

# The Practice of studying the Biochemical Mechanisms of Balneotherapy (sulfuric waters) Effectiveness in the World and Georgia as a Basis for the Development of Evidence-based Rehabilitation Medicine

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**Relevance of the issue** – In conditions of growing technological and pharmacological progress in modern medicine, the expansion of evidence-based knowledge and the introduction of standardized approaches, conventional medicine has increasingly taken its place and narrowed the role of complementary medicine. Accordingly, the role of physical medicine, physio-, balneo-, aqua-, peloidotherapies, which were quite popular in the last century, has declined by the beginning of the 21st century and, to some extent, has even become the subject of denigration by scientists. Their use became increasingly associated with the spa-wellness direction and gradually lost its medicinal value and acquired an aesthetic and health-improving role. The reason for this phenomenon was the paucity of evidence. However, neither earlier nor later studies denied the healing effect of complementary medicine, especially balneotherapy, they simply did not confirm their superior results. Why learning of therapeutic efficiency of apart physical and traditional medicine methods are chosen to analyze the comparative effects of classical treatment methods is a separate question. However, studies that confirm that complementary medicine methods, along with classical ones, achieve much faster and better results than when treating with classical methods alone, are really scarce, and funding is also less!

**Our goal** was to substantiate the role of balneotherapy, namely, the study of the main mechanisms of the impact of sulfur mineral waters on health, in order to increase healing capabilities

**Objectives:** 1. Attitude to the role of balneotherapy in rehabilitation treatment in the modern world and in Georgia 2. Search for materials studying the chemical mechanisms of the healing effect of sulfur waters; 3. Sorting and processing the found materials according to the degree of reliability 4. Drawing conclusions and developing recommendations for more effective use of this natural remedy for therapeutic and rehabilitation purposes in various diseases and planning new studies.

**Materials and methods** – Analysis of the current situation by the method of analogy; Meta-analysis of local and international articles using Meta-essentials.

**KEYWORDS:** Balneotherapy, Evidence-based medicine, Chemical mechanisms of sulfur healing waters

## Discussion

1. At this stage, the study of current practice in the world showed a rather variegated and different picture depending on the level of development of countries and medicine. The use of balneotherapy and, in general, traditional medicine is more typical for traditional countries (India, China, Arabia, Iran, Tibet, South American and African countries) and, accordingly, is either not regulated by the state, or their legislation is adapted to this reality and, representatives of certain knowledge, experience, reputation, school officially have permission to treat people with folk remedies. In certain cases, there is no regulation and does not prohibit self-treatment by the population with traditional medicine methods or treatment with a public healer. In developed countries, due to the intensification of migration processes in recent years, the sharp increase in the cost of modern medical technological methods, low funding and a decrease in trust (and therefore the flow of patients), integrative medicine centers are increasingly appearing. The interests of the pharmaceutical business and a certain hidden struggle with physical and traditional medicine, including balneotherapy, are understandable, however, human rights in healthcare and the obligation to ensure financial, territorial and informational access to medical services force us to think about offering those services that patients want and have the opportunity to do. Also, in the event of ineffectiveness or intolerability of using classical methods, we should be able to offer an alternative and not leave them without treatment due to exhaustion of resources. Taking into account these factors, in recent years, the appointment of complementary medicine methods has again become popular in leading countries of the world, not only integrative medicine centers have been created, but also separate offices and clinics of physical, electro-medicine, balneotherapy, naturotherapy, as well as departments with neurosurgical, neurological, traumatological, rheumatological, cardio-pulmonological centers and clinics. The increasingly widespread use of complementary medicine in parallel with classical treatment or in the period after active treatment has been associated with the development of rehabilitation medicine, the assessment of health as a person not only in terms of physical, mental and social well-being, but also in terms of functional capabilities! This has been accompanied by research to study the biochemical and biophysical mechanisms of the healing effect of various methods of physical and traditional medicine, including balneotherapy and mineral waters, which has been especially intensively carried out over the last 10-15 years.

