CONTRIBUTION OF SULFUROUS MINERAL WATERS TO DIETARY SULFUR INTAKE AND METABOLISM

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ABSTRACT

Sulfur is a non-metal macroelement with critical importance for the human body integrity and homeostasis. Sulfur-containing biomolecules exert important functions in redox balance maintenance, enzyme functionality, DNA methylation and repair, modification of extracellular matrix components, and xenobiotic metabolism.

Many studies related to the sulfur utilization and metabolism are focused on foods rich in organosulfur compounds that are associated with health benefits. It is believed that sulfur-containing mineral water also could have beneficial effects on the human health, but this knowledge is currently based on empirical data.

It could be suggested that the intake of sulfurous mineral waters as a part of the everyday diet would have measurable effects on the human metabolism.

Keywords: *sulfurous mineral water, hydrogen sulfide, health benefits, human metabolism*

INTRODUCTION

Scientific research on the factors influencing human health is limited mainly to the lifestyle, diet, physical activity, social status and unhealthy habits such as smoking and alcohol abuse. Water intake is considered mainly from the point of view of ensuring the water balance without sufficient consideration of the intake of macro- and microelements in regard to the mechanisms behind their biological effects.

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Mineral waters are a valuable natural resource, rich in essential dietary minerals, and may provide important portions of the recommended dietary intake of these minerals (1,2,3). Studies report that some types of mineral water can significantly contribute to the daily intake of calcium and magnesium and may have beneficial effects on bone metabolism, water-electrolyte balance and blood pressure (4,5,6,7,8).

Sulfur is one of the basic structural elements in the human body and its metabolism is extremely important in terms of the role that this element plays in many biochemical processes (9,10,11). It could be assumed that the intake of mineral waters containing hydrogen sulfide and soluble sulfides will have a measurable effect on human metabolism even at the level of intestinal absorption.

The purpose of this study is to provide a brief overview of the available literature sources devoted to the role of sulfur in human metabolism and nutritional sources of sulfur-containing biologically active compounds. Some aspects of the biological effects of sulfurous mineral waters (SMW) are also commented.

SULFUR IN HUMAN METABOLISM AND NUTRITION

Sulfur is one of the seven most abundant elements in the human body (9,12,13). It plays an essential role in various processes such as posttranslational modification of endogenous proteins, maintaining the integrity of extracellular matrix, synthesis of key

Table 1. Natural S-compounds, their sources and scientific data in support of their biological effects:

S-COMPOUND	SOURCES	BIOLOGICAL SIGNIFICANCE/ EFFECTS	REFERENCES
Methionine	Only diet (essential for humans and animals): meat and meat products, bread and other grain products, cheese	• **Required for the synthesis of body proteins;** • **Precursor of SAM for methylation reactions in:** - *Synthesis of phospholipids, epinephrine, creatine;* - *Histone methylation (control of transcription);* - *DNA methylation (epigenetic signal for gene expression and cell differentiation).* • **Ribosomal initiation of protein synthesis;** • **Precursor for the synthesis of Cys.**	(9,11,17-25)
Cysteine	1. Biosynthesis from Met 2. Diet: bread and other grain products, meat	• **Required for the synthesis of body proteins;** • **Included in the structure of GSH;** • **Precursor for the synthesis of taurine;** • **Extracellular reducing agent in the structure of plasma proteins;** • **Maintains the correct folding of proteins by disulfide bonds.**	(9,11,21,25-31)
Taurine	1. Diet is the primary source: meat, tuna, shrimps, milk 2. Biosynthesis from Met and Cys in liver	• **Neuromodulatory potential (agonist of GABA and glycine receptors in CNS);** • **Antioxidant and anti-inflammatory activity:** - *Neutralization of hypochlorous acid generated by myeloperoxidase in neutrophils;* - *Direct scavenging of reactive oxygen species;* - *Enhancing the expression and activities of antioxidant enzymes.* • **Bile acid conjugation;** • **Stimulates bile acid synthesis and reduces serum cholesterol levels;** • **Osmoregulation and membrane stabilization in skeletal muscles and myocardium.**	(32-40)

Glutathione	Biosynthesis from Cys, glutamate and glycine	• **Pivotal role in reducing oxidative stress and maintaining redox balance:** - *Direct scavenger of diverse oxidants;* - *Cofactor of antioxidant enzymes;* - *Neutralization of free radicals produced in Phase I of xenobiotic metabolism.* • **A compound for conjugation of xenobiotics in Phase II of xenobiotic metabolism;** • **Regeneration of vitamins C and E;** • **A potent chelator of heavy metals in brain and liver;** • **Protects mitochondrial DNA from oxidative damage;** • **Protects cells from aging processes;** • **Regulatory factor in the immune system;** • **Reservoir for Cys.**	(30,41-46)
Hydrogen sulfide	Metabolism of Met and Cys	• **Antioxidant and anti-inflammatory activities;** • **Neuromodulator in central and peripheral neuronal system;** • **Neuroprotective potential;** • **Smooth muscle relaxation by opening of ATP-sensitive K+ channels;** • **Protecting factor against mucosal injury.**	(7,47-60)
Organosulfur compounds from plants	Broccoli, cauliflower, cabbage, Brussel sprouts, watercress, garlic, onion	• **Anticancer activity:** - *Modulation of the xenobiotic-metabolizing enzymes (carcinogens are less active or more rapidly excreted);* - *Direct binding of toxins to the SH group.* • **Cardioprotective potential:** - *Reducing thromboxane formation by platelets;* - *Reducing blood cholesterol, triglyceride levels and systolic blood pressure.* • **Antibacterial action;** • **Anthelmintic action;** • **Protection against nephropathy and vascular complications in type 2 diabetes.**	(14,15,61-71)

sulfur-containing metabolites, detoxification processes, and many others. In the structure of sulfur-containing amino acids, it is related to the activity of enzymes containing SH-groups in its active center, as well as to the maintenance of native conformation of proteins by disulfide bonds. In addition, sulfur is a component required for sulfation reactions in detoxification processes.

