by a deficient or insufficient sulfur intake. Without sufficient amounts of sulfur in the diet, human health would be gravely impacted.

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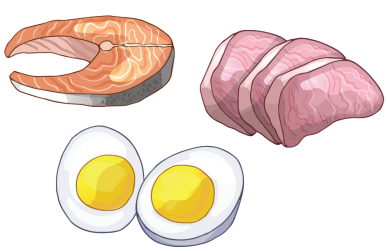
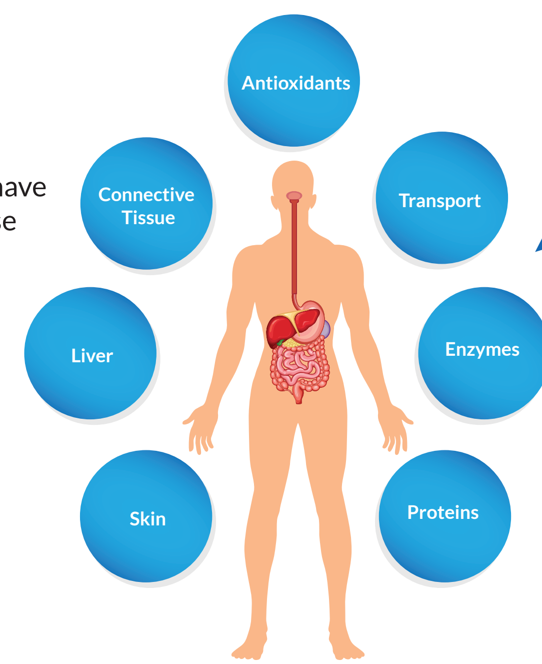
- Sulfur from soil is impacted by environmental and agricultural practices which can lead to low levels in the plants we eat



- Meat, fish, eggs and other animal foods have lower levels of sulfur in them due to these practices, which impacts human intake



- Humans that eat the meats and plant sources have a lower dietary intake of sulfur

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RECOMMENDED INTAKE OF SULFUR

Currently, there is no universal recommended dietary allowance (RDA) for sulfur. However, there are recommended daily intake amounts for sulfur-containing amino acids. For example, intake of the essential sulfur amino acid methionine (combined with cysteine) is recommended at 14 mg/kg BW. However, these recommendations rely on what might be considered inappropriate nitrogen balance studies as an indicator of "sulfur adequacy" and may grossly under-estimate the actual dietary need for sulfur[5]. It is important to point out that the recommendations reflect sulfur's perceived supportive role, and assume that an indirect measurement can adequately account for the body's broad sulfur requirements.

SOURCES OF SULFUR

Sulfur intake is directly correlational to protein intake source. Chicken, fish, and beef proteins contain about 5% of SAA. Dairy products contain around 4% because of casein's lower SAA content. If milk proteins are separated, whey protein contains more SAA than casein. Plant proteins average below 4%. The highest content of SAA is found in egg whites, comprising around 8% of SAA. Drinking water contains varying amounts of sulfur. Brussels sprouts, garlic, and onions typically have considerable amounts of sulfur, but this varies due to soil variability[5]

MSM AS A SOURCE OF SULFUR

Since directly determining sulfur needs is challenging, it is logical to focus on contributing sources of sulfur, especially when considering supplementation. Methylsulfonylmethane (MSM) is one such dietary and supplemental source. MSM is composed of sulfur, oxygen, and methyl groups[3]. Several studies demonstrate sulfur from MSM is incorporated into SAA, proteins, and various tissues [8,9]. MSM is naturally found in a variety of foods, such as milk, fruits, tomatoes, corn, coffee, and tea[10]. As stated earlier, changes in agriculture have also changed the sulfur content of the soil, impacting the natural levels of sulfur in a wide variety of foods. Because the amount found in foods can also significantly decrease during food processing and manufacturing, there has been increased interest in the usefulness or utility of supplementing the diet with MSM.

OptiMSM® is one such commercial MSM product sold in the marketplace. OptiMSM is a branded form of MSM manufactured by Bergstrom Nutrition and is Generally Recognized as Safe (GRAS)[11]. The only MSM produced in the U.S., OptiMSM is recognized for its safety and purity as the singular MSM produced utilizing a multi-stage distillation process to eliminate contaminants or impurities. A recent study proved rapid absorption of OptiMSM's sulfur incorporation into tissue proteins. The research showed OptiMSM provides the body an easily accessible pool of sulfur which spares the essential sulfur-containing amino acids (SAAs) methionine and cysteine from being metabolized for their sulfur. Earlier pharmacokinetic and metabolic research with oral MSM demonstrates it is rapidly absorbed, well distributed, and entirely excreted from the body[12]. In humans, serum MSM levels display the rise and fall pattern consistent with relatively rapid absorption from the stomach (within an hour), followed by slower elimination from the bloodstream (over one or two days).

