

Review

Unveiling the Role of Minerals and Trace Elements of Thermal Waters in Skin Health

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Abstract: The role of thermal spring waters (TSWs) in the treatment of dermatological disease has been described by several authors, as have their benefits in treating certain skin conditions, among which atopic dermatitis, contact dermatitis, seborrhea, seborrheic dermatitis, psoriasis, acne, rosacea, and sensitive skin can be cited. It has been postulated that the mechanisms involved include chemical, thermal, mechanical, and immunological effects, and the chemical composition of thermal water is crucial in its skin effects. Thus, in this review, the effects of the different anions, cations, trace elements, and other compounds present in TSW were investigated, showing that the benefits of TSW can be mainly linked to its content of chloride, sulfate, and bicarbonate anions; calcium, sodium, and magnesium cations; and, among its trace elements, boron, selenium, strontium, manganese, and zinc, which are those with greater influence. Other compounds such as SiO₂, sulfur anions, and CO₂ can also exert specific effects. As a whole, the specific effects can be summarized as anti-inflammatory, antioxidant, wound healing improvement, skin hydration, and skin barrier recovery activities.

Keywords: thermal spring water; mineral–medicinal water; skin care; trace elements; minerals



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1. Introduction

Thermal spring waters (TSWs), also called “mineral–medicinal waters”, “natural mineral waters”, or “spa waters” in some countries, are characterized by their mineral content and healing properties.

According to their mineral composition, TSWs can be classified as chloride, bicarbonate, sulfate, sulfide or sulfurous, carbon-dioxide-rich, and weakly mineralized waters. They can also contain soluble minerals such as Mg⁺², Ca⁺², Na⁺, silicates, SiO₂, etc., and trace minerals such as manganese, selenium, zinc, boron, etc. Taking into account the temperature, several classifications can be used (from a geological or medical point of view); the most widespread is based on the mean annual soil temperature (Ts) or the mean annual air temperature (Ta) as follows: hypothermal (temperature < Ts mean annual + 4 °C), mesothermal (temperature = Ts mean annual + 4 °C), and hyperthermal (temperature > Ts mean annual average + 4 °C). But for therapeutical purposes, the most useful TSW is that related to body temperature: hypothermal (<37 °C), mesothermal (=37 °C), and hyperthermal (>37 °C).

Balneology is defined by the ESPA (European Spas Association) as “the use of local natural resources such as natural healing water, peloids, gases, and climatic conditions for treatment, which is only available at medical spa facilities that are recognized and regulated by state authorities. The treatments offered at these facilities have been thoroughly researched and approved by scientists and medical doctors” [1]. Among the uses of thermal waters, rheumatological, respiratory, and dermatological diseases stand out, but TSWs are also used for well-being and relaxing purposes in so-called wellness centers. Additionally, TSWs are included in dermocosmetics as an excipient and active ingredient.

The role of TSW in the treatment of dermatological diseases has been described by several authors. Cacciapuoti et al. [2] described recent evidence of major dermatologic

diseases that are frequently treated by balneotherapy with a remarkable rate of success. The authors considered that balneotherapy offers several advantages, including the fact that no chemicals or potentially harmful drugs are needed; there are almost no side effects during and after treatment; and there is a low risk to the patient's general health and well-being. The effects of TSW were linked to its mineral and trace element contents [3].

The protocols for the treatment of dermatologic diseases vary depending on the thermal spa center, but spa techniques include bathing in thermal water (temperatures ranging from 30 to 35 °C) [4] and other techniques such as showers, pulverizations, and cataplasms [5]. Thermal mineral baths are sometimes combined with natural or artificial ultraviolet (UV) light to provide a synergistic effect of both treatments, a type of therapy known as balneo-phototherapy [4]. It has been suggested that the observed clinical efficacy of TSW may be related to the penetration of some water-soluble minerals into human skin. Minerals such as selenium, magnesium, sulfur, calcium, and zinc are directly related to the skin structure [6,7].

The mechanisms involved in thermal healing are complex and include chemical, thermal, mechanical, and immunological effects on different dermatologic diseases [4,8], such as atopic dermatitis, contact dermatitis, seborrhea, seborrheic dermatitis, psoriasis, and ichthyoses, as well as skin conditions such as sensitive skin, rosacea, and acne. All these mechanisms seem to be related to each other and act synergistically. Although the hormetic mechanism linked to temperature cannot be ignored, the chemical composition of thermal water is crucial in its dermatological effects.

Furthermore, several companies base their dermo-cosmetic claims on the mineralogical composition of the TSW included in their cosmetics, arguing that the effects on the skin are derived from the different minerals and trace elements, such as anti-irritant, soothing, softening, moisturizing, skin barrier recovery, and antioxidant effects, etc. A recent review of TSWs as an active ingredient in cosmetic formulations showed their beneficial effects on the skin due to their chemical composition [9].

The main objective of this work was to investigate the role of the minerals and chemical elements of TSWs in skin care, revealing the mechanisms of action involved and linking them to the different anions, cations, trace elements, and other compounds present in thermal waters (Figure 1).

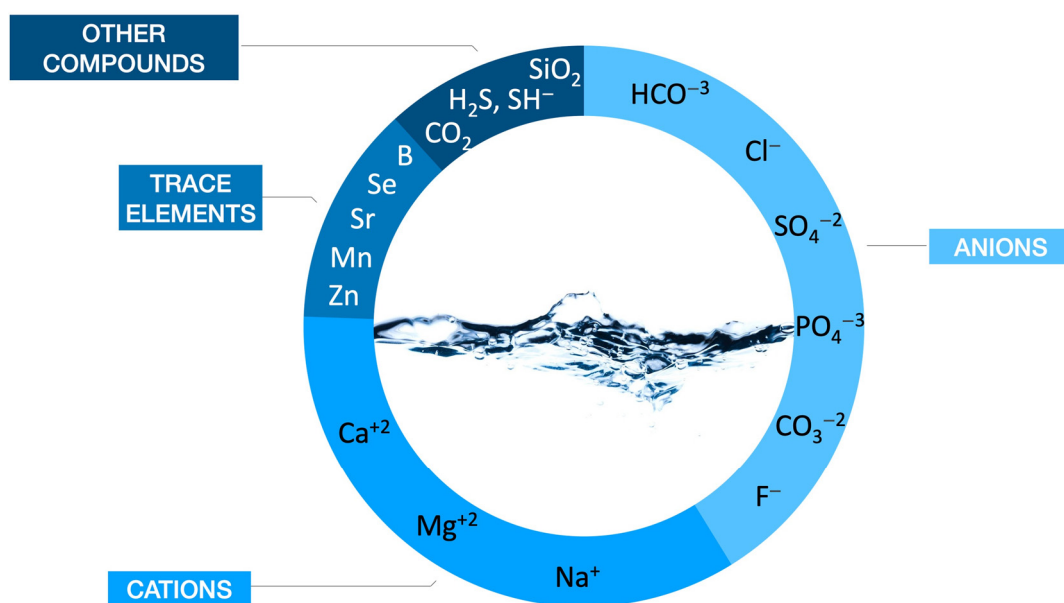


Figure 1. Main anions, cations, trace elements, and other compounds present in thermal spring waters.

