We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,300

Open access books available

172,000

International authors and editors

190M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Chapter

Topical Moisturisers for the Management of Psoriasis Vulgaris

Dalibor Mijaljica, Fabrizio Spada and Ian P. Harrison

Abstract

The aim of this chapter is to provide an overview of basic and tailored topical moisturisers and discuss how and why they form the backbone for the management of psoriasis. Our discussion begins by describing the main characteristics of psoriasis and by indicating how alterations in the skin's integrity and barrier function contribute to the initial development of psoriasis and subsequent changes in psoriasis phenotype. Next, we address the evolution of topical moisturisers to ever more sophisticated and beneficial products, and describe the key biophysical effects exerted on the psoriatic skin by their active ingredients, as well as the myriad benefits offered by fundamental and specialty ingredients. Furthermore, we delineate how topical moisturiser formulation modalities can help to improve compromised skin barrier function and to alleviate the symptoms of psoriasis, cosmetically and/or therapeutically as well as discuss the associated concerns and challenges encountered along the way.

Keywords: active, excipient, formulation modality, ingredient, management, basic moisturiser, tailored moisturiser, psoriatic plaque, skin barrier

1. Introduction

As a common and complex skin condition (Section 1.1), the root causes of psoriasis begin inside our body [1], making it far more than just skin deep. The fact that psoriasis affects the skin's hydration, barrier structure, function and integrity (Section 1.2) [2] means that a combination of several management strategies (Section 1.3) is usually required in order to alleviate associated symptoms [3, 4]. Topical moisturisers (Section 1.4) represent *the* first-line defence strategy that forms the backbone of psoriasis management by reducing and relieving both dryness and the associated itch-scratch cycle, enhancing skin hydration, and strengthening barrier function by influencing its subsequent repair and recovery [5–7] and thus, improving underlying psoriatic symptoms and overall quality of life (QoL) [2].

1.1 Psoriasis at a glance

Psoriasis is a chronic, inflammatory, non-contagious and relapsing skin condition with a strong genetic predisposition and autoimmune pathogenic traits [8]. While psoriasis can present at any age, it most commonly appears for the first time between

the ages of 15 and 25 years, and then again between ages of 57 to 60 years [9], affecting both men and women equally [3, 10]. The worldwide prevalence is about 2–5% on average, but varies according to regions and ethnicities [3, 10]. In general, the higher or lower the latitude, the higher the prevalence; people from Asian and African countries are less prone to psoriasis than people from regions further from the equator such as Northern Europe, North America and Australia [10, 11].

The term 'psoriasis' encompasses several distinct clinical forms of the disease, the most common and well-known of which is psoriasis vulgaris, also known as plaque psoriasis. Given the ubiquity of psoriasis vulgaris relative to other forms of the disease, our focus in this chapter will be on this particular form.

The pathogenesis of psoriasis is multifactorial, with genetics being a primary contributor, especially in those with early onset of the disease. Many of the candidate genes are either involved in antigen presentation, immune cell signalling and activation, or skin barrier function, suggesting an intricate interplay between dendritic cells, T cells and the main skin cell type, known as keratinocytes [12, 13]. Several other factors can either initiate and/or exacerbate psoriasis flare-ups. These include: (a) trauma induced by various physical, chemical and inflammatory skin disruptions (e.g., abrasions, incisions, rubbing); (b) bacterial (e.g., *Staphylococcus aureus*) and viral infections; (c) the use of certain medications or drugs (e.g., lithium, blood pressure reducing medications); (d) poor lifestyle habits such as excessive alcohol consumption and smoking; and (e) stress [10, 13, 14].

