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Review

Cosmeceuticals and Thalassotherapy: Recovering the Skin and Well-Being after Cancer Therapies

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Abstract: Cancer treatments have undergone significant advances in recent years, although they are not exempt from side effects, including skin toxicity. Different studies show that skin care for cancer patients can be effective in reducing sequelae such as inflammation, xerosis, skin rash, and radiodermatitis, among others. This is the reason why research is being carried out on the ingredients of cosmeceuticals for those indicated for oncological skin care. On the other hand, it is necessary to implement measures that improve the patient's well-being and, therefore, thalassotherapy techniques and the marine environment could be an effective resource to achieve this goal. This article reviews the publications related to skin care after cancer treatment, including thalassotherapy techniques that can also contribute to well-being.

Keywords: oncology; cancer; thalassotherapy; hydrotherapy; cosmetics; skin care

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1. Introduction

The increase in the incidence of cancers in the population has multiplied efforts for the development of new therapeutic agents in order to achieve greater patient survival. Cancer treatments improve but are accompanied by side effects, some of which limit the patient's quality of life, both during therapy and years after its cessation. One of the aspects that both therapists and patients value is the care for the skin and physical appearance to ameliorate the side effects and sequelae in the skin and its annexes.

It is well known that the improvement of the cancer patient's well-being and self-esteem contributes positively to their recovery. That is why the use of suitable cosmetics for oncological skin care is of increasing interest given the benefits it offers. Several studies on quality of life (QOL) in which patients who received cosmetic care were compared with those who did not receive treatment showed significant differences between the group that received cosmetic care and the control group in two areas of QOL: mood state and self-perception of the disease [1,2].

Another study by Oliveri et al. [3] compared two groups of patients treated for breast cancer, in which the experimental group received aesthetics treatment for oncologic side effects on the skin, and the control group did not. The alterations treated were hand–foot syndrome, nail damage, edema, xerosis, rash, and radiodermatitis, and the aesthetics treatments were manicure and pedicure with anti-flakiness cream, massage, emollient oil, nourishing and lenitive emulsion. The health-related quality of life (HRQoL) questionnaire was applied before and after 28 days of treatment, twice a week. The study concluded that there were significant differences between the two groups; the treated patients perceived that the symptoms of the indicated disorders improved, and distress was also reduced [3]. Recently, a study conducted by Wakeda [4] showed that camouflage makeup is useful for masking skin changes, improving quality of life scores regardless of age, diagnosis, and site of skin changes.

On the other hand, although there are few publications on the matter, it has been shown, mainly through experiences, that the treatment of the sequelae of oncological therapies in

thermal spring and thalassotherapy centers through the use of hydrothermal techniques can also help improve well-being and faster recovery from skin disorders and fatigue [5].

To recover the skin and improve well-being after an oncological treatment, various techniques can be used, mainly cosmeceuticals, which can be combined with hydrothermal treatments, massage and other well-being techniques such as yoga, mindfulness, etc. This article reviews the publications related to skin care after cancer treatment, including thalassotherapy techniques that can also contribute to regaining well-being.

For this review, Web of Science, SciFinder, and Scopus databases were reviewed up to September 2022. Search terms included "oncology and thalassotherapy", "hydrotherapy and cancer", "cosmetics and oncological skin care", "skin care and cancer", and "post-oncological skin care".

2. Skin Disorders after Oncological Therapies

Before reviewing the cosmetics and care necessary for the skin of cancer patients, the most frequent alterations are briefly described below.

There are differences between the skin manifestations and reactions caused by chemotherapy and by radiotherapy. With chemotherapy, xerosis, skin rash, and hand–foot erythema mainly occur; in radiotherapy, a series of symptoms are produced, grouped under the name of radiodermatitis. Different adverse reactions are also seen with targeted treatments and immunotherapy; thus, acneiform eruptions are more frequent in patients treated with Epidermal Growth Factor Receptor inhibitors (EGFRi) and inhibitors of Mitogen-Activated Protein Kinase (MAPK) pathway; BRAF inhibitors frequently produce secondary skin tumors (squamous cell carcinoma and keratoacanthomas), modifications in preexisting pigmentary lesions, and hand–foot reactions. Immune checkpoint inhibitors (ICIs) produce maculopapular rash, and eczema-like or psoriatic lesions, lichenoid dermatitis, xerosis, and pruritus. Mucositis and oral hyperkeratotic lesions can also appear. Furthermore, targeted treatments and endocrine therapy frequently produce late alopecia, and targeted therapies can also damage the nail plate, with paronychia and periungual pyogenic granuloma distinct from chemotherapy-induced lesions. Delayed nail growth, onycholysis, and brittle nails may also occur [6–8].

2.1. Xerosis

Cutaneous xerosis, or extremely dry skin, consists of an increase in the dryness of the skin and/or mucosa, which in certain cases can be very intense. It is one of the most frequent side effects of systemic therapies that appears several weeks after treatment. When aggravated, it can be complicated by secondary *Staphylococcus aureus* or Herpes simplex (HSV) infections [9]. Usually, it is a simple cutaneous dryness, mainly in the extremities and trunk, which manifests itself with fine scales and sometimes rough skin, a feeling of tightness, and pain. Sometimes it is accompanied by skin inflammation, eczematiform eruption, and more or less intense itching. With Epidermal Growth Factor Receptor (EGFR) inhibitors, cracked eczema can occur in the lower extremities or as painful fissures in the toes or heels. Sometimes, less frequently, they present a form of ichthyosis [10].

2.2. Skin Rash

This is one of the most frequent manifestations and follows a typical chronological pattern that peaks in severity during the first 1–2 weeks of chemotherapy [11]. It manifests with papules and pustules, intense itching, pain, and sometimes spontaneous bleeding from the lesions [6]. Some studies indicate that it may appear in a large percentage of patients treated with EFGF inhibitors [12]. However, the lesions tend to fade after a few weeks or months. Skin rash is located in areas where sebaceous glands abound, such as the face and scalp, the trunk (pre-sternal and interscapular area), and much less frequently in the limbs. The impact on the quality of life is very high. It should be borne in mind that although it may look like an acneiform rash, it is not, since there are no obstructive lesions

characteristic of acne, such as microcysts and blackheads, and it is not common for acne to have a burning sensation, itching, and pain [13].

2.3. Toxic Erithema in Chemotherapy

This term was proposed by Bolognia in 2008 in order to group together the clinical manifestations induced by chemotherapy. It comprises a set of skin reactions that are sometimes described separately or by other names (e.g., Chemotherapy-related bilateral dermatitis associated with eccrine squamous syringometaplasia (CBDESS) or, to a lesser extent, Symmetrical drug-related intertriginous and flexural rash (SDRIFE)). The main manifestations are painful erythematous, violaceous, and/or edematous plaques on the hands, feet, and intertriginous regions that may appear dark and develop blisters with subsequent erosions [14].

Many of these symptoms are associated with other skin disorders such as palmar–plantar erythrodysesthesia, acral erythema, hand–foot syndrome, toxic erythema of the palms and soles, eccrine squamous syringometaplasia, epidermal dysmaturation, and neutrophilic eccrine hidradenitis [13,15,16]. It is usually a toxic, non-immune allergic mechanism and therefore it is dose-dependent and displays an often similar histological pattern [17,18].

2.4. Pruritus

Pruritus can be a consequence of dry skin or occur due to internal organs being affected by treatment (e.g., in the case of jaundice or kidney dysfunction). It can be accompanied by itching and can also be generalized [19].

2.5. Ulcerations

Cutaneous ulcers are characterized by tissue loss that affects the deeper layers of the dermis and hypodermis, with scarce tendency for spontaneous healing. They may occur due to the tumor itself, but very often they are associated with the chemotherapy treatment with EGFR inhibitors, Angiogenesis inhibitors, Platelet-Derived Growth Factor (PDGFR) inhibitors, etc. [20].