For the non-systematic literature review, the PubMed, Web of Sciences, and Google Scholar databases were consulted; the search terms used were as follows: “thermal spring water”, “balneotherapy and dermatology”, “trace elements and skin health”, “chloride water and skin health”, “sulfate water and skin health”, “sulfur water and skin health”, “hydrogen carbonate water and skin health”, “silica water and skin health”, and “carbon-dioxide water and skin health”.

2. Minerals, Trace Elements, and Other Compounds of TSW in Skin Health

In TSW, the minerals are dissolved, and each spring water has its own “signature”. A spring water can contain several anions and cations, and they are classified by the predominant ion, but other ion contents must be taken into account. For example, a TSW can be chlorinated and also rich in sulfate and bicarbonate, and its name will be chloride, sulfate, bicarbonate, sodium, calcium, . . . thermal water. Despite this, each mineral or trace element can be responsible for a specific effect and, as has been mentioned before, the synergy between minerals/compounds (chemical effects) and mechanical, thermal, and immunological effects make thermal water a unique natural treatment.

In this review, the data collected were organized by minerals, trace elements, and other compounds. Table 1 summarizes the data, and, in the following subsections, selected research is discussed.

Table 1. Anions, cations, trace elements, and other compounds of thermal spring waters, effects, and specific activities.

Anions	TSW ¹	Type of Study	Observed Effects	Specific Activities	Reference
Chloride	Leopoldine (chloride, sodium, sulfate)	Clinical and in vitro studies	Decrease in the numbers of epidermal CD4+ and CD8+ T lymphocytes and CD1a+ Langerhans cells Decrease in the epidermal keratinocyte expression of intercellular adhesion molecule-1 and interleukin-8 and the dermal expression of CD4+ and CD8+ T lymphocyte	PASI score improvement	[10]
		In vivo study	Reduce erythema on inflammation induced by sodium lauryl sulfate	Anti-inflammatory	[11]
	Hae-Un-Dae (sodium chloride, sulfate-rich)	In vivo study	Reduction in severity of skin erythema and scales Decrease in serum levels of IL-4 and IL-5	Immunomodulatory effects	[12]
	Salies de Béarn (hypersaline mineral water, chloride, sodium, sulfate)	Clinical study	PASI score improvement	Pruritus reduction	[13]
		In vivo study	Anti-inflammatory on induced AD	Anti-inflammatory on AD	[14]
	La Solía (chloride, sodium, sulfate)	In vitro study	Attenuation of the induced levels of different pro-inflammatory mediators (IL-6, IL-1, TNF α , NF- κ B, and CCL1) at the level of gene expression	Anti-inflammatory	[15]
Sulfate	Uriage (sulfate, chloride, sodium, calcium)	In vitro study	Activation of taurine transporter, regulation of TauT expression, and sodium-dependent vitamin C transporter 1 expression	Protection against UVB irradiation	[16]
		In vitro study	Increased expression of claudin-4, claudin-6, filaggrin, and aquaporine-3	Skin hydration	[17]
		In vitro study	Reduction in the lipid peroxidation induced by the HX/XO stress and restoration of the reduction in skin claudin-6 expression	Protection against UVA + UVB radiation Antioxidant and DNA protection	[18]
		In vitro study	Counteracting the increase in biofilm formation of RT4 acneic strain of <i>Cutibacterium acnes</i> after exposure to epinephrine	Antibiofilm activity (prevent biofilm formation)	[19]

Table 1. Cont.

Anions	TSW ¹	Type of Study	Observed Effects	Specific Activities	Reference
Bicarbonate	Avène (bicarbonate, calcium, magnesium, silica)	In vitro study	Inhibition of histamine and prostaglandin D2 antigen-induced release, inhibition of histamine release triggered by substance P	Antiallergic and anti-inflammatory activity	[20]
		In vitro study	Reduction in percentage and area of dilated vessels after VIP stimulation, decrease in TNF- α release	Anti-inflammatory activity	[21]
		In vitro study	Inhibition of TNF- α -induced expression of E-selectin and intercellular adhesion molecule 1 (ICAM-1)	Anti-inflammatory effect on AD	[22]
		In vitro study	Protection of cell membranes, genomic DNA, and proteins from UVA-induced oxidative stress	Antioxidant activity	[23]
		In vitro study	Suppression of induction of inflammatory cytokine (IL-6) and the formation of ROS after UVB stimulation	Anti-inflammatory and antioxidant activity	[24]
		Clinical and inflammatory biomarkers study	Reduction in SCORAD and PASI, Reduction in IL-8 and <i>Staphylococcus aureus</i> colonization	Anti-inflammatory properties Preventing growth bacteria	[25]
		Clinical study	Reduction in scaling on patients treated with retinoic acid	Soothing properties	[26]
		Clinical trials	Decreased erythema Pain reduction Pruritus reduction after phototherapy	Soothing properties Anti-irritant activity	[27,28]
		Ex vivo study and clinical study	Maintaining mechanical properties and hydration after a chemical peeling Redness reduction Skin sensitivity reduction	Protection against dehydration Anti-irritant activity	[29]
		In vivo study	Decreasing inflammation	Anti-inflammatory activity	[30]
	Comano (bicarbonate, calcium)	In vitro studies	Interference with vascular endothelial growth factor-A isoform expression and secretion by psoriatic keratinocytes Reduction in intracellular levels and secretion rates of IL-6 Downregulation of intracellular levels of TNF- α and also reduction in the intracellular levels and secretion rates of IL-8 Interference with TNF- α expression and IL-8 production and secretion	Anti-inflammatory activity	[31–33]

Table 1. Cont.

Anions	TSW ¹	Type of Study	Observed Effects	Specific Activities	Reference
		In vitro study	Increase in keratinocyte proliferation and migration and favorable modulation of regenerated collagen and elastic fibers in the dermis	Skin regeneration	[34]
		Ex-vivo study	Reduction in overall cell infiltration, evidence of fibroblasts, stimulation of cell proliferation, and collagen and elastic fiber regeneration	Skin regeneration	[35]
		Observational prospective study	Improvement in QoL and SAPASI	Psoriasis improvement	[36]
		Controlled, randomized, double-blind clinical study	Reduction in PASI and hydration improvement	Psoriasis improvement	[37]
		Observational study	Reduction in AD severity Improvement in QoL	Anti-inflammatory on AD	[38]
	Nitrodi (bicarbonate, silica)	In vitro study	Induction of alpha-SMA expression in dermal fibroblasts, promoting transition to myofibroblast-protein ECM deposition	Wound healing improvement	[39]
Carbonate	Nagano hot spring water (carbonate-rich)	In vitro study	Enhancement of wound healing process, increasing vessel density and reducing inflammatory cells in the granulation tissue of the wound area	Wound healing improvement	[40]
Cations	TSW	Type of Study	Observed Effects	Specific Activities	Reference
Calcium	La Roche-Posay (bicarbonate, calcium, magnesium, strontium, selenium)	Clinical study	Reduction in the inflammatory aspect of scars, relieving itching, facilitating the removal of the crusts, and preventing infections	Wound healing improvement	[41]
Sodium	Yuda hot spring (alkaline spring water)	In vivo study	Wound healing acceleration	Wound healing improvement	[42]
	Sungai Lalang (sodium-rich spring water)	Clinical study	Enhancement of stratum corneum hydration Reduction in local inflammatory symptoms Improvement in QoL	Acne symptom improvement	[43]
Magnesium	Dead Sea (hypersaline, calcium, magnesium-rich)		Improvement in skin barrier function, increase in skin hydration, and reduction in inflammation	Atopic dermatitis improvement	[44]

Table 1. Cont.