Psoriasis manifests in several distinct clinical forms according to appearance and the body part affected but predominantly presents as well-demarcated salmon pink plaques (dry and piled up skin cells) and/or lesions with silvery-white scale, accompanied by skin tightness, itchiness, a burning sensation and, in severe cases, even bleeding [1, 3, 10, 13, 15]. These plaques typically appear in a symmetrical distribution and affect extensor areas such as the elbows, knees, lower back, limbs, the scalp, tips of the fingers and toes, palms and soles, the fingernails and toenails, and occasionally, the genitals [3, 10, 13–15]. Patients suffering from psoriasis are frequently categorised into two main groups: (1) mild or moderate psoriasis (most common category; affecting 3–10% of total body area) and (2) severe psoriasis (rare; affecting more than 10% of total body area). Such categorisation primarily depends on the following three aspects: (1) the clinical severity score (also known as Psoriasis Area Severity Index—PASI) of the plaques, which is an assessment tool based on the degree of plaque redness, thickness, itchiness and scaling; (2) the percentage of affected body surface area (BSA); and (3) patient QoL [13, 14, 16].

As alluded to in the introduction, psoriasis is not only a skin condition, it also involves multiple organ systems (e.g., cardiovascular, hepatic, respiratory and haematological) and people with psoriasis regularly display a broad spectrum of symptoms and significant co-existing conditions such as obesity, cardiovascular disease, non-alcoholic fatty liver disease, cancer, diabetes and metabolic syndrome, with rates being especially elevated in those with more severe psoriasis [1, 13]. For example, diabetic patients with psoriasis appear to be more likely to require pharmacological management and suffer from micro- and macrovascular diabetes complications than diabetic patients without psoriasis [17].

1.2 Skin barrier alterations in psoriasis

The barrier function of the skin resides in the outermost layer of the epidermis, known as the stratum corneum (SC) and is linked to the protein enriched corneocyte

(dead keratinocytes lacking vital cellular organelles) layers and the intercellular membrane lipid matrix mostly composed of ceramides, cholesterol and free fatty acids [18–21]. Corneocytes are continually and efficiently replaced to maintain skin hydration, flexibility and structural integrity, and to repair any perturbation and damage [21]. Continuous exposure to environmental insults such as harsh climatic conditions (e.g., extreme temperatures, wind) and chemicals (e.g., harsh detergents and soaps) can significantly impact the skin's structural and functional properties, which in turn can cause acute or chronic damage of the skin barrier resulting in unfavourable changes in skin morphology and physiology over time [19, 20, 22–24].

Skin dryness is a major underlying problem of the dysfunctional psoriatic skin barrier as it reflects an abnormal and defective desquamation (shedding) process, where corneocytes are shed as visible scales, causing the cosmetically unattractive rough texture associated with dry skin and excessive transepidermal water loss (TEWL), ultimately leading to discomfort and itchiness. Such compromised, dry and fragile skin that is unable to efficiently bind and hold water is also susceptible to the penetration of irritants, allergens and microorganisms that can result in irritation, inflammation and infection [3, 10, 13–15, 19, 20, 22–24].

Normally, healthy skin cells mature and are shed from the skin's surface every 28 to 30 days [25]. However, when psoriasis develops, these skin cells mature much faster, usually in 3 to 6 days, and subsequently move to the skin surface. Due to such a rapid turnover of skin cells, it is possible that even live and healthy cells can reach the surface and accumulate with the dead cells. Instead of being shed, the skin cells pile up, causing the development of thick plaques that are characteristic of psoriasis [14]. There are two main schools of thought as to the exact pathological process that leads to the development of such psoriatic plaques, however, neither of these can stand independently from each other. The first considers psoriasis primarily as an unregulated condition of excessive growth and regeneration of skin cells, characterised by abnormal keratinocyte differentiation and hyperproliferation. Such a problem is simply seen as a 'fault' of the epidermis and its keratinocytes [3, 14, 26]. The second considers psoriasis as an immune-mediated skin condition in which the excessive regeneration of skin cells is secondary to factors produced by the immune system, suggesting that the inflammatory mechanisms are immune-based and most likely initiated and maintained primarily by T cells found within the deeper layer of the skin, the dermis [14, 27, 28]. Given that keratinocytes, dendritic cells and activated T cells are all crucial to the development and persistence of psoriatic plaques, the pathophysiology of psoriasis cannot be explained by the role of a single cell type exclusively – it is likely a dynamic and complex interplay between those cell types. Furthermore, the contribution of each cell type is equally essential in different phases (e.g., initiation, formation, maintenance) of psoriatic alterations. Therefore, the exact sequence of events that lead to the development of psoriatic plaques remains unknown [28].