2.6. Hand–Foot Syndrome

Hand–foot syndrome, also known as palmar–plantar erythema, acral erythema, and palmar–plantar erythrodysesthesia, is a relatively frequent dermatologic toxic reaction to anti-cancer therapies both in chemotherapy treatments and in targeted therapies, although in the former case they are more diffuse, and with targeted therapies they appear earlier and are more localized. It is a painful scaling and sloughing along an extensive inflammatory erythema on hand's palms of and feet soles (usually bilateral), sometimes with edema and varying degrees of desquamation, hyperkeratosis, or blisters. It has a great impact on the QoL of the patient, so it may be needed to reduce the dose of and even stop treatment [21,22].

2.7. Linphedema

Cancer patients who have had axillary lymph nodes removed during a mastectomy are at risk of developing lymphedema (swelling, redness, heat, tight skin, or a heavy sensation in the affected limb). This condition usually affects the extremities (arms and legs) and it could be also consequence of radiotherapy treatments in the area. It can appear immediately or years after the end of treatment [23].

2.8. Alopecia and Other Hair Disorders

The most notable alteration is alopecia, which occurs due to chemotherapy treatment that causes toxicity in hair that is in its active growth phase (anagen). In the studies conducted by Naveed et al. [24], it is highlighted that in a large percentage of patients suffering from alopecia, this is related to an anagen effluvium, and in a lower percentage it is with a telogen effluvium. Due to the psychological impact, patients consider this

the main burden of the disease, sometimes constituting a stigma, because through this alteration, the disease is visible to others. Rarely, hirsutism or hypertrichosis can occur [24].

2.9. Nail Disorders

Different alterations can occur, mainly color alterations (melanonychia and leukonychia), followed by nail ridging, onycholysis, Beau's line, paronychia, brittle nail and nail infection, fragility, striations and changes in thickness and color [21].

2.10. Mucosal Disorders

Oral mucositis is quite frequent and manifests with redness in the mouth with a burning sensation. It can be very painful and therefore prevents normal food intake, sometimes making necessary treatment with powerful anti-inflammatory drugs. The endobuccal epithelium is especially sensitive to the cytotoxic effect of chemotherapy. Mucositis corresponds to inflammatory phenomena induced by chemotherapy, radiotherapy, and to a lesser extent targeted therapy that develops in the entire mucosa of the digestive tract, from the mouth to the anus. Clinically, chemotherapy-induced mucositis appears after the first or several first cycles (inflammatory ulcerations varying from limited to diffuse, on the ventral and lateral sides of the tongue, base of the mouth, soft palate, or mucosa of the cheek); if radiation therapy is associated, it affects more areas and can be complicated by pain, which will limit feeding and even speech. These chemotherapy-induced lesions can occur with induced but more limited therapies in the form of aphthoid ulcerations. Xerostomia (endo-oral dryness) has also been observed after radiotherapy, with frequent sequelae such as dysgeusia and mucous pigmentation [13].

2.11. Other Skin Alterations Derived from Chemotherapy

There are a set of alterations, dermatoses or facial imperfections, that all affect personal self-image to a great extent.

2.11.1. Hyperpigmentation

These appear mainly in the acral areas but can also be generalized [24]. They usually disappear once the treatment is finished; they are often accentuated by sun exposure, so the use of sunscreen is beneficial.

2.11.2. Photosensitivity

The skin is sensitive to sun exposure, so specific protectors must be applied. The sensitivity is induced by ultraviolet A (UVA) light, and it is more of a phototoxicity than a photoallergy. Aggravation of preexisting dermatoses (e.g., subacute lupus) or the phenomenon of UV recall (or reappearance of an erythema) may occur after the injection of certain chemotherapeutic substances, in which an erythema reappears in the area that had previously been irradiated [25].

2.11.3. Vascular Disorders

There can be vasculitis-like lesions, periorbital edema and flushing, among others [24].

2.12. Radiodermatitis

As a side effect of radiotherapy treatments, multiple skin reactions occur that have been grouped under the term radiodermatitis. These reactions are produced by the aggression that radiotherapy inflicts on the cutaneous barrier, diminishing the regenerative capacity of the skin cells; there is damage to blood vessels and therefore to the nutritional supply necessary for skin regeneration. Symptoms of acute radiodermatitis have been classified into three levels: grade 1 (mild erythema), grade 2 (dry desquamation), and grade 3 (severe moist desquamation) [26].

The main manifestations during the acute phase are erythema, which appears in the first weeks; dry desquamation, occurring due to a reduction in the mitotic capacity of the

germ layer of the epidermis, with itching and peeling; moist desquamation (a complication of the previous stages), occurring due to damage not only to the basal layer of the epidermis but also to the vessels of the dermis; and ulceration and necrosis, which rarely appear, but can occur due to reirradiation, usually several weeks or months after irradiation if the connective tissue has been damaged. Re-epithelialization develops from 6 to 8 weeks after the undamaged cells. As a side effect, hyperpigmentation, reduction or suppression of sebaceous and sweat glands can occur, as well as hair loss due to the high sensitivity of anagen follicles to the radiation [27]. In the subacute phase (6 months to 1 year after completing radiotherapy), hyperpigmentation and hypopigmentation, telangiectasias, skin atrophy, or ulcerations could appear. In the chronic phase (1–5 years later), the most common manifestations are atrophy, dermal fibrosis, telangiectasias, and permanent skin depilation. In the final phase (which begins 5 years later), there is a high risk of developing skin cancer [27].

2.13. Other Skin Problems

Other facial alterations or imperfections that affect personal self-image are as follows [28]:

- Hypersensitivity to certain cosmetics, with a tendency to redden.
- Color changes, vascular or brown spots.
- Alteration of the pores, which become more evident.
- Facial telangiectasias.
- Flaccidity increases (cheekbones accentuate and eyes sink).
- Sallow tone and loss of luminosity.

All these alterations not only cause discomfort to the patient but also contribute to modifying the patient's perception of his or her own body and body image, which is why an approach to cosmetic care from different points of view—medical, psychological, and aesthetic—is necessary [2].

3. Cosmeceuticals for Skin Care of Oncologic Patient

When providing care to the cancer patient, it is necessary to distinguish the different phases, since the cosmetic products (and aesthetic care) that can be applied will vary in each of them. Thus, in the phases prior to chemotherapy and/or radiotherapy, there are fewer limitations since it is a matter of preparing the skin to minimize side effects, but during the treatment itself, the actions and cosmetics will be limited. Therefore, preventative strategies are recommended, including topical barrier-protecting agents, moisturizers, and sunscreen protection [29]. Once medical treatment is finished, the objective is to aid recovery of the skin and its adnexa in the shortest possible time.

There is scarce scientific evidence to support the use of cosmetics for skin care of an oncologic patient. Most of the guidelines of the cancer treatment centers indicate that hydration and emollience are necessary. The treatment must always be personalized and adapted to each specific case. Recently, Lacouture et al. developed an algorithm focused on general measures and skin care to prevent or reduce the severity of cutaneous adverse events. The skin care regimen, including hygiene, moisturizing and sun care products should be safe and effective in helping to minimize these events and improve skin conditions such as xerosis, pruritus, erythema and photosensitivity [30]. In 2021, the Nordic European Cutaneous Oncodermatology Management (NECOM) project developed five consensus statements—Evidence and Opinion-Based Best Practices Recommendations—for skin care in cancer patients. The statements included: (1) Dermatologic toxicities associated with cancer treatment are common and can significantly impact QoL and disrupt cancer treatment; (2) Early education and appropriate skin care, including cleansing, hydration and photoprotection, may improve quality of life and prevent severe skin side effects for cancer patients an survivors; (3) Effective skin care for cutaneous toxicities should be based on evidence; it should be safe, effective, non-sensitizing, and a have a pH close to that of the skin surface; (4) Effective management of dermatologic toxicities associated with cancer treatment is a multidisciplinary effort requiring the participation of dermatolo-

gists, oncologists, primary care physicians, and other HCPs involved in cancer treatment; (5) Camouflage can mitigate some of the stigmas of cancer and contribute to a better quality of life [31].

According to European regulations, cosmetics are considered "any substance or mixture intended to be placed in contact with the external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odors". Cosmeceuticals, although a term not officially recognized, are defined as "cosmetic products with biologically active ingredients purporting to have medical or drug-like benefits" [32].