Trace Elements	TSW	Type of Study	Observed Effects	Specific Activities	Reference
Selenium	La Roche-Posay (bicarbonate, calcium, magnesium, strontium, selenium)	In vitro study	Protective effect against oxidative stress induced by UVB light	Antioxidant	[45]
		In vitro study	Selenium-glutathione peroxidase and superoxide dismutase activity higher than control	Antioxidant	[46]
		In vitro study	Better resistance with better cell survival and a reduction in IL-1 α cytokine release compared to control after exposure to increasing UVB doses	Antioxidant	[47]
		Ex-vivo study	Inhibitory effect for TNF- α	Anti-inflammatory	[48]
		In vitro study	Reduction in IL-1 α release in irradiated keratinocytes, increase in selenium-dependent glutathione peroxidase activity, and decrease in the production of lipoperoxides after UV irradiation	Antioxidant	[49]
		In vitro study	Reduction in IL-6 levels and the formation of ROS after UVB irradiation	Antioxidant	[24]
		Clinical study	Reduction in PASI score	Psoriasis improvement	[50]
Strontium	La Roche-Posay (bicarbonate, calcium, magnesium, strontium, selenium)	Ex-vivo study	Inhibitory effect for TNF- α Decrease in IL-6 production	Anti-inflammatory	[48]
Manganese	Saint-Gervais (boron- and manganese-rich)	In vitro	Acceleration of wound closure	Wound healing improvement	[51]
Boron	Saint-Gervais (boron- and manganese-rich)	In vitro	Promotion of keratinocytes migration	Wound healing improvement	[51]
Zinc	Avène (bicarbonate, calcium, magnesium, silica)	Clinical study	Reduction in pruritus after a photodynamic therapy procedure	Anti-inflammatory in post-photodynamic therapy	[27]

Table 1. Cont.

Other Compounds	TSW	Type of Study	Observed Effects	Specific Activities	Reference
Silica	Sao Pedro do Sul (bicarbonate, silica-rich)	Clinical study	Reduction in skin irritation and promotion of skin barrier recovery	Anti-inflammatory Skin barrier recovery	[52]
	Monfortinho (bicarbonate, silica-rich)	Clinical study	Improvement in skin hydration	Skin hydration improvement in psoriasis and eczema	[53]
		In vitro	Skin barrier recovery	Skin barrier improvement	[53]
		In vitro	Reduction in cell metabolism and proliferation of keratinocytes and macrophages	Improvement of hyperkeratotic conditions	[54]
	Blue Lagoon (silica-rich)	Clinical study	Reduction in PASI	Psoriasis improvement	[55,56]
Sulfur ²	La Bourbule (chloride, sodium, sulfurous water)	Observational study	Wound healing improvement by controlling keratinocyte physiology	Wound healing improvement	[57]
	Name not mentioned (bicarbonate, sulfurous water)		Reduction in PASI score Increase in stratum corneum hydration Improvement in itching and skin dryness	Psoriasis improvement Skin hydration improvement	[58]
	Molitg-Les-Bains (sodium sulfurous water)		Reduction in PASI score DLQI improvement VAS pruritus score improvement	Psoriasis improvement	[59]
Carbon-dioxide	CO ₂ -enriched water	In vivo	Improvement of blood flow and increase in plasma level of NO in diabetic rats	Improvement blood flow	[60]

¹ Chemical profile. ² (SH⁻; H₂S). AD: atopic dermatitis. DLQI: Dermatology Life Quality Index. HX/XO: xanthine oxidase/hypoxanthine free radical. PASI: Psoriasis Area Severity Index. QoL: quality of life. SAPASI: self-administered Psoriasis Area Severity Index. VAS pruritus score: Visual Analogue Scale pruritus score.

2.1. Anions

As mentioned before, TSWs are classified by their predominant ion. In this subsection, the effects of the most important anions are discussed, taking into account the fact that spring waters are endowed with a “physical–chemical dynamism”, in which most of their ions are interrelated, and part of that balance is lost when the water is carried away from the spring.

Tarnowska et al. [61,62] performed several studies and reviews on the skin permeation of ions and the mechanisms involved. In short, the skin absorption of ionic species is much more complex than just passive diffusion due to the complexity of the skin structure being organized in layers, with the *stratum corneum* being a simple passive barrier (high content of lipids) and with the viable epidermis and dermis being characterized by a higher water content (up to 70%) where the facilitation of ion transport operates. Therefore, various types of skin–ion interactions are possible. Furthermore, based on the Hofmeister series of anion classifications (F^- , Cl^- , Br^- , NO_3^- , I^- , SCN^- , ClO_4^-), which is based on their interactions with macromolecules in aqueous solutions, and the concept of “salting in” or “salting out” properties, the authors postulated that similar effects can be expected within the *stratum corneum*, such that the adsorption/absorption of anions into/onto the hydrophobic *stratum corneum* and the protein-facilitated anion transport depend on the nature of the anions in the same order as the Hofmeister series. Several transport pathways are involved, such as chloride channels (CIC), calcium-activated chloride channels (CaCC), volume-regulated anion channels (VRAC), etc.

2.1.1. Chloride

The chloride anion, along with the sodium cation, is essential for the water balance of tissues. Furthermore, it has been shown that the osmotic forces of water with sodium chloride play an important role in the loss of transepidermal water, favoring the skin’s renewal capacity and the recovery of its barrier function [63].

The anti-inflammatory potential of sodium chloride waters has been demonstrated in different studies. Tsourelis-Nikita et al. [10] studied the effects of bathing in Leopoldine water (salso-sulfate thermal water) in psoriatic patients, showing a decrease in PASI after 4 weeks of treatment. Further, in vivo studies showed the anti-inflammatory effects of Leopoldine mineral water on human skin affected by modest inflammatory reactions caused by the direct application of the chemical irritant sodium lauryl sulfate (SLS) [11].