1.3 Management of psoriasis

Choosing the best management strategy for psoriasis can often be problematic and frustrating for both patients and healthcare professionals, and usually there are several factors to consider: the type, severity and localisation of the condition; the patient's age and medical history; the impact the disease has on QoL; and the patient's expected goals [1]. Before embarking on a management strategy, it is absolutely crucial to establish expectations and goals. The 'ideal' goal would be complete clearance of psoriatic plaques but this is currently not achievable in most patients. Thus, it is necessary to set

a minimal target to allow modification of the management strategy if the target is not achieved within a set time [29]. In very basic terms, management for ‘generalised’ psoriasis follows a 1-2-3 step-ladder approach (**Figure 1**), starting with topical therapies (e.g., topical moisturisers) (Section 1.4) followed by phototherapy and then systemic medications that can include a range of oral drugs and small biologicals [1, 10, 30].

Topical therapy as monotherapy is useful in psoriasis patients with a mild to moderate condition. Topical moisturisers are also used as an adjuvant strategy for moderate to severe psoriasis that is concurrently treated with either phototherapy or systemic medications [10].

Phototherapy represents a second-line defence strategy in the management of psoriasis (**Figure 1**). It involves exposure of the psoriatic skin to ultraviolet (UV) radiation, which can decrease the appearance of plaques on the skin [10, 31]. Many types of phototherapy have been developed and used for the treatment of psoriasis over the last few decades. Broadband ultraviolet B light (BB-UVB, 290–320 nm) was the first such therapy developed, but was later replaced by narrowband ultraviolet B light (NB-UVB, 311 nm) as the latter is more effective than the former. The excimer laser/lamp of 308 nm was next invented and used as a monochromatic (single wavelength) UVB source for psoriasis treatment. The advantage of using excimer is its targeting ability that can spare unaffected skin while providing high doses targeted directly at psoriatic skin [32]. In short, phototherapy acts by causing cutaneous immuno-suppression, slowing down excessive growth of skin cells and altering cytokine expression [10, 31]. The drawbacks to phototherapy include the extensive time investment that is required; usually, three to five therapy sessions per week are needed, with the total therapy period ranging from approximately 2–3 months. Additionally, the response to phototherapy can vary from individual to individual, and there can be health implications to consider, such as the risk of skin cancer [10].

Figure 1.
Schematic of psoriasis 1-2-3 step-ladder management approach [1, 10, 30].

The decision to progress to systemic therapy (**Figure 1**) should be based not only on objective disease severity (where PASI $\geq 10\%$ or QoL index $\geq 10\%$ or BSA $\geq 10\%$; indicating more than 10% of involvement of the skin) [33], but also on social and psychological factors. The patient should understand the risks (e.g., higher risk and more adverse effects) (**Figure 2**) associated with systemic medications and should be allowed to determine whether the risk of therapy outweighs the benefit [10]. Indications for systemic therapy include widespread plaque psoriasis, erythrodermic (potentially life-threatening inflammation) psoriasis, or the need for repeated hospitalisation for topical therapy. The therapies for extensive and severe forms of psoriasis usually have long-term side effects [34].

The order in which these management strategies are employed should progress in a stepwise fashion from lowest to highest risk (**Figure 2**), hence, the concept of a management ladder (**Figure 1**). The management strategy with the fewest side-effects (e.g., topical moisturisers) should be employed first. If this strategy proves ineffective or if the psoriasis is more severe, strategies with greater toxicity (e.g., phototherapy and systemic medications) may be initiated (**Figure 2**) [10, 34].