Oral MSM appears to be absorbed in a dose-dependent manner without a direct dose-dependent impact on sulfate metabolism[13]. Its role as a sulfur donor and its ability to preserve SAAs explains the broad range of health benefits observed with OptiMSM.

MSM is sold on the commercial dietary supplement market and often utilized or promoted for joint health. Research has suggested that MSM, alone or along with glucosamine, reduces osteoarthritis (OA) related pain, swelling, and improves function. Results from several human studies demonstrate MSM's ability to improve function using validated quality of life scores[14-17]. This improved quality of life may be explained by findings of animal studies that have shown that sulfur-depleted joints affected by OA showed signs of decreased joint degeneration when supplemented with MSM, perhaps due to the abundance of sulfur found in MSM[18]. In a study performed on mice, pretreatment with MSM in doses of 200 and 400 mg/kg significantly decreased ethanol/HCl-induced increase in NF-κB mRNA expression, a key regulator of inflammation in gastric mucosa[19]. The decrease in the severity of ethanol/HCl-induced gastric mucosal injury upon supplementation of MSM is explained by the inhibition of oxidative stress and inflammation (antioxidant and anti-inflammatory activity), which may be of interest to prevent peptic ulcer disease as well as other gastrointestinal disorders[19]. MSM may also be effective in suppressing seasonal allergic rhinitis, interstitial cystitis, autoimmune diseases, and supporting cancer chemoprevention[20].

In vivo studies have shown it has an antioxidative effect by reducing the production of reactive oxygen and nitrogen species (RONS)[21]. MSM supplementation may reduce exercise-induced oxidative stress and muscle damage in humans. In untrained males, supplementation of 50 mg/kg/day reduced markers of oxidative stress after an acute bout of exercise, when compared to placebo[22], and also increased the total antioxidant capacity (TAC) and reduced creatine kinase (CK, a marker of muscle damage) and bilirubin levels (an antioxidant substrate, a surrogate marker of oxidative stress) after exhaustive exercise compared to placebo[23]. Another study reported reduced muscle soreness and fatigue and increased antioxidant activity in moderately-trained men with an increased MSM dose of 3.0 g/day[24]. Similarly, MSM has been shown to decrease inflammatory molecules in response to strenuous exercise[25]. When physically active men were supplemented with either placebo or MSM (3 g/day), MSM not only dampened IL-1β and IL-6 in response to an intense bout of exercise (suggesting that MSM works as an antioxidant) but also increased IL-10 levels in response to exercise[25]. As IL-10 is increased in response to exercise-induced muscle damage and acts as an anti-inflammatory mediator by downregulating proinflammatory cytokines IL-1β and TNF-α, supplementation with MSM reflects anti-inflammatory mechanisms[25]. Therefore, while the proposed mechanisms of action for MSM are most likely related to its anti-inflammatory[20] and antioxidant activity[21], its demonstrated ability for sulfur donation and the potential contribution to its mechanism should not be overlooked. Dosages of MSM between 1.5 and 6 g/day taken for several weeks to months have been used in human clinical studies with no significant adverse events reported[14,15,20]. While there is abundant research to support the role of MSM in human health[3,14-18,20-22,24-25], less has been reported on the specific role of MSM as a dietary source of sulfur and a vital component of the sulfur cycle.