Hae-Un-Dae TSW sodium chloride, sulfate-rich spring water showed immunomodulatory effects. A murine model of imiquimod-induced psoriasis-like skin inflammation was used to test HUOTSW compared to distilled water (DW); mice were bathed in HUOTSW for 5 min a day for 2 weeks, and the severity of skin erythema and scales were evaluated, and serum levels of inflammatory cytokines were measured. The results showed that the HUOTSW group had faster improvement in terms of skin erythema and scales than the DW bathing group. A substantial reduction was observed in the lesional mRNA levels of IL-17A and IL-23 in the mineral water group. Serum levels of IL-4 and IL-5 were significantly decreased in the HUOTSW group but not in the DW group, and normalized T-cell proportions were observed after bathing [12].

A clinical study compared bathing in hypersaline mineral water (chloride: 152,140 mg/L, sodium: 102,630 mg/L) (A group) with 311 nm UVB phototherapy (B group) and a combination of both mineral water and phototherapy (C group) in patients with stable psoriasis vulgaris of more than 1 year’s duration and a PASI score of more than 10. After a regimen of 3 weeks with 5 days of treatment a week, the results showed that groups B and C were similar (reduction in PASI of –64% and –55%, respectively), and for group A, the change in PASI was –29%, indicating less efficacy than in groups B and C [13]. In any case, the treatment of psoriasis with hypersaline water has proven to be an effective alternative for patients in whom phototherapy is contraindicated.

An in vitro study compared standardized water and highly mineralized natural mineral spring water (HMW) of a chloride-sodium-sulfate type to test the effects on atopic dermatitis-like inflammation in hairless mice. The results showed that the 100% pure

(PHMW) and 10% diluted (DHMW) HMW significantly decreased the scratching behavior; the serum IgE level was also significantly decreased in the DHMW group as compared to the control group. Additionally, the level of inflammatory cytokines in the serum, such as interleukin (IL)-1 β , IL-13, and tumor necrosis factor- α , were significantly inhibited in the PHMW and DHMW groups. Furthermore, the total serum reactive oxygen species (ROS) level was significantly decreased in the PHMW group, and the serum malondialdehyde level in the PHMW group was lower than in the control group [14]. As HMW contains other ions and trace elements (Ca, Mg, Sr, and Mn), the effects cannot be attributed solely to the presence of the major ions; the minor ones and trace elements must also be considered.

Recently, a combination of La Solia TSW (chloride-sodium-sulfate-type, rich in calcium and magnesium), and a diatom extract (species found in the sources of this spring water) demonstrated anti-inflammatory properties. The mixture was assessed during pro-inflammatory stimulation in an in vitro system mimicking keratinocytes under skin irritation. The mentioned ingredient effectively attenuated the induced levels of different pro-inflammatory mediators (IL-6, IL-1, TNF α , NF- κ B, and CCL1) at the level of gene expression. The authors highlighted the potential benefits of this combination in skin irritation, and it could therefore be useful for sensitive skin care [15].

2.1.2. Sulfate

Costantino et al. [64] revised the medical use of sulfate mineral waters, including in treating skin disorders, citing the expression of Com   (expert on thermalism in dermatology), who coined the term “mineral eudermic water” to identify waters able to provide an organism with all the factors necessary for nutritional, eutrophic, and rehydrating action. In this review, the authors highlighted the effects of sulfate mineral water stimulating skin turnover and toxin removal, and several types were cited as sodium-chloride sulfate, magnesium-sulfate, carbonate-sulfate alkaline, carbonate-sulfate-calcium, and bicarbonate-sulfate-rich mineral waters.

One of the most studied sulfate-rich spring waters is Uriage thermal spring water (Uriage TSW), which is also rich in chloride, sodium, calcium, magnesium, silica, and trace elements. Verdy et al. [26] investigated the effect of Uriage TSW on skin protection by evaluating taurine transporter (TauT) and sodium-dependent vitamin C transporter 1 (SVCT1) expressions in normal human keratinocytes at a basal level and under stressful conditions (irradiation UVB). Keratinocytes were incubated with Uriage TSW at increasing concentrations after irradiating the cells with UVB, and the effect of UVB was slightly reduced after 24 h, and a high level of TauT expression was maintained after 72 h. The results showed that the Uriage TSW slightly reduced the effect of UVB after 24 h of incubation but permitted the maintenance of a high level of TauT expression after 72 h of incubation. The authors suggested that Uriage TSW could act to efficiently protect the skin from dehydration through its effect on TauT and SVCT1 expression and additionally permit a more efficient taurine and vitamin C supply to the epidermis in order to protect it from other aggressions such as oxidant stress. In addition, the UTSW could also be useful for the skin in fighting against situations such as dehydration, UVB irradiation, and aging.

Other in vitro studies performed by Joly et al. [17,18] investigated the effects of a cosmetics cream formulated with Uriage TSW. In the first study, the Uriage TSW cream showed a very good effect on *stratum corneum* reparation, and the filaggrin labelling and AQP-3 labelling were equivalent to that observed in control explants. The results showed that this formulation was also able to enhance the expression of claudin-4 and claudin-6 in the delipidated explants, and the authors concluded that the use of Uriage TSW in cosmetic formulations contributes to increasing their efficacy in treating dry skin conditions. The second study focused on an evaluation of the protective effects of Uriage TSW on skin barrier function, investigating its antioxidant properties through TBARS and SOD activity assays. The Uriage TSW was able to reduce the lipid peroxidation induced by HX/XO (xanthine oxidase (XO)/hypoxanthine (HX) free radical) stress and also to restore the reduction in skin claudin-6 expression when skin explants were exposed to UVA +

UVB radiation. These results demonstrated the antioxidant and DNA-protecting effect of Uriage TSW.

Later studies investigated UTSW in *C. acnes* biofilm formation. One study evaluated the effect of catecholamines on acneic (RT4) and non-acneic (RT6) strains of *C. acnes* in a medium with Uriage TSW compared with sterile physiological water. On strain RT4, grown in a sterile physiological medium, the biofilm formation was studied after exposure to epinephrine; the results showed a significantly lower basal biofilm production with Uriage TSW compared to a medium containing sterile physiological water [19].

2.1.3. Bicarbonate

Balneotherapy in bicarbonate-sulfate-rich spring water improves the healing of patients with contact dermatitis due to their moisturizing and softening action related to the buffer capacity of the bicarbonate anion [65]. Additionally, several studies showed the benefits of bicarbonate TSW in treating inflammatory skin diseases such as atopic dermatitis.

Avène TSW is a bicarbonate-rich spring water that has been shown to exert an anti-inflammatory effect on atopic dermatitis and acne. Joly et al. [20] studied two different thermal spring waters (“Sainte Odile” and “Val d’Orb”) from Avène on rat peritoneal mast cell activation, finding that both were able to inhibit histamine and prostaglandin D2 antigen-induced release and also inhibit histamine release triggered by substance P, which could explain their anti-inflammatory and antiallergic properties. The anti-inflammatory effect of Avène TSW has also been shown in a model of human skin explants stimulated by a neurotransmitter (vasoactive intestinal peptide VIP), in which the Avène TSW showed that the percentage and area of dilated vessels stimulated by VIP treatment was significantly reduced when an Avène-TSW-soaked cotton disk was applied on the skin fragments, and a concomitant decrease in TNF- α release was also observed after the Avène TSW treatment [21].