Three main groups of skin care cosmetics can be established: cleansers, moisturizing and maintenance products, and sun-screens. In addition, hair cleansers (shampoos) and cosmetics are used to repair the hair structure and to maintain the scalp. For nails, emollient products are used; for the maintenance of the nail plate, and in post-oncological care, toxic-free decorative cosmetics could be included.

There are no specific active ingredients for the skin care of the cancer patient; those that repair the skin barrier will be used, respecting the natural cycle of epidermal renewal, with little or no toxicity, and high quality and purity.

3.1. Oils and Butters

Vegetable oils and butters provide numerous properties to the skin, since they have a good affinity for the skin and display protective, emollient, and regenerative effects. They are therefore the active ingredients of choice in skin care to alleviate many of the cutaneous symptoms resulting from oncological treatments, such as xerosis, flaking, and irritation. They must be selected from those of adequate purity, and in the case of oils, those derived from first cold pressing are preferred because they retain all their active compounds (unsaturated fatty acids, vitamin E, etc.). The most used are murumuru, shea, cocoa, mango, and kokum butters; olive, borage, jojoba, argan, babassu, baobab, macadamia, kukui oils, and so on. Rose hip oil is also used for its regenerative potential, especially reported to improve healing. The oils rich in polyunsaturated fatty acids (PUFAs) are of great interest, since it has been shown that their lack can cause skin dryness, flaking, and eczema, and they have also been shown to improve the health of the epidermal immune system. They are abundant in the oil of flax, evening primrose, hemp, pumpkin, safflower, borage, black cumin, and sunflower, among others [33]. Sacha Inchi (*Plukenetia volubilis*) seed oil is also used in regenerative cosmetics for its richness in PUFAs, tocopherols and phytosterols, and its antioxidant activity [34]. Other oily active ingredients of interest are unsaponifiables, which contain carotenoids (precursors of vitamin A), tocopherols (such as vitamin E), and phytosterols; an example is avocado unsaponifiables (ASU) [33].

3.2. Vitamins

There are numerous studies showing the role of various vitamins in skin health.

3.2.1. Vitamin A and Its Precursor Beta-Carotene

Vitamin A is involved in the maintenance, repair, and formation of new epidermal cells regulating epidermal keratinization; additionally, in its acidic form (retinoic acid), together with vitamin C, it has been shown to intervene in the synthesis of collagen [35]. However, retinoic acid, due to its irritancy, cannot be used in formulations for oncological skin care, since it would increase irritation, further weakening the skin barrier.

3.2.2. B Vitamins

B vitamins contribute to a greater or lesser extent to maintaining the health of the skin and hair; they are also coenzymes in energy production. They are water soluble and

quite stable, penetrating through the stratum corneum, and are frequently used for the production of cellular energy and to improve the protection of the skin barrier.

Vitamin B_3 (Niacinamide) is perhaps the most studied in regard to treatment of skin inflammation and erythroses, calming irritation. Niacinamide exerts anti-inflammatory effects due to inhibition of proinflammatory factors, as well as its ability to increase the expression of serine palmitoyl transferase, the enzyme involved in ceramide synthesis [36]. Therefore, studies have been carried out to evaluate the protective effect of a cosmetic preparation with 4% niacinamide during radiotherapy, obtaining a significant improvement in symptoms [37].

Vitamin B_5 or D-Panthenol acts as a moisturizer, improving stratum corneum hydration, reducing transepidermal water loss and maintaining skin softness and elasticity. It is also known to accelerate re-epithelization in wound healing. Dexpanthenol has been shown to have an anti-inflammatory effect on experimental ultraviolet-induced erythema. The stimulation of epithelization, granulation and mitigation of itching were the most prominent effects of formulations containing dexpanthenol, and also improved the symptoms of skin irritation, such as pruritus, erythema, roughness, scaling, and likewise erosion/fissures, after a few weeks [38]. Another study compared the reduction of incidence of moist desquamation with a hydroactive colloid gel versus dexpanthenol; a clear clinical benefit of a hydroactive colloid gel over an oil-in-water emulsion containing 5% dexpanthenol has been shown for the prevention of radiotherapy-induced moist desquamation [39].

Vitamin B_6 (pyridoxine pure crystalline powder or pyridoxine hydrochloride forms) acts as a coenzyme in numerous enzymatic reactions, many of them necessary for the maintenance of healthy skin. A review by Chen et al. [40] concluded that, although there is insufficient scientific evidence, vitamin B_6 in doses of more than 400 mg may improve some of the manifestations of hand–foot syndrome. Pyridoxine could be converted into pyridoxal phosphate in red blood cells, and it acts as a potent antagonist of P2X purinergic receptor, which accelerates the skin barrier repair and prevents epithelial hyperplasia [41].

Biotin B_7 is a water-soluble vitamin that acts as a prosthetic group of carboxylases. In addition to its function as an enzyme cofactor, it participates in embryonic development, cell proliferation, immune functions and metabolism, while pyridoxal participates in regeneration of tetrahydrofolate and in glutathione biosynthesis. Both vitamins play important roles in the energy metabolism. Further progress in biotin function investigation revealed its epigenetic properties and a role in cell signaling and in defense against reactive oxygen species [42,43]. Using a PAMAM G3 dendrimer with measured linkages of nine biotin molecules and ten molecules of pyridoxal phosphate (BC-PAMAM), these authors carried out a study in which managed to reduce inflammation in HaCaT keratinocytes, which opens an interesting perspective for the treatment of skin inflammation [44].

3.2.3. Vitamin C or Ascorbic Acid

Along with vitamin E, vitamin C has been shown to be able to neutralize free radicals. Furthermore, it is essential for the synthesis of collagen fibers, and it plays a protective role for the skin against the erythema produced by the aggression of UV light [45]. For topical use, magnesium ascorbyl phosphate, magnesium ascorbyl palmitate, and ascorbyl tetraisopalmitate formula is used which is more soluble and stable, more easily penetrating the skin.

3.2.4. Vitamin D (Cholecalciferol, Ergocalciferol)

Among other effects, this vitamin intervenes in the differentiation of keratinocytes. The European Cosmetics Directive explicitly bans the use of vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol) in cosmetics; however, calcitriol is used topically to control the proliferation of keratinocytes in psoriasis. Calcitriol is closely involved in the proper maintenance of the calcium gradients in the skin; in addition, it stimulates the formation of antimicrobial effective peptides such as cathelicidins and defensins involved in the inflammatory process in several inflammatory processes. Calcitriol could participate

in the skin defenses, prolonging the self-protection of the skin during the exposure to UVB radiation as it stimulates the heat shock proteins [46,47]. However, a study by Nasser et al. [48], in which treatment with calcitriol ointment was compared with an O/W emulsion in patients undergoing radiotherapy, concluded that topical vitamin D ointment is not superior to a conventional aqueous cream for prevention of radiation-induced dermatitis in women treated with adjuvant radiation for breast cancer [48].

3.2.5. Vitamin E (α-Tocopherol)

Vitamin E is well known for its antioxidant capacity and the ability to counteract free radicals and protect cells against photoaging caused by UV light. In addition, when applied to the skin, it reduces erythema, swelling, lipid peroxidation, and DNA damage [49]. In cosmetics, it is applied in the form of esters (mainly tocopherol acetate); when associated with vitamin C (in the form of ascorbyl phosphate), its protective effect on the skin against damage caused by UV radiation is enhanced. Moreover, vitamin E acetate and sodium ascorbyl phosphate showed that they can be transformed, respectively, into vitamin E and vitamin C and therefore significantly improve photoprotection of sunscreens against free radical formation in viable epidermal layers [49]. Vitamin E analogues can also protect healthy skin against the aggression of radiotherapy treatments [50].

3.2.6. Antioxidants

Antioxidants are essential for protection of cell membranes from lipid peroxidation and capture of free radicals that reduce the skin's antioxidant defenses. It should be remembered that many free radicals are generated with chemotherapy and radiotherapy treatments, so once the therapy is finished, it is necessary to bring the skin back to its natural balance.