1.4 Topical moisturisers are the backbone of psoriasis management

Most topical moisturisers are specifically formulated to promote and maintain healthy skin, but may also serve to manage dry and itchy skin conditions such as psoriasis. Moisturisers are crucial to achieving a reduction in clinical signs of irritation and dryness, scaling and roughness, and a decrease in perceived feelings of tightness and itching [6, 20, 35, 36]. There are no specific rules on what is the best or ‘correct’ type of topical moisturiser to use. Since topical moisturisers are effectively used either as cosmetics (providing basic skin moisturisation) or therapeutics (e.g., managing psoriasis and preventing its exacerbation), the patients’ considerations will be mainly influenced by their personal preferences and lifestyle, and the nature and severity of their skin condition. Individual patient preferences and history may have an impact on the choice of moisturiser or moisturising base to use. A psoriasis patient presenting with severe dryness may benefit most from an occlusive ointment, yet their distaste for this particular base may dissuade them from using the product consistently, which could lead to increased morbidity. Conversely, while a lotion or

Figure 2.
The order in which management strategies for psoriasis should be implemented [10, 34].

cream may not provide as much hydration as an ointment, the patient’s preference for such ingredient base may improve compliance and, therefore, outcome. Patient expectation can also impact the choice or use of moisturiser. Despite wide management options being available, psoriasis is still an incurable disease, so expectation needs to be carefully managed. Complete psoriatic plaque clearance and relief from symptoms is often very difficult, if not impossible, a fact that can lead to patient dissatisfaction, as well as poor adherence and compliance with the current management options [10, 37].

The ‘ideal’ topical moisturiser (**Figure 3**) is one that the user prefers and will use regularly and liberally, keeping in mind that it should be: (a) cosmetically acceptable and elegant; (b) absorbed rapidly providing immediate skin moisturisation and achieve the intended cosmetic and/or therapeutic effect(s); (c) free from common irritants and allergens such as fragrance, colour and soap to minimise irritation and aggravation of the skin or underlying skin condition; and (d) non-sensitising, non-comedogenic (will not block pores), long-lasting [36, 38] and pH-balanced [39].

The efficacy of topical moisturisers is related to its basic skin moisturisation and ‘conditioning’ benefits, as well as its therapeutic effects. This is achieved most commonly through a well-designed combination of fundamental and specialty ingredients and actives, formulated and delivered in a range of topical formulations (Section 3) [20, 40, 41].

Figure 3.
The ‘ideal’ topical moisturiser characteristics [36, 38–41].

2. The evolution of moisturisers: from fundamental ingredients to tailored products

The evolution of topical moisturisers is basically equivalent to an odyssey from fundamental ingredients (e.g., emollients, humectants, occludents, excipients) [6, 35, 42] (Section 2.1) to specialty molecules (e.g., ceramides, Panthenol, nicotinamide) [6, 35] (Section 2.2) and functionally distinct actives (e.g., corticosteroids, tar-based ingredients, keratolytics) [43, 44] (Section 2.3). Therefore, understanding the interplay and synergism amongst different ingredients as well as being familiar with their ever expanding biophysical effects is essential to get a cosmetically acceptable and/or therapeutically stable tailored product (Section 3) with the desired impact on both healthy and diseased skin [6, 35].

2.1 Fundamental ingredients

Topical moisturisers usually contain, at a minimum, one or a combination of the key moisturising ingredients, namely emollients (e.g., dimethicone) (Section 2.1.1), humectants (e.g., glycerin) (Section 2.1.2) and occludents (e.g., petrolatum/petroleum jelly) (Section 2.1.3), as well as numerous excipients (e.g., penetration enhancers, preservatives, pH adjusters) to stabilise the formulation (Section 2.1.4). Additional ingredients often include selected specialty ingredients (Section 2.2) and actives (Section 2.3). Ingredient selection, and moisturiser composition and formulation are crucial considerations when choosing an appropriate moisturiser. Specifically for psoriasis, these considerations can determine whether the product will repair and strengthen or further deteriorate the psoriatic skin barrier [6, 35, 45].