Additionally, in an in vitro study, Avène TSW significantly inhibited TNF- α -induced expression of E-selectin and intercellular adhesion molecule 1 (ICAM-1), and through the inhibition of adhesion molecules involving NF- κ B, the ATSW exhibited a regulation of inflammatory parameters, thus minimizing the inflammatory reaction in atopic dermatitis [22].

The antioxidant effect of Avène TSW has also been investigated. In vitro experiments in normal keratinocytes irradiated with ultraviolet-A (UVA) demonstrated that Avène TSW was able to protect cell membranes, genomic DNA, and proteins from UVA-induced oxidative stress [23]. Later research confirmed the antioxidant activity of Avène TSW; Zöller et al. [24] compared the effect of culture media supplemented with (a) thermal spa waters (La Roche-Posay, Avène) and (b) two natural mineral drinking waters (Heppinger, Adelholzener) on physiological parameters in HaCaT keratinocytes, concluding that, despite having different compositions, they both efficiently suppressed the induction of a prototypical inflammatory cytokine (IL-6) and the formation of ROS after UVB stimulation.

Clinical studies have also demonstrated the anti-inflammatory effects of Avène TSW. Patients suffering from psoriasis and AD were treated with several therapeutical techniques, including spraying with Avène TSW. The decrease in both in the SCORing atopic dermatitis (SCORAD) and psoriasis area severity index (PASI) scores was associated with a significant reduction in IL-8 and *Staphylococcus aureus* colonization [25].

Patients suffering from acne were treated with a topical application of retinoic acid alone or in association with a water spray used ad libitum; the results showed a significant reduction in scaling, observing an overall tolerance when applying the combined treatment [26]. In addition, two clinical trials evaluated the use of Avène TSW in terms of efficacy and tolerance when used as an adjunctive care in post-procedure skin care with photodynamic therapy in dermal melasma or acne vulgaris and/or actinic keratoses (spraying Avène TSW after the procedure for a week). In both studies, the Avène TSW reduced erythema and pruritis and relieved pain. The studies showed that spraying Avène TSW after photodynamic therapy significantly reduced the short-term adverse effects associated

with the procedure. The results obtained showed the smoothing and anti-irritant properties of Avène TSW due to the involvement in the reduction in the sensitivity of cells and the anti-inflammatory effects [27,28]. Furthermore, a recent *ex vivo* and clinical study showed that Avène TSW was able to decrease redness and reduce the overall sensitivity scale after a dermatological chemical peeling [29].

Comano thermal spring water (Comano TSW) is a low-mineralization, bicarbonate, calcium thermal spring water that has also been investigated for its anti-inflammatory and beneficial therapeutic effects on patients with psoriasis and atopic dermatitis and also in wound healing.

Gregotti et al. [30] investigated the anti-inflammatory and antiphlogistic effects of Comano TSW when applied to the skin of an albino rabbit treated with TCA 25% (a potent exfoliant) and then treated with a cold pack of Comano TSW, showing a significant decrease in inflammation compared to the control. Authors suggested that these anti-inflammatory effects were probably due to the buffer activity that bicarbonate-calcium Comano TSW has, as well as to its rehydrating effect observed in the experimental burning.

Chiarini et al. [31,32] performed two studies to investigate the effect of CTSW in psoriatic epidermal keratinocytes. In the first assay, the results showed that CTSW was able to interfere with vascular endothelial growth factor-A isoform expression and secretion via psoriatic keratinocytes. These effects reduced all the vascular endothelial growth factor-A-mediated angiogenic, vessel-permeabilizing, and chemotactic effects. In the second study, the researchers used IL-6-hypersecreting keratinocytes isolated from six psoriatic patients and found that intracellular levels and secretion rates of IL-6 were drastically curtailed when cells were cultivated with Comano TSW. Additionally, CTSW downregulated the expression of cytokeratin-16, a marker associated with the keratinocyte psoriatic phenotype. Later studies conducted by the same research group investigated the effects of Comano TSW on cultures of epidermal keratinocytes isolated from the lesion areas of nine psoriatic patients, concluding that Comano TSW exposure significantly downregulated the intracellular levels of TNF- α and also reduced the intracellular levels and secretion rates of IL-8 [33]. All these results may explain the anti-inflammatory effect of Comano TSW in psoriasis.

Comano TSW has been shown to exert regenerative effects on wound healing. One *in vitro* study demonstrated that Comano TSW improved skin regeneration by increasing keratinocyte proliferation and migration and by favorably modulating the regenerated collagen and elastic fibers in the dermis [34]. In addition, Nicoletti et al. [35], in an *ex vivo* study, compared the regenerative effects of Comano TSW and a control. Human 6 mm punch skin biopsies harvested during plastic surgery sessions were injured in their central portion to induce skin loss and were cultured in either conventional medium (controls) or medium powder reconstituted with filtered Comano TSW (treated samples). At 24, 48, and 72 h, the specimens were observed following staining with hematoxylin and eosin, Picrosirius Red, orcein, and anti-proliferating cell nuclear antigen. The results showed that compared with the controls, the treated samples exhibited reduced overall cell infiltration, evidence of fibroblasts, stimulation of cell proliferation, and collagen and elastic fiber regeneration. Despite this evidence, other studies have shown that the regenerative effects cannot be attributed solely to the chemical composition, as metabolites from the Comano TSW microbiota may have a role in these properties, and a combination of the biological properties of several bacterial species within this spring water might be responsible for its regenerative effects on human skin [66–68].

Taboli et al. [36] conducted an observational prospective study in which patients bathed in Comano TSW alone or combined with UVB phototherapy for two weeks once a day. The results showed an improvement in quality of life and self-administered Psoriasis Area Severity Index (SAPASI) scores in both groups. Additionally, a controlled, randomized, double-blind clinical study was performed to compare Comano TSW with tap water, showing a reduction in PASI scores and hydration improvement in the studied group. Histologic reports showed a significant reduction in hyperkeratosis, acanthosis, and papillomatosis; no undesired side effects were described [37].

An observational study was conducted on children with mild-to-severe atopic dermatitis who underwent balneotherapy at the Comano thermal spring water center. The results showed a statistically significant improvement in AD severity after the Comano TSW balneotherapy, and the therapy was well tolerated. Furthermore, no relevant adverse effects were reported during the treatment course [38].

Nitrodi thermal spring water (Nitrodi TSW) is medium-mineral water classified as bicarbonate and rich in silica. Several studies have shown its potential anti-inflammatory activity [69,70]. Recently, Napolitano et al. [39] conducted a study with the aim of studying the biological effects of Nitrodi TSW on human dermal fibroblasts to determine whether the water exerts in vitro effects that could be relevant to skin wound healing. The results showed that Nitrodi TSW exerts strong promotional effects on dermal fibroblast viability and a significant stimulatory activity on cell migration; in short, Nitrodi TSW induces alpha-SMA expression in dermal fibroblasts, thus promoting their transition to myofibroblast-protein ECM deposition. Furthermore, Nitrodi thermal spring water reduces intracellular reactive oxygen species (ROS), which play an important role in human skin aging and dermal damage. Additionally, a significant stimulatory effect on the cell proliferation of epidermal keratinocytes was observed, as well as an enhancement of their response to the oxidative stress caused by external stimuli.