The primary dietary source of sulfur are proteins and particularly the two sulfur-containing amino acids methionine (Met) and cysteine (Cys). It is believed that these amino acids, along with taurine, provide most of the sulfur amount needed for maintaining the body's homeostasis (11).

Apart from their role as building monomers for protein synthesis, the sulfur-containing amino acids Met and Cys are precursors for synthesis of important sulfur-containing metabolites such as gasotransmitter hydrogen sulfide (H_2S), the powerful redox buffer glutathione (GSH), the universal methyl donor S-adenosylmethionine (SAM), the amino acid taurine known to play various metabolic functions as well as the universal donor of sulfate and a mandatory co-substrate in sulfating reactions 3'-phosphoadenosyl 5'-phosphosulfate (PAPS).

A significant amount of nutritional studies has been devoted to organosulfur compounds in edible plants such as garlic and crucifers, suggesting that their anticancer and antioxidant activities are due to the potential of these compounds to induce or inhibit the expression of detoxification enzymes (14,15,16).

Some of the most significant biological effects of natural sulfur-containing compounds (S-compounds), supported by scientific data, are summarized in Table 1.

SULFUROUS MINERAL WATERS: WHAT DO WE KNOW AND WHAT LIES AHEAD?

Sulfur containing mineral waters have a long history of use in the treatment of various clinical conditions and some of their healing effects are attributed to possible antioxidant and anti-inflammatory activities (72-79) The application of SMW is recommended for treatment of various pathological conditions such as liver, gastrointestinal, urological and cardiovascular disorders (80-82). Also, SMW baths are applied for relief of atopic dermatitis, psoriasis, infected wounds (16,17,75,83-85), and degenerative osteoarthritis (74,86-89).

The mineral water from the Varna basin is classified as sulfurous because of its H_2S content (89). According to Vladeva and Kostadinov, 1996 (90) the mineral water from the most actively used boreholes in the Varna basin has a neutral pH and is defined as low-mineralized and appropriate for everyday use (90-92). Recently new data were obtained assessing the content of the biologically active compounds such as potassium, dissolved sulfides and free hydrogen sulfide (S2, SH-, H_2S), selenium and chromium (93).

The role of sulfurous active compounds contained in thermal waters, in particular, and the effects of drinking therapies involving H_2S-rich waters on the human metabolism are poorly studied. Knowledge about the healing properties of Varna mineral waters are based currently on empirical data describing their health effects when used as a daily drinking water in kidney and gastrointestinal disturbances.

Hydrogen Sulfide

It is considered that the beneficial effects of sulfur thermal therapies in the treatment of osteoarthritis are due to dissolved H_2S and soluble sulfides therein. In the recent years the interest in H_2S has increased because of data accumulation in support of its beneficial effects on the human health.

Like nitric oxide (NO) and carbon monoxide (CO), H_2S is a lipophilic molecule with signaling functions that passes freely through membrane structures and can be measured in blood serum and tissues where it is present in concentrations of the order of 50 μM (94). H_2S is produced in most tissues but was estimated in highest amounts in the brain, cardiovascular system, liver, and kidney (95). It is considered as a gasotransmitter with various biological effects, such as vasodilation, neurotransmission, angiogenesis, pro-and anti-inflammatory effects, and others (54,96,97). By its chemical nature, hydrogen sulfide is a good reducing agent, which determines its potential antioxidant role. In addition, hydrogen sulfide is a highly reactive molecule and readily reacts with active oxygen and nitrogen forms, thus neutralizing them (54,58). Another mechanism of its antioxidant action involves stimulating cysteine transport and glutathione synthesis (52). Effects of hydrogen sulfide on various signaling pathways have been reported, such as stimulation of ATP-dependent potassium channels (50), activation of adenylate cyclase cascades, influence of extracellular signaling kinase (ERK), and inhibition of inducible NO synthase (iNOS) under inflammatory stimuli (58,98,99).

In addition to its anti-inflammatory action, several pharmacological studies have demonstrated the protective role of endogenous and exogenous H_2S against ulcerogenesis, induced by nonsteroidal anti-inflammatory drugs (8,47,49,100). Based on these intriguing results, new hybrid H_2S-releasing drugs have been developed with safer gastrointestinal profile (8).

CONCLUSION

The pivotal importance of S-compounds in many complex biochemical and physiological mechanisms could be a basis for the interpretation of beneficial effects observed during SMW applications. It could be expected that the thermal waters rich in H_2S will have an impact on many metabolic processes commensurable with the beneficial effects of other, well-studied natural sources of sulfur-containing compounds.

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