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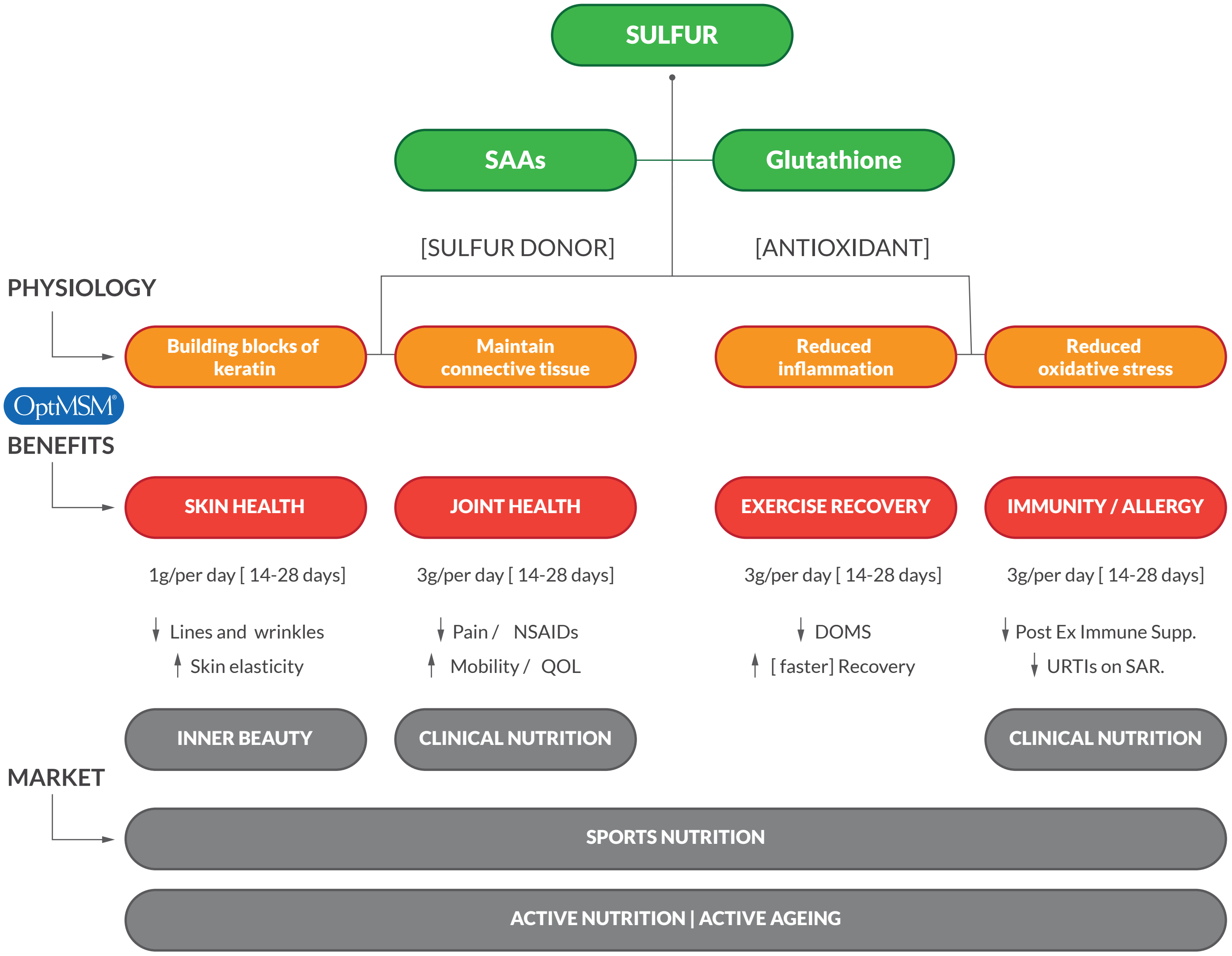
CONCLUSION

Considering the multitude of physiological functions that require sulfur, it is justified to give it credit as a nutrient in its own right, while maintaining recognition of it as part of MSM, SAA, Glutathione and other compounds. Furthermore, awareness that dietary intake may be marginal or insufficient warrants consideration of sulfur supplementation such as that provided by OptiMSM.