Other studies have suggested that bathing in hot springs may affect the gut microbiota in healthy individuals, showing that the relative abundance of *Bifidobacterium bifidum* was increased significantly after seven consecutive days of bathing in a bicarbonate spring, and significant increases in other gut microbiota were also observed after bathing in simple, bicarbonate, and sulfur springs [71].

2.1.4. Fluoride

Despite the recognition of the benefits of fluoride waters in balneology [72], studies on fluoride's effect on skin health were not found in our literature research.

2.1.5. Phosphate

Phosphate is found in thermal spring waters in the form of orthophosphate. Although it is essential for the maintenance of bones and teeth, there were no specific studies on phosphate in balneology.

2.1.6. Carbonate

There are few studies about carbonate waters. Liang et al. [40] investigated the effects of Nagano hot spring water (rich in carbonate ions, 42 °C) on the healing process of the skin using a nude rat skin wound model, finding that this water enhanced the wound healing process, increasing vessel density and reducing inflammatory cells in the granulation tissue of the wound area.

Some TSWs are also carbon-dioxide-rich, and these are described in Section 2.4.

2.2. Cations

2.2.1. Calcium

Many mineral spring waters are classified as calcium spring waters, since this cation is found in solutions linked to bicarbonate and sulfate waters.

Calcium is well known for its participation in numerous skin processes, such as wound healing, the regulation of keratinocyte proliferation, the formation of certain proteins, the regulation of hyaluronic acid expression, and its role in the homeostasis of the epidermal barrier through calcium channels, among others [73–78].

Examples of calcium-rich TSW are Avène and Comano, which have been already discussed in Section 2.1.3.

La Roche-Posay TSW is a spring water rich in calcium and selenium, with specific anti-inflammatory and antioxidant properties. Several in vitro and clinical studies have

been carried out in the last few decades; some examples are described below and in Sections 2.3.1 and 2.3.2.

La Roche-Posay TSW spray was effective in treating scars after pediatric plastic surgery, showing a reduction in the inflammatory aspect of scars, easing of itching, facilitating the removal of crusts, providing a careful cleaning method after non-traumatic surgery, and preventing infection [41].

2.2.2. Sodium

Sodium is an essential nutrient that the body needs in relatively small amounts (as long as there is no substantial sweating) to keep body fluids in balance and muscles and nerves healthy. In addition to the classic two compartments (intracellular and extracellular), new investigations have shown that sodium can be stored without commensurate water retention in the interstitium and endothelial surface layer, forming a dynamic third compartment for sodium. Sodium storage in the skin and endothelial surface layer may function as a buffer during periods of dietary depletion and excess, representing an extra-renal mechanism for regulating sodium and water in the body [79].

Most sodium-rich thermal waters are chloride waters, but sodium sulfate waters can be also found; chloride and sulfate TSWs were already discussed in Sections 2.1.1 and 2.1.2.

Inaka and Kimura [42] investigated the wound-healing effects of Yuda hot spring water in female albino guinea pigs. Yuda hot spring water is classified as a thermal alkaline spring water; the main cations are sodium ions, the main anions are chloride ions, and sulfur is also present. Animals were bathed in Yuda TSW, and the control group was bathed in tap water. Differences in the concentrations of several amino acids associated with wound healing were found between the two groups, and image analysis showed that wounds made on the abdominal skin of guinea pigs were significantly contracted by hot spring bathing compared to bathing with tap water, and their histopathological findings demonstrated that wound healing was accelerated.

A single-center, evaluator-blinded, split-face, randomized study investigating the effects of sodium-rich thermal spring water in improving the efficacy and tolerability of standard acne therapy showed an improvement in skin hydration and a feeling of skin suppleness; QoL also improved [43].

2.2.3. Magnesium

Magnesium salts are known for their anti-inflammatory properties and wound-healing properties. A topical application of a cream containing 2% magnesium and calendula was able to reduce the recovering time in diaper dermatitis [80]. All of the magnesium salts, except magnesium dihydrogen phosphate, accelerated barrier repair, but research performed by Denda et al. [81] demonstrated that magnesium chloride aqueous solutions contained calcium chloride at different molar ratios. When the calcium-to-magnesium ratio was lower than 1, the mixture accelerated barrier repair. The application of an aqueous solution of 10 mM magnesium chloride and 10 mM calcium chloride was found to hasten the barrier recovery more effectively than a solution of 10 mM magnesium chloride. Magnesium exerts a pivotal role in the growth and differentiation of keratinocytes, and it is responsible for helping the skin preserve a lack of water, thus acting as a natural moisturizing agent. These effects are very useful in treating and managing pathologies such as psoriasis and atopic dermatitis [64,82].

Several studies have been performed with magnesium-rich TSW, mainly in the Dead Sea, where the content of magnesium salts is very high. Studies have shown that magnesium-rich Dead Sea salt solutions are able to improve skin barrier function, increase skin hydration, and reduce inflammation in atopic dermatitis [44]. When TSWs rich in calcium and magnesium are added to cosmetics formulations, the penetration of both cations is enhanced, and they can reach viable skin layers in a formulation-dependent manner [61].

2.3. Trace Elements

The content of trace elements, such as selenium, zinc, boron, and strontium, among others, has been suggested to be involved in the healing effects of TSW. Deficiencies in some of them could also be entailed in skin diseases. For example, Kirmit et al. [83] studied the serum levels of trace elements in patients suffering from psoriasis, finding that Se and Zn levels were significantly lower in the psoriatic patients compared to the control group.

2.3.1. Selenium

The most-studied TSW containing selenium is La Roche-Posay TSW. In addition to calcium, La Roche-Posay TSW is rich in selenium and strontium, to which researchers attribute the antioxidant properties of this thermal water [84]. Studies comparing La Roche-Posay TSW with distilled water and water with the same selenium concentration as La Roche-Posay TSW showed that the La Roche-Posay TSW had a greater protective effect against oxidative stress induced by UVB light than controls in human skin fibroblasts [45].

To investigate the effects of La Roche-Posay TSW, several studies have been performed over the last twenty years. In vitro studies were performed in which human skin fibroblasts were cultured and exposed to oxidative stress from UVA radiation in the presence or absence of La Roche-Posay TSW, showing that selenium-glutathione peroxidase and superoxide dismutase activity was higher in fibroblasts cultured in medium containing La Roche-Posay TSW than in other media [46]. A study carried out on human keratinocytes after exposure to increasing UVB doses, showing better resistance with better cell survival and a reduction in IL-1 α cytokine release in cells cultured in medium containing La Roche-Posay TSW in comparison with cells cultured in medium containing demineralized water [47]. An in vitro study evaluated the modulatory effects of media containing selenium or strontium salts as well as La Roche-Posay TSW. These effects were evaluated using a reconstructed model of biopsies of healthy skin or skin with atopic dermatitis for the production of IL-1 α , IL-6, and TNF- α . In the three media, after 10 days of culture, the production of these three cytokines was lower in the inflamed skin than in the healthy skin. With strontium salts, the skin's selective inhibitory effect on IL-1 α production was less evident, but the inhibitory effect for TNF- α was greater. At intracellular and extracellular levels, selenium and strontium salts showed a modulating effect in decreasing IL-6 production [48].