The most used antioxidants are superoxide dismutase, a natural enzyme of human skin that needs the presence of selenium and zinc, which can be provided through the diet. These antioxidants are also used as an active ingredient in cosmetics. Glutathione, which is generated from the amino acid cysteine, glutamic acid and glycine, also displays antiradical effect, which similarly requires the presence of selenium and zinc; its topical use to prevent radiodermatitis has therefore been studied [51]. Other antioxidants of interest are N-acetyl cysteine, lipoic acid, grapefruit seed extracts and lycopene for tomato [52].

3.2.7. Hydrophilic Film-Forming Substances

Among the most widely used hydrophilic film-forming compounds in cosmetics is hyaluronic acid. Hyaluronic acid (HA) is a major constituent of the extracellular matrix of the skin. It has demonstrated remarkable rheological, viscoelastic, and hygroscopic properties that are relevant to wound healing [53]. Several studies demonstrated that HA creams can considerably reduce intensity and duration of unwanted reactions during radiotherapy [54,55].

3.2.8. Thermal Spring Waters

The use of thermal spring waters for anti-inflammatory treatment has been endorsed by numerous clinical studies. They are generally mineral–medicinal waters (or natural minerals in their most common denomination) of low or medium mineralization, rich in selenium, zinc, and magnesium, among other minerals and trace elements [56,57]. Several studies have been carried out to demonstrate the mechanisms of action of the spring waters. Research with two thermal spring waters (Avène and LaRoche-Posay) demonstrated that both waters are able to reverse the induction of interleukin-6 and the formation of reactive oxygen species after UVB stimulation, and it seems likely that trace elements such as selenium and zinc are critical for the observed effects [58]. Furthermore, Avène thermal spring water mediated inhibition of TNFα-induced E-selectin and ICAM-1 expression, and this inhibition could be attributable to the suppression of NF-κB transcription factor pathway activation [59]. Additionally, a cream containing an extract obtained from *Aquaphilus dolomiae*, isolated from the deep aquifer of Avène thermal spring water, showed

to be particularly useful for treating pruritus and persistent itch [60]. Others such as Vichy volcanic spring water seem to be capable of repairing the skin barrier, protecting against the aggressions of the exposome through improving antioxidant status and strengthening the immune defenses [61].

Other studies showed that thermal spring waters can have immunomodulatory effects; thus, a study showed that Avène spring water is endowed with an immunomodulatory potential. Avène spring water limits the DC stimulatory capacity of Th1 and Th17 cell responses by impairing their maturation, IL-12 and IL-23 production and accessory cell function [62]; another study with the same spring water showed that mast cells, dendritic cells (DCs) and CD4+ T cells are modulated [63]. The antinociceptive effect of a cream made with thermal water rich in calcium and sulfur derivatives has also been shown [64]. Other recent studies showed that the microbial communities detected in hot springs may be involved on the improvement of skin homeostatic defense linked to the control of its physiological microbiota and innate immunity [65,66], with anti-inflammatory and immunomodulatory effects [67], and in the re-epithelialization of damaged skin or reinforcing the epidermal barrier [68–73]. In addition, other studies showed that skin care with these types of products is very well tolerated, so cosmetic skin care is recommended to minimize skin reactions [74,75].

The interest in the prevention of burns caused by radiotherapy treatment has also led to the formulation of a gel with thermal water that is compared with a cream with trolamine, observing a similar efficacy to the latter in the prevention of burns, although tolerance is better with the thermal spring water gel and the onset of itching occurs at a later stage [76].

Finally, it is worth mentioning that some thermal spa initiatives have been launched to improve the management of chronic alterations and patient education, among which oncological alterations are included [77].

3.2.9. Clays

Clays have antiphlogistic properties and have been used therapeutically since time immemorial. The best-known clays are bentonites, a type of smectite, and kaolin, the common name for the mineral kaolinite [78]. Kaolin can be applied to skin lesions, offering soothing effects, as long as it is kept moist and a gauze moistened with thermal water is applied between the affected area and the clay plaster. Otherwise, when it dries, it is more difficult to remove and can cause discomfort. Green clay from France (montmorillonite) is also used for its soothing and antibacterial properties; in fact, there are experiences in thermal spa centers in which a decrease in skin irritation caused by chemotherapy treatments has been observed, although more studies are needed to confirm these first impressions. For use in cancer patient care, they must be of high purity, with the guarantee that they do not contain heavy metals that could be harmful [79].

3.2.10. Peloids

Peloids are products made from a solid substrate, generally clay or mineral water sediments, mixed with a liquid substrate that is always mineral–medicinal water, from the sea or salt lake. They are also called thermal mud or thermal peloids. They are widely used in spas to treat various dermatological conditions such as dermatitis, psoriasis, burns, etc. There are few studies of its efficacy in the care of alterations derived from oncological treatment, although there are some experiences in spas that indicate that they can be effective in calming itching and reducing erythrose. Their use is supported by their applications in the aforementioned dermatological disorders [80–83].

Additionally, the influence of the skin microbiome on different skin disorders including cancer is increasingly being studied [84,85], and it is being discovered that peloids can modify the skin microbiome. It has been postulated that the actions of the peloids, in addition to the substances that are generated in the maturation process, could also exert

their effect through the modulation of the microbiota through an indirect influence on the immune system [86].

3.2.11. Plant Extracts and Other Botanicals

Various plant extracts have calming and anti-inflammatory effects. The most studied and used extracts are marshmallow (*Althaea officinalis*), roman chamomile (*Anthemis nobilis*), marigold (*Calendula officinalis*), mallow (*Malva sylvestris*), and black elder (*Sambucus nigra*). Others are used for their epithelializing and regenerating properties of the skin, such as centella or gotu kola (*Centella asiatica*), licorice (*Glycyrrhiza glabra*), milk thistle (*Silybum marianum*), mimosa or jurema (*Mimosa tenuiflora*) and comfrey (*Symphytum officinale*) [33].

It is important to consider that, like oils and butters, when these types of extracts (or derived active substances) are used as ingredients in cosmetic formulations for oncological skin care, they must originate from controlled organic farming without pesticides or other substances that can affect oncological skin.

The case of aloe (Aloe vera) is controversial, since despite the fact that its juice or gel has been considered a good pain reliever, anti-inflammatory and healing aid [87], it has been observed that there are people in whom skin reactions to it have occurred, although Bosley et al. [88] suggested that these reactions appeared to be associated with anthraquinone contaminants in the preparation. Likewise, a recent study concluded that the administration of aloe gel to prevent oral mucositis was not more effective than the application of the base of the gel without active ingredient [89]. Another study by Hoopfer et al. [90] drew similar conclusions on the use of aloe extract formulations to reduce the symptoms or severity of skin reactions after treatment with radiotherapy. The recommendations of the nursing guidelines for the management of radiodermatitis do not include them either, since they have not been shown to be more effective than external aqueous phase creams [91,92].

In an open-labeled phase II study, patients with grade 2 or 3 skin toxicity after chemotherapy were treated twice daily with a soap made of oil extracted from *Pistacia terebinthus*; the results showed that this product could be effective and safe in the treatment of skin toxicity induced by cetuximab [93].