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REFERENCES

1. Komarnisky LA, Christopherson RJ, Basu TK. Sulfur: its clinical and toxicologic aspects. Nutrition (Burbank, Los Angeles County, Calif). 2003;19(1):54-61.
2. van de Poll MC, Dejong CH, Soeters PB. Adequate range for sulfur-containing amino acids and biomarkers for their excess: lessons from enteral and parenteral nutrition. The Journal of nutrition. 2006;136(6 Suppl):1694s-1700s.
3. Parcell S. Sulfur in human nutrition and applications in medicine. Alternative medicine review : a journal of clinical therapeutic. 2002;7(1):22-44.
4. Flagg EW, Coates RJ, Eley JW, et al. Dietary glutathione intake in humans and the relationship between intake and plasma total glutathione level. Nutrition and cancer. 1994;21(1):33-46.
5. Nimni ME, Han B, Cordoba F. Are we getting enough sulfur in our diet? Nutr Metab (Lond). 2007;4:24.
6. S. CJC. Sulfur Deficiency. Purdue University Department of Agronomy: Soil Fertility Update. 2017.
7. Palego L. Sulfur Metabolism and Sulfur-Containing Amino Acids: I- Molecular Effectors. Biochem Pharmacol. 2015;4(1).
8. Wong T, Bloomer RJ, Benjamin RL, Buddington RK. Small Intestinal Absorption of Methylsulfonylmethane (MSM) and Accumulation of the Sulfur Moiety in Selected Tissues of Mice. Nutrients. 2017;10(1).
9. Richmond VL. Incorporation of methylsulfonylmethane sulfur into guinea pig serum proteins. Life sciences. 1986;39(3):263-268.
10. Pearson TW, Dawson HJ, Lackey HB. Natural occurring levels of dimethyl sulfoxide in selected fruits, vegetables, grains, and beverages. Journal of agricultural and food chemistry. 1981;29(5):1089-1091.
11. Borzelleca J.F. SIG, Wallace K.B. . Dossier in Support of the Generally Recognized as Safe (GRAS) Status of Optimsm (Methylsulfonylmethane; MSM) as a Food Ingredient. Food and Drug Administration. 2007;Vero Beach, FL, USA.
12. Magnuson BA, Appleton J, Ames GB. Pharmacokinetics and distribution of [35S]methylsulfonylmethane following oral administration to rats. Journal of agricultural and food chemistry. 2007;55(3):1033-1038.
13. Kalman DS, Hewlings, S.J. A randomized prospective comparative pharmacokinetic and pharmacodynamic dose-escalation study of oral methylsulfonylmethane in healthy male volunteers. EC Nutrition. 2018; 13(11):684-695.
14. Usha PR, Naidu MU. Randomised, Double-Blind, Parallel, Placebo-Controlled Study of Oral Glucosamine, Methylsulfonyl methane and their Combination in Osteoarthritis. Clinical drug investigation. 2004;24(6):353-363.
15. Kim LS, Axelrod LJ, Howard P, Buratovich N, Waters RF. Efficacy of methylsulfonylmethane (MSM) in osteoarthritis pain of the knee: a pilot clinical trial. Osteoarthritis and cartilage. 2006;14(3):286-294.
16. Debbi EM, Agar G, Fichman G, et al. Efficacy of methylsulfonyl methane supplementation on osteoarthritis of the knee: a randomized controlled study. BMC complementary and alternative medicine. 2011;11:50.
17. Lubis AMT, Siagian C, Wonggokusuma E, Marsetyo AF, Setyohadi B. Comparison of Glucosamine-Chondroitin Sulfate with and without Methylsulfonylmethane in Grade I-II Knee Osteoarthritis: A Double Blind Randomized Controlled Trial. Acta medica Indonesiana. 2017;49(2):105-111.
18. Rizzo R, Grandolfo M, Godeas C, Jones KW, Vittur F. Calcium, sulfur, and zinc distribution in normal and arthritic articular equine cartilage: a synchrotron radiation-induced X-ray emission (SRIXE) study. The Journal of experimental zoology. 1995;273(1):82-86.
19. Amirshahrokhi K, Khalili AR. Methylsulfonylmethane is effective against gastric mucosal injury. European journal of pharmacology. 2017;811:240-248.
20. Butawan M, Benjamin RL, Bloomer RJ. Methylsulfonylmethane: Applications and Safety of a Novel Dietary Supplement. Nutrients. 2017;9(3).
21. Beilke MA, Collins-Lech C, Sohnle PG. Effects of dimethyl sulfoxide on the oxidative function of human neutrophils. The Journal of laboratory and clinical medicine. 1987;110(1):91-96.
22. Nakhostin-Roohi B, Barmaki S, Khoshkhahesh F, Bohlooli S. Effect of chronic supplementation with methylsulfonylmethane on oxidative stress following acute exercise in untrained healthy men. The Journal of pharmacy and pharmacology. 2011;63(10):1290-1294.
23. Barmaki S, Bohlooli S, Khoshkhahesh F, Nakhostin-Roohi B. Effect of methylsulfonylmethane supplementation on exercise - Induced muscle damage and total antioxidant capacity. The Journal of sports medicine and physical fitness. 2012;52(2):170-174.
24. Kalman DS, Feldman S, Scheinberg AR, Krieger DR, Bloomer RJ. Influence of methylsulfonylmethane on markers of exercise recovery and performance in healthy men: a pilot study. Journal of the International Society of Sports Nutrition. 2012;9(1):46.
25. van der Merwe M, Bloomer RJ. The Influence of Methylsulfonyl methane on Inflammation-Associated Cytokine Release before and following Strenuous Exercise. Journal of sports medicine (Hindawi Publishing Corporation). 2016;2016:7498359.