Furthermore, it has been suggested that selenium-rich thermal water could play an important role in the prevention of UV damage, as studies have shown that La Roche-Posay TSW is able to reduce IL-1 α release in irradiated keratinocytes, increase selenium-dependent glutathione peroxidase activity, and decrease the production of lipoperoxides in irradiated fibroblast [49].

Additionally, Zöller et al. [24], comparing different waters, showed that La Roche-Posay TSW was able to reduce IL-6 levels and the formation of ROS after UVB irradiation. The authors suggested that the observed effects could be related to the high selenium content (53 $\mu\text{g/L}$), which is a co-factor for glutathione peroxidase, a key enzyme in the elimination of ROS.

As has been previously mentioned, La Roche-Posay selenium-rich spring water was also used in the treatment of scars after pediatric plastic surgery and has been shown to be able to reduce pruritus, soften the inflammatory appearance, and facilitate the elimination of crusts and prevent the formation of new ones [84].

Additionally, La Roche-Posay selenium-rich spring water was found to reduce PASI scores by $47 \pm 4\%$ ($p < 0.05$), and interestingly, 8% of patients were completely cleared and 48% improved by more than 50%. Changes in the microbiome profile were also found [50].

2.3.2. Strontium

The antipruritic effect of strontium salts was demonstrated in a study performed by Papoiu et al. [85]. After inducing itching in healthy subjects, who were divided into four groups, the participants were topically treated with either a gel containing 4% SrCl₂,

a control vehicle, topical 1% hydrocortisone, or topical 2% diphenhydramine. The results showed that strontium significantly reduced the peak intensity and duration of itching compared to the control, and it was significantly superior to the other two antipruritic formulae. Additionally, in a randomized, double-blind clinical trial, Fatemi et al. [86], by using biometric skin measurements, demonstrated that strontium chloride salts are able to reduce acute skin irritation.

The main studies about the effects of strontium-rich TSW were performed by La Roche-Posay; this research has been described above in Section 2.3.1.

2.3.3. Manganese

The role of manganese superoxide dismutase on the skin is very well known to exert antioxidant activities, and it is important in the defense against UV-induced photoaging [87]. A serum containing a manganese tripeptide-1 was applied topically in patients suffering from photoaging, showing an overall improvement in hyperpigmentation [88], and chitosan nanovesicles loaded with bioactive manganese were effective in protecting against infections and promoting the wound healing process [89].

Chebassier et al. [51] studied the effects of Saint Gervais boron- and manganese-rich TSW on wound healing. They incubated keratinocytes for 24 h with boron salts at concentrations of between 0.5 and 10 mg/mL or manganese salts at concentrations of between 0.1 and 1.5 mg/mL. The results showed that these salts accelerated wound closure compared with the control medium, but they did not increase keratinocyte proliferation, so the authors suggested that they could promote keratinocyte migration.

2.3.4. Boron

The mechanisms implicated in the effects of boron in wound healing [90–93] and in photoaging prevention [94] have been discussed by several authors.

Boron can be found in volcanic spring water in the form of boron-based acids (e.g., boric, metaboric, tetraboric, and pyroboric acid), but studies on its effects on the skin are scarce.

The effects of boron of Saint Gervais TSW were studied by Chebassier et al. [51]. The results of this research were already discussed in Section 2.3.3.

2.3.5. Zinc

It is very well known that several human diseases that are accompanied by skin manifestations are linked to mutations or dysregulation in Zn transporters [95]. Zinc salts intervene in wound healing and also have antibacterial properties [96,97]. Zinc-rich Avène TSW has been shown to reduce pruritus after a photodynamic therapy procedure, but more studies are needed to understand the mechanism of action [27].

2.4. Other Compounds

Several other compounds can be found in thermal spring waters, with SiO₂ (silica spring waters) and sulfur compounds such as hydrogen sulfide H₂S (in addition to sulfate, described in Section 2.1.2.) being of interest. Carbonate-rich and carbon-dioxide waters can also have specific effects on the skin.

2.4.1. Silica (SiO₂)

Silica TSWs are known for their anti-irritant properties. A clinical study performed by Ferreira et al. [52] demonstrated that Sao Pedro do Sul TSW, which is rich in silica, is able to reduce skin irritation and promote skin barrier recovery. Water-based creams formulated with silica-rich Monfortinho TSW improved skin hydration, and an in vitro study showed that it promoted skin barrier recovery [53]. Water-based creams formulated with silica-rich Monfortinho TSW reduced cell metabolism and the proliferation of keratinocytes and macrophages, which could explain the observed benefits of this TSW in hyperkeratotic conditions, such as psoriasis and atopic dermatitis [54].

Blue Lagoon TSW is a highly mineralized water with an extremely high concentration of silica (137 mg/L). Studies have demonstrated that this TSW is able to reduce PASI scores in psoriatic patients [55,56].

2.4.2. Sulfur and Hydrogen Sulfide

Coavoy-Sánchez et al. [98] revised the role of H₂S in dermatological diseases, stating that most of the effects of H₂S are strongly dose- or concentration-dependent, and the effects of several H₂S-releasing compounds, such as Na₂S, NaHS, and GYY4137 (H₂S donor), among others, can be potential therapeutic tools for the treatment of a variety of skin diseases by exerting anti-inflammatory, anti-pruriginous, cytoprotective, pro-angiogenic, and immunomodulatory actions. And, later on, Xiao et al. [99] summarized the latest research progress on H₂S-mediated effects, highlighting its antioxidant effect. Li et al. [100] investigated the role of H₂S in wound healing, concluding that, overall, H₂S suppressed skin fibroblast proliferation via oxidative stress alleviation and necroptosis inhibition.

Sulfur occurs with four main valences, i.e., 2[−], 3⁺, 4⁺, and 6⁺, and depending on the oxidation state, large amounts of oxyacids can be produced, as well as sulfides. In mineral–medicinal waters, compounds with valence 2[−], such as hydrogen sulfide (SH₂), sulfhydrates (SH[−]), and sulfides (S⁼), and with 6⁺ status, such as sulfates are of interest [101]. To exert its beneficial effects, sulfur spring water must contain a reasonable amount of H₂S or HS[−] and thus have a relatively acidic pH [102]. Studies, both in vitro and in vivo, on primary psoriatic lesions have demonstrated that hydrogen sulfide can not only reduce the basal expression and secretion of IL-8 but also interfere with IL-17- and IL-22-induced IL-8 production [103].