Regarding the prevention of radiotherapy injuries, in a review by Hall et al. [94], several plants and botanicals are cited as emergent radioprotectants, including curcumin (*Curcuma longa*) as having antioxidant, anti-inflammatory, and anti-proliferative effects; quininic acid (coffee, cocoa) with antioxidant effects, and decreasing DNA damage; lycopene (*Lycopersicon esculentum*) as antioxidant, peroxidation inhibitor, and free radical scavenger; rutin (a bioflavonoid from different plants and extracts as *Ruscus aculeatus* or *Prunus avium*) as antioxidant; hemocyanin (*Rapana thomasiana*) as radiomitigator; black tea extract (*Camellia sinensis*) as free radical scavenger; silymarin (*Silybum marianum*) as anti-apoptotic agent, and reducing DNA damage. This author also considers other emerging therapies as the use of genistein (antioxidant and anti-inflammatory), manganese superoxide dismutase-plasmid liposome (MnSOD-PL) gene therapy (antioxidant, decreases free radical production and inflammatory cytokine release), caffeine (antioxidant and anti-inflammatory), and tetrahydrobiopterin, an enzymatic cofactor involved in neurotransmitters and nitric oxide synthesis (modulation of free radical-induced damage), among others [94]. Glutamine, a non-essential amino acid that has been widely studied for its potential beneficial effects in a number of pathologies associated with radiation toxicity including mucositis, dermatitis and esophagitis, is cited in the same review [94]. Likewise, Wang et al. [93] conducted a double-blind, randomized controlled study to assess the efficacy and safety of topical soaks of a mixture of Chinese plants (*Astragalus radix*, *Angelica sinensis*, *Gerainii herba*, *Arnebiae radix*, and *Cartami flos*) for hand–foot skin reaction induced by molecular targeted anticancer drugs, showing that the product alleviated the symptoms [95]. Another study with a cream made with olive oil and *Silybum marianum* applied after chemotherapy or radiotherapy sessions increased skin hydration. The authors postulated that the cosmetic products for oncological patients improve and restore the adequate level of skin hydration, aid in repair of the epidermal barrier, soothe irritations,

accelerate the healing of pathological lesions and prevent their development, and may delay the occurrence of adverse effects, which prevent further treatment [96].

3.2.12. Algae and Derivatives

Algae have been used since immemorial times for their important applications in health, both in food and in the preparation of drugs and cosmetics. Some algae compounds may be of interest in cancer patient care, mainly those that have moisturizing, demulcent, and antioxidant properties. Among them are sulfated polysaccharides, fucoidan, laminaran as antioxidants; astaxanthin and phlorotannins as anti-inflammatories; alginates and carrageenans as moisturizing and protective agents; fucoxanthin that promotes repair of the protein filaggrin involved in the epidermal barrier; and mycosporine-like amino acids (MMAAs) for their potential use in sunscreens. It is also worth mentioning ectoine, an osmoprotectant present in halophilic bacteria that improves skin inflammation and is currently being investigated for the treatment of moderate atopic dermatitis [32]. In a review carried out by Pereira [97,98], the moisturizing, anti-inflammatory and calming effects (among others) of the extracts or bioactive compounds (proteins, phycobilins, phytosterols, sulfated polysaccharides, phlorotannins, etc.) of a large number of algal species of marine origin, either Rhodophyta, Phaeophyceae or Chlorophyta, which reveals the great potential of this type of natural resources in skin care [97,98].

There are already algae-based products on the market (e.g., INCI name *Ascophyllum nodosum* (Phaeophyceae) extract; *Asparagopsis armata* (Rhodophyta) extract) that help prevent radiodermatitis; some emulsions have been tested for this type of application, showing preventive activity and reducing the symptoms of itching and scaling [99].

3.2.13. Other Compounds of Interest

In this review on active ingredients for cosmetic use in cancer patient care, it is important to mention the ingredients of sunscreens, which are essential for protecting the skin against the most harmful solar radiation. Sunscreens with inorganic filters (also called physical filters) are recommended, because they form a barrier on the epidermis that reflects radiation and does not penetrate the skin. The most used components are titanium dioxide and zinc oxide. We can also include so-called biological filters, which are antioxidants and free radical scavengers, among which are vitamin E and some of the botanicals mentioned earlier.

Among the moisturizing compounds, in addition to those mentioned, is urea, which is used in creams in concentration of 5–10% to prevent and improve cutaneous xerosis [100]. Emollients with urea have also been shown to be effective in preventing hand–foot syndrome induced by sorafenib [101,102].

An asset of interest that has also been used in creams for the prevention and treatment of dermatitis is β-Glucan. β-Glucans are polysaccharides which are found in cereals (barley and oat), yeast, mushrooms and algae, with immunomodulatory properties, among others [103–105]. Emulsions containing β-Glucan have been used to prevent radiodermatitis, causing an increase in skin hydration and reduction of itching [99].

Another study where patients were prescribed moisturizers to prevent radiation-induced damage with measurement of hydration using biometric techniques (Corneometer) showed that in all cases it is possible to reduce the symptoms of skin toxicity. The products used included product A with pure vitamin E; product B with Omega-3,6,9; product C with natural triglycerides–phytosterols, product D with beta-glucan and sodium hyaluronate; and product D with *Vitis vinifera* extract, the latter two being the most effective ones [106].

There are few studies on the use of growth factors, although some describe their effects on healing, which seems to be a promising area of research. In a multicenter prospective cohort study of 1172 patients undergoing radiotherapy for variable malignancies, an EGF-based cream was used to assess the effectiveness and safety in the prevention of radiation dermatitis in patients with cancer. The cream contained a 0.005% recombinant human EGF with additional ingredients such as ceramide, hyaluronic acid, Inca omega oil (*Plukenetia*

volubilis seed oil), *Portulaca oleracea* extract, mango butter, and meadowfoam oil. The results suggested that a recombinant human EGF-based cream could be safely applied to prevent or alleviate radiation dermatitis [107]. It may also be of interest to use copper peptides for improving wound contraction and epithelization [108].

Taking into account the important role that calcium plays in maintaining the epidermal barrier [109], products that contain calcium in their formulation may be appropriate, constituting a possible area of research; there are already patents on the market (patent US8535904B2) that also include plant extracts. Other studies show that the use of sucralfate with Cu and Zn salts can delay the onset of radiodermatitis, although more studies are needed that compare results with the control group [110].

Dressing films are also of interest in both prophylaxis and the treatment of radiotherapy-induced skin reactions. Silicone dressings are suitable for patients with fragile skin and do not cause tissue trauma during removal [111]. However, for patients with moist desquamation it is important to minimize excess of moisturizing and skin maceration, so another dressing was launched into the market to prevent this problem (Mepitel). Mepitel dressing is vapor permeable, which allows excess moisture to evaporate through the dressing; it is therefore intended for superficial wounds in which moist environment promotes healing. It is also used to protect fragile and sensitive skin from microbial contamination, fluid penetration and other external contamination [112,113].

Another research by Mepilez Lite (self-adhesive dressing consisting of a thin flexible sheet of absorbent hydrophilic polyurethane foam bonded to a backing layer of water vapor permeable polyurethane film) in radiation-induced erythema concluded that compared with aqueous cream, Mepilex Lite dressings did not significantly reduce the incidence of moist desquamation, but did reduce the overall severity of skin reactions [114].

Calcium alginate dressings are also widely used in the management of severe bio-radiation dermatitis, and their use allows to improve treatment tolerability and reduces treatment interruption [115].

Silver foam dressing, used in the treatment of burns and ulcers, exerted antibacterial activity against wound bacteria, promoted wound healing and shortened recovery time, effectively relieving the pain of patients [116]. When used in oncology, it proved to be effective in reducing radiation dermatitis, apparently because of its antibacterial properties [117]. Nevertheless, another study conducted by Aquino-Parsons [116] concluded that silver leaf nylon dressing use has not been effective in reducing the incidence of moist inframammary desquamation, although itching was reduced 1 week after radiotherapy completion [118]. Later studies showed that nano-silver medical antibacterial dressing combined with high-flow oxygen therapy can reduce inflammation, relieve pain and accelerate the healing of superficial wounds, as well as improve the frequency of dressing changes in patients [119].

Finally, it is necessary to mention medications for frequent topical use that contain ingredients to reduce inflammation despite not being dermocosmetics; this is the case with corticosteroid creams and Biafine, one of the most used creams whose main asset is trolamine, but which has not been shown to be more effective than cosmetic creams [120]. Later studies showed that Mepitel Film is superior to Biafine cream in reducing the severity of acute radiation-induced skin reactions and moist desquamation incidence in head and neck cancer patients [121]. And also should be mentioned Bimatoprost, a prostaglandin analogue, widely used to treat hypotrichosis of the eyelashes by promoting the growth of longer and thicker lashes [122].