The importance of rehabilitation treatment in our country has been recognized again since 2017, when, within the framework of the European Association commitment, the government and the Ministry of Health were tasked with working on a state strategy for rehabilitation treatment. As a result, at this stage, Georgia has a state program that defines and finances standards for outpatient rehabilitation after stroke and head and spinal cord

injuries. However, precisely because of the lack of evidence, our protocols recognize the effectiveness of only physical therapy and neurostimulation, while therapeutic massage, physiotherapy, and balneotherapy procedures are neither included nor financed. 2. Based on the given reality and the natural capabilities of the Tbilisi balneological resort (sulfur mineral thermal water), we searched for materials studying the chemical mechanisms of the healing effect of sulfur waters (Georgian sources – 1955-1995, foreign articles – 1995-2025). A total of 78 works were found, of which 46 were Georgian, 32 were foreign. 3. Taking into account modern requirements for the validity of research, 1 Georgian and 19 foreign works were considered valid, where the chemical reactions that develop when a sulfur molecule enters the body in various ways, its interaction with other chemical elements/compounds, and the impact of this interaction on health were studied and substantiated. 4. Analysis of the materials showed that the use of sulfur thermal waters for treatment all over the world, including in Georgia, dates back centuries. However, the study of the physicochemical mechanisms of its impact on various organs and systems did not occur until the second half of the last century, and even then, the issue was mainly limited to establishing a correlation between the use of sulfur waters and the dynamics of certain symptoms – that is, in fact, to the Clinical Scoring System (CSS). Georgian studies of the Soviet period are mainly based on the use of this method, however, the antioxidant and microcirculation-improving properties of hydrogen sulfide when it penetrates the skin are also emphasized in an attempt to explain the mechanisms. That is, studies conducted here and abroad in the second half of the last century confirmed that the main pathogenic mechanism of the healing effect is the improvement of microcirculation, although the separation of physical and chemical effects and the precise description of the chemical reactions that occur in the body under the influence of the main active molecule of sulfuric waters – hydrogen sulfide (H<sub>2</sub>S) – have only begun to be actively pursued in recent years.

For example, Jose Manuel Carbajo 1, Francisco Maraver in the work "Sulphurous Mineral Waters: New Applications for Health" reviewed the chemistry and actions of hydrogen sulphide in sulphurous mineral waters and its natural role in body physiology. This is followed by an update of available data on the impacts of exogenous hydrogen sulphide on the skin and internal cells and organs including new therapeutic possibilities of sulphurous mineral waters and their peloids. In this paper, they revisit the chemical properties of H<sub>2</sub>S in sulphurous mineral waters and describe how environmental factors such as pH, temperature, and the presence of oxygen can affect its concentrations and thus the final activity of the waters or their products. "Finally, we review the impacts of H<sub>2</sub>S on mammalian cells and organs, with special attention paid to the new therapeutic possibilities of sulphurous mineral waters and their peloids." – write the authors and indeed, the detailed chemistry of sulphur under different conditions, where ultimately H<sub>2</sub>S exhibits a therapeutic effect, is discussed. For example, the authors note that "the main functions of H<sub>2</sub>S are vasodilation and promoting new vessel growth. The proangiogenic effects of hydrogen sulphide have been associated with increased vascular endothelial growth factor (VEGF) expression and activation of its receptor. Hydrogen sulphide-based therapies have therapeutic potential in diseases such as renal ischemia-reperfusion disorders, hypertension, and hypertensive-associated heart disease." Interestingly, the effects of sulfur baths and sulfur-containing mud are transmitted through

the skin. Here too, there are new findings that explain what chemical changes occur when the skin is penetrated – "within the epidermis, H<sub>2</sub>S is transformed into sulphur, which may also interact with oxygen radicals in the deeper layers of the epidermis. Here, sulphur may be converted into pentathionic acid (H<sub>2</sub>S<sub>5</sub>O<sub>6</sub>), which could explain the antibacterial and antifungal properties of sulphurous mineral waters" – the article notes. Based on the works of other authors, the article also explains the physiological changes caused by the effect of sulphur mineral water on the skin: "Sulphurous mineral water may be absorbed through the skin causing vasodilation, analgesia, immune response inhibition, and keratolytic effects that reduce skin desquamation. The therapeutic action of sulphurous mineral waters is related mainly to sulphur's keratolytic, or peeling, effect. Sulphurous mineral water exerts beneficial anti-inflammatory, keratoplastic, and antipruritic effects. Its bactericidal and antifungal properties have determined its use for the treatment of infected leg ulcers, tinea versicolor, tinea corporis, and tinea capitis. It is also known that the topical application of H<sub>2</sub>S will also have an effect on the internal organs".