Sulfur thermal spring waters (also called sulfurous TSW and sulfide TSW) are used in balneo-dermatology to treat dermatological disorders such as psoriasis and AD. They have anti-inflammatory, keratoplasty, antipruritic, antibacterial, and antifungal effects [104]. Other research has reported that sulfurous TSW could induce the release of IL-10, an anti-inflammatory cytokine, as demonstrated in an in vitro study [105], despite the fact that the precise mechanism has not been completely elucidated. In vitro studies have shown the important dose-dependent inhibitory effect of sulfur spring waters on mitogen-induced T lymphocyte proliferation and IL2 production [106]. Additionally, sulfurous TSW boosts the antioxidant capacity and reduces oxidative stress levels in the human body [107]. Other studies have shown that La Bourboule TSW, a sulfurous spring water, could improve wound healing by controlling keratinocyte physiology; the authors suggested that one of the mechanisms of La Bourboule TSW could be the modulation of various inflammation regulators at the mRNA and/or protein levels [57].

An observational study in patients suffering from psoriasis was carried out to assess the efficacy and safety of balneotherapy with hydrocarbonate- and sulfur-rich water in combination with emollient application in mild-to-moderate plaque psoriasis, as well as to study the influence on the skin physiology of lesional and non-lesional skin. The results showed an improvement in PASI scores, stratum corneum hydration, and itching and skin dryness [58].

Finally, it is worth mentioning the PSOTERMES study on psoriasis, which included five French thermal baths, including Molitg-Les-Bains with sulfurous waters, which showed that thermal spring curing is effective in psoriasis, although the compounds in the thermal waters that may be involved in the observed improvements were not specified. In addition, it should be noted that an improvement was obtained in the VAS pruritus score, one of the most annoying symptoms of psoriasis [59].

2.4.3. Carbon-Dioxide

The three main effects of CO₂ hydrotherapy during whole-body or partial immersion include a decline in core temperature, an increase in cutaneous blood flow, and an elevation in thermal sensation scores [108].

Elimban et al. [60] investigated the effect of a CO₂ water bath at 37 °C for 6 weeks in diabetic rats with or without peripheral ischemia, concluding that peripheral ischemia augmented the increase in blood flow and development of angiogenesis in diabetic skeletal muscle upon CO₂ therapy. It was suggested that the greater beneficial effects of the CO₂ therapy in the diabetic–ischemic animals in comparison to the diabetic group may have been a consequence of differences in changes in redox-sensitive signal transduction mechanisms.

Carbon-dioxide waters are used for the treatment of chronic venous insufficiency, as some evidence supports the idea that CO₂ baths might represent an efficient therapeutic means for the rehabilitation of coronary heart disease, myocardial infarction, and stroke, as well as in the treatment of chronic venous insufficiency, certain inflammatory diseases, and functional disturbances [109,110], but more studies are needed to support this evidence.

In summary, Table 2 lists, in alphabetical order, the thermal spring waters studied and their main beneficial effects on the skin.

Table 2. Thermal springs waters and beneficial effects on the skin.

TSW	Main Composition	Beneficial Effects
Avène	Bicarbonate, calcium, magnesium, silica, zinc	Soothing properties Protection against dehydration Antiallergic and anti-inflammatory Antioxidant Preventing growth of bacteria
Blue Lagoon	Silica-rich	Psoriasis improvement
Comano	Bicarbonate, calcium	Skin regeneration Anti-inflammatory effects Psoriasis improvement
Dead Sea	Hypersaline, calcium, magnesium-rich	Atopic dermatitis improvement
Hae-Un-Dae	Sodium chloride, sulfate-rich	Immunomodulatory effects
La Bourbule	Chloride, sodium, sulfurous water	Wound healing improvement
La Roche-Posay	Bicarbonate, calcium, magnesium, strontium, selenium	Anti-inflammatory effects Antioxidant Psoriasis improvement Wound healing improvement
La Solía	Chloride, sodium, sulfate	Anti-inflammatory effects
Leopoldine	Chloride, sodium, sulfate	PASI score improvement, anti-inflammatory effects
Moligt-Les-Bains	Sodium sulfurous water	Psoriasis improvement
Monfortinho	Bicarbonate, silica-rich	Skin hydration improvement in psoriasis and eczema Skin barrier improvement Improvement in hyperkeratotic conditions
Nagano hot spring water	Carbonate-rich	Wound healing improvement
Nitrodi	Bicarbonate, silica	Wound healing improvement
Saint-Gervais	Boron- and manganese-rich	Wound healing improvement
Salies de Béarn	Hypersaline mineral water, chloride, sodium, sulfate	PASI score improvement Anti-inflammatory on AD
Sao Pedro do Sul	Bicarbonate, silica-rich	Anti-inflammatory effects Skin barrier recovery
Sungai Lalang	Sodium-rich	Acne symptom improvement
Uriage	Sulfate, chloride, sodium, calcium	Skin hydration Protection against UVB irradiation Antioxidant Prevent biofilm formation
Yuda hot spring	Alkaline spring water (sodium-rich)	Wound healing improvement

3. Conclusions and Future Perspectives

Thermal spring waters have been shown to be effective in several dermatologic diseases and skin conditions, exerting anti-inflammatory activities in atopic dermatitis, pso-

riasis, seborrhea, seborrheic dermatitis, and ichthyosis, among others, and they can also improve wound healing. Other skin conditions such as rosacea and acne benefit from TSW, and, in addition to the anti-inflammatory effects, skin barrier recovery is an important part of topical treatment with TSW, both by spraying and by applying cosmetics made from them. It is considered that the synergy between minerals/compounds (chemical effects) and the mechanical, thermal, and immunological effects are responsible for the actions on the human body and, specifically, on the skin, where minerals and trace elements play a crucial role.

In this review, studying each anion and cation separately, it has been proven that the main anions involved in the actions of TSW on the skin are chloride, which exerts anti-inflammatory and immunomodulatory actions and also maintains skin hydration; sulfate, which also has anti-inflammatory properties as well as antioxidant and antibiofilm activity (and can prevent the formation and growth of complex microbial communities); bicarbonate, which exerts anti-irritant, anti-inflammatory, and antioxidant activities as well as having soothing properties, protecting against dehydration, and also promoting skin regeneration; and carbonate, which enhances the wound healing process. Among the cations, calcium and sodium can improve wound healing, and magnesium improves skin barrier function, increases skin hydration, and reduces inflammation. Trace elements have also been found to exert several activities; selenium is characterized by its antioxidant properties, and strontium seems to have similar properties; manganese and boron promote wound closure; and zinc has been shown to reduce pruritus after a photodynamic therapy procedure. Other compounds found in TSW are considered to be involved in skin care, such as SiO₂, which has been shown to have anti-inflammatory activity and participate in skin barrier recovery; sulfur and its derivatives (SH[−]; H₂S), which has been demonstrated to improve wound healing and psoriasis; and CO₂-rich waters, which are able to improve blood flow.

This evidence can support the chemical action of TSWs, but more research is needed to elucidate the exact mechanism of action of each specific thermal spring water.

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