4. Thalassotherapy for Improving Well-Being and Post-Oncology Recovery

Thalassotherapy is the combined use of marine elements (water, algae, mud and climate), in a marine environment for healing and well-being improvement purposes [123]. In 2010, Gutenbrunner et al. offered a proposal for a worldwide definition of health resort medicine, balneology, medical hydrology and climatology; even though the authors do not mention the word “thalassotherapy”, Climatotherapy (the use of climatic factors) is included as a part of Health Resort Medicine [124]. Later on, Maraver et al. suggested

including the use of seawater and its peloids (thalassotherapy), including its modalities, full-body or local baths, showers, inhalations, irrigations and peloid packs, and its agents, seawater, marine peloids and sand, among others [125]. Recently, other authors mentioned the "thalassotherapy" concept in journal articles or book chapters, despite the fact that they are not specialized publications in the use of the sea water [97,126]. To offer thalassotherapy, the establishment must be on the edge of the sea, have adequate facilities and duly qualified medical and technical personnel. Although the use of seawater for healing purposes is an ancient practice, the main development of thalassotherapy centers took place in France in the 20th century, which, together with research on the properties of seawater and derivatives and its effects on health, led to thalassotherapy becoming a cure financed by health systems in some European countries. The main therapeutic effects are linked to functional rehabilitation, joint pathology, stress or fatigue, some dermatoses, circulatory pathologies and, additionally, sports rehabilitation [123].

4.1. Sea Water: Effects on Skin

The composition of seawater is similar in all oceans and seas, with variations in component concentration. Table 1 shows the average composition of seawater in the world, expressed in mg/L [127].

Table 1. Seawater composition: major ion concentration (mg/L) in seawater around the world.

Parameter	Worldwide Average
Chloride, Cl^-	18,980
Sodium, Na^+	10,556
Sulphate, $SO_4{}^{-2}$	2649
Magnesium, Mg^{+2}	1272
Calcium, Ca^{+2}	400
Potassium, K^+	380
Bicarbonate, $HCO_3{}^-$	140
Bromide, Br^-	65
Borate, $H_2BrO_3{}^-$	26
Strontium, Sr^{+2}	13
Fluoride, F^-	1.0
TDS	34,482

(TDS: Total Dissolved Solids).

Seawater is very well known for its curative effects in the treatment of skin diseases such as eczemas, dermatoses, psoriasis, respiratory problems such as nasopharyngeal inflammations, gynecological diseases such as vaginitis, and other infections of the external genital organs. For skin care, it has been used as a moisturizing agent; it also regularizes the sebaceous production, avoiding the consequent formation of scaling of the scalp (dandruff). It is worth to mention the important role of seawater in the absorption of saline and metallic ions, favoring the excretion of toxic residues and a certain oxygenation of tissues [98].

Seawater has been shown to have important effects on skin hydration and regeneration, although there are few scientific studies, since mostly testimonials are available. Most of the studies focus on the hypersaline water of the Dead Sea; a few of them examine the seawater of the Atlantic coasts and others do the deep seawater.

From the studies of the last ten years, those carried out by Yoshikawa et al. [128,129] deserve to be cited. In the first study, the effects of sea water and its main components on experimental irritant contact dermatitis induced by sodium lauryl sulphate (SLS) cumulative irritation were investigated, and it was concluded that the effect of sea water may be attributed to skin barrier preservation by NaCl and KCl, and an emollient effect by NaCl [128]. In the second study, the effects of three types of mineral water with NaCl and KCl with different concentrations (500 nM NaCl + 10 nM KCl; 250 nM NaCl + 10 nM KCl, and 250 nM NaCl + 50 nM KCl) were studied in order to assess the most effective water concentration to prevent disruption of skin barrier. The authors suggested that mineral

water with 250 mM of NaCl and 50 mM of KCl may be useful as adjunctive therapy in atopic dermatitis and other chronic dermatitis [129].

Bathing in the Dead Sea waters (with an average concentration of 280 g/K) has been extensively studied: magnesium salts are known to bind water, influence epidermal proliferation and differentiation, and enhance permeability barrier repair [130]. In a study by Proksch et al. [131], immersion in magnesium-rich salt solutions from the Dead Sea was investigated (Mavena® Dermaline Mg Dead Sea). The experiment consisted of 15 min bathing in a solution containing 5% Dead Sea salt daily for 6 weeks; transepidermal water loss (TEWL), stratum corneum hydration, and skin redness in atopic dry skin (xerosis) were measured, concluding that bathing with Mavena® Dermaline Mg Dead Sea salt solution, owing to its high content of magnesium ions, enhanced stratum corneum hydration, improved skin barrier function and reduced skin roughness and inflammation [131].

On the other hand, as has been mentioned, in recent years, the effect of deep-sea water on different skin disorders has been studied. A study in NC/Nga mice model carried out by Bak et al. [132] with mineral water from deep-sea bedrock, rich in minerals such as Ca, Mg, Na, K, Fe, and others, investigated the preventive effects of natural deep-sea water on developing Atopic dermatitis, concluding that this water inhibits the development of atopic dermatitis-like skin lesions [132]. Lee et al. [133] studied, in a skin equivalent model, Jeju lava sea water, showing that this water (rich in sodium, magnesium and calcium) increased the CD44 (hyaluronic acid receptor) which is related to skin hydration; the authors conclude that the Jeju lava sea water may help to improve skin hydration [133].

Moreover, Chun et al. [134] studied the effect of deep-sea water (high levels of Mg and Ca) on lipopolysaccharide (LPS)-induced inflammatory response in RAW 264.7 macrophage cells and determined that this water suppressed inflammatory responses via the MAPK/AP-1 and NF-κB Signaling Pathway [134]. Recently, Lee et al. [135] evaluated the effects of mineral-balanced deep-sea water (DSW) on Atopic dermatitis-like skin damage both in vitro and in vivo. The results showed that DSW is effective in the treatment and prevention of atopic-type skin lesions. The mechanism of action involved seems to be the suppression of the expressions of proinflammatory chemokines and cytokines, as well as the inhibition of histamine and IgE production underlying the STAT1 and JNK1/2 signaling pathways. In addition, other mechanisms involved are the positive regulation of filaggrin and the recovery of involucrin expressions and the inhibition of IL-4 production, which help restore skin health. The authors suggested that mineral-balanced DSW may be useful in preventing and treating skin inflammation caused by skin disorders, including atopic dermatitis [135].

On the other hand, Carbajo et al. [136] revised the mechanism of action specific to saline waters; when topically administered, this water rich in sodium and chloride penetrated the skin where it was able to modify cellular osmotic pressure and stimulate nerve receptors in the skin via cell membrane ion channels known as “Piezo” proteins. They postulated that the effects of salt mineral waters are mediated by mechanisms linked to the concentration and type of salts involving cellular osmosis-mediated activation/inhibition of cell apoptotic or necrotic processes, and in turn, this osmotic mechanism modulates the mechanosensitive piezoelectric channels [136].

Another aspect of great interest in the use of seawater is wound healing. In a study carried out by Huynh et al. [137], it was demonstrated that short-term rinsing with NaCl promoted hGFs migration and increased the expression of extracellular matrix as well as cytoskeletal proteins; the authors concluded that these data strongly support the empirical use of NaCl mouth rinse [137]. Cantore et al. [138], in a single-blinded randomized controlled trial, studied the effects of sea salt mouth rinse on subjects undergoing oral surgery; the results showed an appreciable wound healing in the experimental group when compared to the control, with no reported adverse effects [138]. Another study demonstrated that the use of a sea salt-based mouthwash in daily oral hygiene reduces the bacterial levels of *Streptococcus mutans* linked to the combined action of xylitol and lysozyme, together with the action of sea salt [139]. In addition, another research showed that soaking in 7% of table salt concentration can significantly accelerate the wound healing process compared to the

control group, with a decrease in wound diameter on the 3rd day and complete healing on the 7th day [140].

4.2. Procedures and Techniques of Thalassotherapy

Seawater is applied to the body using different respiratory (aerosol) or topical techniques such as bathing and pressure techniques, whether partial (legs and feet, arms and hands) or full body, as well as algae and marine mud applications. The so-called complementary techniques are also used, which include saunas and steam baths, mechanical techniques, electrotherapy or different types of massages. The most used techniques are summarized in Table 2 and some examples are shown in Figure 1A–C.