Sara Cacciapuoti, Maria A. Luciano and All in the article "The Role of Thermal Water in Chronic Skin Diseases Management: A review of the Literature" note that "Mineral waters (in particular salty and sulfur waters) are considered particularly useful for therapeutical applications in dermatology due to their keratolytic, regenerative, and antioxidant effects", although they also substantiate the chemical basis of the immunomodulatory and anti-inflammatory properties both by creating an unfavorable microenvironment for microbes and by inhibiting the proliferation of T-cells. "Among the minerals, sulfur can dose-dependently inhibit T-cell proliferation and cytokine production such as interleukin (IL)-2, IL-8, IL-23, IL-17, and interferon (IFN)- $\gamma$ . It also impairs keratinocyte cell growth and adhesion inhibiting mitogen-activated protein kinase signaling" – the authors note based on their analysis of the literature they have found and then discuss in detail the biochemical basis of the healing properties of sulfur thermal water in the treatment of chronic skin diseases.

In the article "Effect of Sulfur Baths on Antioxidative Defense Systems, Peroxide Concentrations and Lipid Levels in Patients with Degenerative Osteoarthritis", the authors Cem Ekmekcioglu, Wolfgang Marktl and others went further and used the measurement of indicators such as antioxidative defense systems, peroxide concentrations, and lipid levels in patients with degenerative osteoarthritis to study the mechanisms of the healing effect of sulfur thermal water. "After randomization one group of patients (n = 19) received sulfur baths during their stay at a health resort (sulfur group), whereas the other age-matched patient group served as controls (n = 19, control group), only receiving spa therapy. Total cholesterol levels, HDL, LDL, triglycerides and the antioxidative status, glutathione peroxidase, and superoxide dismutase (SOD) activities, and peroxide concentration, as an oxidative stress parameter, were evaluated at the beginning and end of therapy. A 17.2% decline in peroxide concentrations (p = 0.10, n.s.) and significant lower SOD activities (p < 0.001) were detected in the sulfur group at the end of the therapy. 40.45 mg/dl) and in the control group (from 197.63 +/- 34.66 mg/dl to 207.95 +/- 33.02 mg/dl). A similar significant group difference was found for LDL (p = 0.017), with a 5.9% reduction in the sulfur group and a 6.1% increase in the control group. Triglyceride concentrations were nonsignificantly reduced in both groups after 3 weeks at the health resort (sulfur group 11.2%, control group 20.2%). HDL values only



minimally changed in both groups. The results presented here suggest that a sulfur bath therapy could cause a reduction in oxidative stress, alterations of SOD activities, and a tendency towards improvement of lipid levels" – we read in their abstract.

It is interesting that the mechanisms of the therapeutic effect of sulfur water have been studied not only in skin and bone-joint diseases, but also in internal diseases. For example, the article "Thermal Water Applications in the Treatment of Upper Respiratory Tract Diseases: A Systematic Review and Meta-Analysis" by Sarah Keller, Volker König, Ralph Mösges is interesting, where the authors conclude that "Thermal water applications with radon or sulphur can be recommended as additional nonpharmacological treatment in upper airway diseases. Also in comparison to isotonic saline solution it shows significant improvements and should be investigated further", because by analyzing the data of 840 patients, they found significant improvement in Mucociliary clearance time, Nasal resistance and Nasal flow. "For the IgE parameter only sulphurous thermal water ( $P < 0.01$ ) and ISCS ( $P > 0.01$ ) were analyzable. Adverse events of minor character were only reported for sulphurous treatment (19/370)".

In the same and other works, new ideas were also expressed that  $H_2S$  plays the role of a signaling molecule and protein sulfhydration in various cytoprotective biochemical reactions of our body, contributing not only to the improvement of existing capillary blood circulation, but also to the formation of new microcirculation networks thanks to various complex mechanisms. We have seen that there are a number of studies that describe in detail all the chemical reactions, compounds, conditions, influencing factors that are associated with the anti-inflammatory, immunomodulatory, proliferative and other activities of the sulfur molecule and are included in the literature reviews that we have already familiarized ourselves with as ready-made conclusions.

## Conclusion

1. Meta-analysis of studies shows that the chemical mechanisms of the effect of sulfur waters on various tissues and organs have been studied, which explains the therapeutic effect and should be considered by the medical authorities and DMPs of Georgia MoH as evidence based method of treatment. 2. Further, deeper and more thorough studies are needed in different conditions and in different diseases. 3. It is necessary to develop evidence-based protocols and use sulfur healing waters more widely, correctly and purposefully. This, in some cases, will be a much easier, cheaper and more effective way to treat various diseases, which is so important in today's expensive healthcare conditions.

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