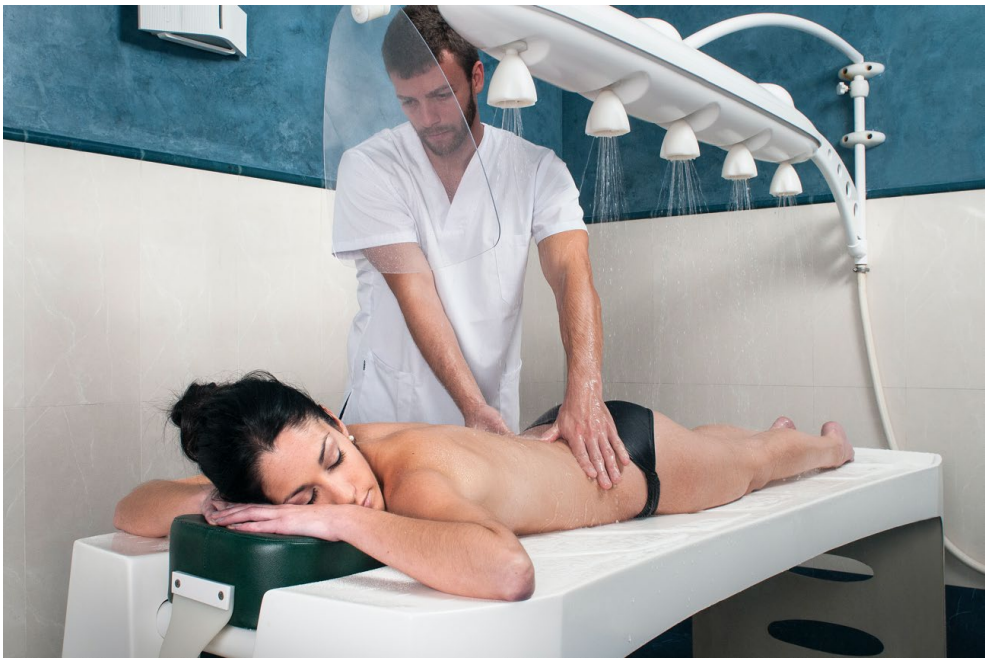
Table 2. Procedures and techniques of thalassotherapy.

Thalassotherapy Techniques	Other Complementary Techniques
Aerosols	Sauna and steam baths
Bubbling bath	Pressotherapy
Hydromassage bath	Electrotherapy
Underwater massage	Thermo- and Criotherapy
Jet showers	Lymphatic draining
Affussion showers	Massages (therapeutic, antistress, etc.)
Vichy showers	Osteopathy
Scottish showers	Oriental massages (Shiatsu, Thai, etc.)
Phlebologic path	Yoga, Tai-chi and others
Hand and Foot Baths	Reeducational therapies
Hydrotherapy pool	Nutritional therapies and counselling
Seaweed wrappings	Water therapies: Watsu, Ai Chi, etc.
Marine mud applications	Aquagym, Aquabike, etc.

(**A**)

Figure 1. *Cont.*

(**B**)



(**C**)

Figure 1. Thalassotherapy techniques: (**A**) Hydromassage bath; (**B**) jet shower; (**C**) Vichy shower (Courtesy of Talaso Atlántico, Spain).

Added to this is the marine environment, used in the treatment of non-allergic bronchial asthma and also in psoriasis [141,142] and, in certain cases, the use of heliotherapy [143].

4.3. Thalassotherapy and Post-Oncological Recovery

There is sufficient scientific evidence on the benefits of hydrotherapy techniques with seawater and mud or marine mud in functional rehabilitation [144–148]. Hydrotherapy treatments carried out with ordinary water show the benefits in the rehabilitation of different traumas and joint pathologies, as well as hydrothermal techniques carried out with thermal

spring water [149]. Some studies whose conclusions could be extrapolated to rehabilitation and recovery after an intervention or oncological therapy are described below.

Dalenc et al. [150], in a randomized, multicenter controlled study 1–5 weeks after completing radiotherapy, investigated the efficacy of post-treatment hydrotherapy as supportive care for management of persistent/long-lasting dermatologic adverse events (dAEs). Both groups received supportive care and the intervention group received 3 weeks of specific hydrotherapy. The study demonstrated that a 3-week supportive care program with hydrotherapy initiated after completion of radiotherapy is an effective and safe supportive treatment and is of significant benefit to these patients resulting in an improvement of dAEs, therefore reducing the impact of breast cancer and its treatment on overall physiological well-being and dermatological and health-related QoL [150].

Likewise, there are experiences of care and recovery of cancer survivors in thermal spa centers in which the main base is also the hydrothermal techniques and the effect of the minerals and trace elements of the mineral–medicinal waters in the organic balance [151,152]. Thus, in 2005, Strauss-Blachet et al. [153] conducted a study on the efficacy of adding spa therapy to a rehabilitation program after breast cancer. One hundred forty-nine women, 32 to 82 years, participated in a study 3 to 72 months after breast cancer surgery; quality of life (QoL, EORTC QLQ-C30), anxiety, and depression (HADS) were measured 2 weeks before, at the end, and 6 months after rehabilitation; the tumor maker CA 15-3 was measured at the beginning, end, and at 6-month follow-up. Patients received an individualized rehabilitation program incorporating different hydrothermal techniques such as carbon dioxide baths and mud packs, as well as other complementary ones such as manual lymph drainage, massages, exercise therapy, psychological counseling, and relaxation training. The results showed that quality of life and mood improved significantly, the greatest short-term improvements were observed for mood-related aspects of quality of life, the most lasting improvements detected for physical complaints (e.g., fatigue) [153].

Another study on oncological patients showed that spa therapy increased clusterin serum concentration (a stress-associated cytoprotective glycoprotein involved in many physiological and pathophysiological processes which is up-regulated by various apoptotic triggers in many cancers and neurodegenerative diseases). Authors suggested that this result is probably due to the positive effects of balneotherapy; however, the sample was very small and further research is required [154].

Galvez et al. revised the effects of balneotherapy considering it a clinically effective complementary approach in the treatment of low-grade inflammation- and stress-related pathologies; the physiological effects are exerted through both physical mechanisms—mainly linked to heat therapeutic effects—and chemical and biological properties of the agents. Therefore, thermotherapeutic effects are the basis of these treatments with a range of temperatures from 38 to 42 °C. It is well known that severe heat stress leads to cellular damage and cell death, and mild heat stress induces heat shock response which protects cells and organisms from severe damage, allows resumption of normal cellular and physiological activities. In this review, the authors postulate that hormesis can play a role in the biological effects of balneotherapy, and these effects can be related to non-specific factors such as heat—which induces the heat shock response, and therefore the synthesis and release of heat shock proteins—and also to specific biochemical components such as hydrogen sulfide (H_2S) in sulfurous water and radon in radioactive water [151].

Kwiatkowski et al. [155,156] studied the improvement of the quality of life of breast cancer survivors with 2 weeks of physical and educational intervention in thermal spa centers, concluding that balneotherapy is effective in improving the quality of life and that the effects are maintained for at least 6 months, recommending a second intervention after that time.

Furthermore, another study investigated the effectiveness of a warm-water footbath on relieving fatigue and insomnia problems in patients undergoing chemotherapy. Two groups were investigated (control and experimental group) in a longitudinal study design. Women diagnosed with gynecologic cancer and receiving a 4-series platinum chemotherapy

regimen were recruited and then followed up for 6 months. They completed fatigue and insomnia items on the 1st, 2nd, 4th, 7th, and 14th day after each scheduled chemotherapy. Participants in the experimental group soaked their feet in 41 °C to 42 °C warm water for 20 min every evening, starting from the eve of receiving the first chemotherapy, whereas participants in the comparison group did not do so. The results showed that participants in the experimental group reported a significant reduction in fatigue and improvement in sleep quality from the second session of chemotherapy and continued to improve during the study period [157].

Recovery post-breast cancer was also studied; Cantarero-Villanueva et al. [158] carried out a study with 40 women aged 29–71 years with stage I–III breast cancer who reported arthralgia. The hydrotherapy intervention consisted of 24 sessions 3 days a week over 2 months; each session included 5 min of warm-up, 15–20 min of aerobic exercise, 15 min of mobility exercise, and 20 min of recovery techniques. The results showed that participants experienced a decrease in pressure pain threshold measured in neck, hand, shoulder and leg, as measured by algometry pressure and waist circumference; body mass index and cancer-related fatigue did not show significant improvement [158].

Later on, a randomized controlled trial was conducted by the same research group in breast cancer survivors. They compared two groups of patients: the experimental group followed aquatic exercise in deep water pool and the control group followed the usual care; the intervention group attended aquatic exercise sessions 3 times per week for 8 weeks in a heated deep swimming pool (sessions were 60 min in duration: 10 min of warm-up, 40 min of aerobic and endurance exercises, and 10 min of cool-down exercises). Patients allocated to the usual care group followed the oncologist's recommendations in relation to a healthy lifestyle. Values for fatigue (Piper Fatigue Scale), mood state (Profile of Mood States), and abdominal (trunk curl static endurance test) and leg strength (multiple sit-to-stand test) were collected at baseline, after the last treatment session, and at a 6-month follow-up. Immediately after discharge, the aquatic exercise group showed a large effect size in total fatigue score, trunk curl endurance, and leg strength, but negligible effects in vigor, confusion, and disturbance of mood. At the conclusion of the 6-month follow-up period, the aquatic exercise group maintained large to small effect sizes in fatigue scores, multiple sit-to-stand test, and trunk curl static endurance and negligible effects for the fatigue severity dimension and different scales of the Profile of Mood States. The authors concluded that an aquatic exercise program conducted in deep water was effective for improving cancer-related fatigue and strength in breast cancer survivors [159].

Mourgues et al. [160], in a multicenter randomized controlled trial with and intervention group that included women in complete breast cancer remission without contraindication for physical activities or cognitive disorders, undergoing spa therapy and nutritional consultation, confirmed that spa treatment is a cost-effective strategy to improve resumption of occupational and non-occupational activities and the abilities of women in breast cancer remission [160]. Finally, it is worth mentioning that in a review carried out by Reger et al. [161], several studies are detailed showing the efficacy of aquatic hydrotherapy for the improvement of lymphedema.

Therapies in the Dead Sea are an example of dermatological treatments with highly mineralized waters; in addition to treating psoriasis and atopic dermatitis, skin recovery treatments have been carried out on cancer patients. In a phase II study, researchers compared the outcomes of 24 treated patients with Dead Sea water and 30 conventionally treated patients matched for age, tumor site, and type of treatment. The Dead Sea products comprised a mouthwash solution (Lenom®) and a skin cream (Solaris®) used three times daily for 1 week before, during, and up to 2 weeks after completion of radiotherapy. Mucositis and dermatitis were evaluated using common toxicity criteria. The two Dead Sea products were shown to decrease skin and mucosal toxicity in head and neck cancer patients receiving radio-chemotherapy [162].

It is also worth mentioning the studies carried out with thalassotherapy treatments in fibromyalgia in which an improvement in fatigue and sleep disturbances were observed,

aspects that are common to some of the side effects that occur after oncological therapies. These results can show the beneficial use of the thalassotherapy for the rehabilitation of cancer survivors [163].

Another study attempted to demonstrate the effects of the combination of thalassotherapy treatments (hydrotherapy with sea water) with sleep management and its influence on sleep, mood states, well-being, health outcomes and cognitive (sustained attention) and physical capacities in healthy middle-aged workers. Despite a short period of treatment (3 days) and a small group (11 participants), the results showed beneficial effects of 3 days of thalassotherapy care combined with sleep management for mood states, well-being, health outcomes, and cognitive and physical capacities in the general working population. The authors suggested that hydrotherapy care (3 days with two 2-h sessions of care) and sleep management resulting in increased total sleep time (TST) in the second night may explain immediate positive effects on self-reported psychological outcomes and objectively measured vigilance attention but also delayed positive effects on lower limb flexibility. It also would be interesting to evaluate the effectiveness of thalassotherapy in the prevention and management of professional burnout that has been previously described as associated with anxiety and sleep disorders [164]. In addition, thalassotherapy with deep-sea water was shown to be effective in recovery from fatigue and muscle damage [165].

As mentioned above, some thermal centers have implemented programs for post-cancer patient care; such is the example of Avène, La Roche-Posay, Balaruc-les-Bains, Saint-Gervais, La Bourboule or Uriage, some specialized in lymphedema such as Luz-Saint-Sauveur. Others focus on programs for the treatment of chronic diseases [166], which may also be of interest for cancer patient care.

Although there are no publications on the results of treatment programs for post-cancer patients, thalassotherapy centers have also joined this initiative. Table 3 lists some of them, which are mainly located in France.

Table 3. Post-oncologic care programs in thalassotherapy centers.

Thalassotherapy Center	Program Web Page
Thalasso Deauville	https://www.thalasso-deauville.com/en/12-day/125-post-cancer-stopover.html (accessed on 25 November 2022)
Atlanthal Hotel & Thalasso	https://www.atlanthal.com/es/curas/178-thalasso-post-cancer.html (accessed on 25 November 2022)
Roscoff-Hôtel Valdys, Beau Rivage Thalasso & Spa	https://www.thalasso.com/destination/roscoff (accessed on 25 November 2022)
Hôtel Thalasso & Spa Emeria Dinard	https://www.emeriadinard.com/ (accessed on 25 November 2022)
Thalasso Concerneau	https://www.concarneau-thalasso.com/ (accessed on 25 November 2022)
Côte Thalasso Banyuls-sur-Mer	https://www.cote-thalasso.fr/banyuls-sur-mer/cures (accessed on 25 November 2022)
Hotel Talaso Atlántico	https://www.talasoatlantico.com/es/talaso.html (accessed on 25 November 2022)

Another aspect of great interest in the care of cancer survivor patients is physical activity (either through active exercise or relaxation activities such as yoga) and adequate nutrition [167–171]. In whose programs, thalassotherapy centers can also be main actors. Likewise, although scarce, there are studies on the influence of phototherapy for the immunological improvement of cancer patients [172], an aspect that may be of interest in thalassotherapy centers where heliotherapy is applied.

On the other hand, nowadays, more and more importance is assigned to healing environments (understanding that the environment of a thalassotherapy center has healing effects), highlighting cures in natural environments; by way of example, the studies by Ray et al. [173] assert that the natural environment can counteract attentional fatigue in recently diagnosed breast cancer survivors, and therapeutic landscapes can reduce the state of

anxiety, improving the health of survivors. Likewise, Liamputtong and Suwankhong [174] also described the importance of healing landscapes for the "the emotional healing".

5. Conclusions

Cutaneous anticancer toxicities may occur at any time during treatment, including long after discontinuation of treatment in the case of radiation and immunotherapy; these toxicities can have a major impact on HRQL [175] as well as on the perception of the disease. There is currently a general consensus that it is necessary to advise patients on skin care before, during, and after treatment. Cosmeceutical care is therefore essential to minimize cutaneous toxicities and their manifestations, as well as the reactions derived from radiotherapy. Although the scientific literature is scarce, several studies have shown that certain active substances can be included in cosmeceuticals to calm and regenerate the epidermal barrier damaged by oncological therapies, as well as be effective as emollients, moisturizers and protectors against external aggressions. Vegetable oils and butters, vitamins, antioxidants, clays, peloids, thermal spring waters, various algae and plant extracts, among others, have been shown to be useful in alleviating the side effects and skin sequelae of oncological treatments. However, more clinical studies are necessary to show their efficacy and determine in which cases they can be used.

On the other hand, thalassotherapy, through the use of seawater and other marine resources, is considered a natural therapy which is applied in healthy environments and has proven to be effective in the rehabilitation of various traumas and the treatment of certain skin conditions. For this reason, it can be a resource of great interest for the well-being of post-cancer patients' recovery through providing an adapted methodology for the development of specific cures that attempt to reduce fatigue and stress and increase vitality and quality of life, improving the health of cancer survivors and facilitating their rehabilitation process.

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