2.1.1 Emollients

Emollients are used to improve the appearance and texture of skin by filling in the crevices between corneocytes. This contributes to increased softness, smoothness and suppleness of the skin and improves its overall appearance [42, 46, 47]. The most common types of emollients are silicones such as dimethicone, which is a hypoallergenic and non-comedogenic polymer and is used extensively in topical moisturisers. It exerts a protective effect on the skin by locking in moisture and decreasing TEWL [48]. Dimethicone's low surface energy and highly flexible silicone polymer backbone allows for effective spreading on the skin and a pleasant skin feel. The physical and aesthetic properties of silicones can be controlled by varying the chain length and molecular weight of the polymer. As chain length increases, the viscosity of silicones also increases, and vice-versa. Low viscosity means that the silicone is able to spread quickly and easily while providing a light, silky skin feel, whereas higher viscosities enable silicones to form more persistent hydrophobic (water-repelling) films with good water barrier properties [49].

2.1.2 Humectants

Humectants are hygroscopic (water-attracting) substances that are able to increase the water content of the skin by enhancing water absorption from the underlying skin layers, namely the deeper epidermis and dermis. Humectants penetrate the SC readily and act like biological sponges that promote water retention in the skin [47].

In addition, humectants are also able to hydrate the SC by absorbing water from the external environment. As a consequence, the SC tends to have greater water content in areas in which humectants are localised [42, 46, 47].

Glycerin is the most widely-studied and used humectant. It is also an endogenous component of the human skin. Glycerin is transported from the dermis through the keratinocytes by a transmembrane water/glycerol transport protein, Aquaporin 3 (AQP3) [50–52], and its hygroscopic properties enable it to increase the water holding capacity of an impaired SC. Glycerin functions in a way similar to the skin's own natural moisturising factor (NMF), which is an essential skin process responsible for appropriate SC hydration, barrier homeostasis, desquamation and plasticity. When used topically, glycerin protects the skin from irritant-associated skin conditions and accelerates recovery of irritated skin, while also improving overall skin hydration. Topical glycerin also helps barrier recovery through corneocyte desquamation regulation and is able to restore skin hydration at low usage levels (from as little as 2% v/v up to 10% v/v) [47, 52].

2.1.3 Occludents

Occludents are lipophilic (lipid-loving) substances that form a protective film on the skin and restrict TEWL, trapping water in the skin's uppermost layers and protecting against moisture loss [42, 46, 47, 53]. The most commonly used occludent, petrolatum or petroleum jelly (a long, aliphatic/straight chain of hydrocarbons) [54], can enter the intercellular space of the SC and become part of its lipid structure to provide internal occlusion of the SC, resulting in an increased barrier to water loss. In this regard, petrolatum is often considered to be the most effective moisturising ingredient for dry skin [42, 46, 47, 53].

2.1.4 Excipients

Non-active ingredients, commonly termed excipients, are extensively used in the formulation of topical moisturisers and typically make up the majority ($\geq 90\%$) of topical product content [41, 55]. By their physicochemical nature, different classes of excipients are used to enhance the functionality of active ingredients in therapeutic products, as well as to aid with formulation challenges. Excipients are often used to: (1) improve solubility to allow incorporation of an active; (2) control the release, penetration and permeation of an active; (3) improve the overall aesthetics of the product to increase patient compliance; (4) improve active and product stability; (5) prevent microbial growth and contamination (e.g., preservatives) and (6) balance the pH of water-based moisturisers, so that they are compatible with the skin's naturally slightly acidic pH [41].

2.1.4.1 Penetration enhancers

Penetration enhancers are chemicals that readily disrupt the structure of the SC and are commonly used to facilitate active (drug) delivery. The cutaneous inflammation experienced by patients with psoriasis promotes hypersensitivity and also suppresses skin barrier function. Therefore, the effective delivery of anti-inflammatory actives such as corticosteroids, aided by appropriate penetration enhancers, can bring about a net improvement in the skin's barrier function [41]. Many penetration

enhancers, like propylene glycol, are also solvents, and so can be used alone or in combination with other penetration enhancers to help facilitate both the partitioning into and the passage through the SC. However, care must be taken when selecting and using chemical penetration enhancers since their excessive use can potentially lead to systemic absorption of the active [41, 56]. As such, a careful tradeoff must be made between delivering a therapeutic active dose and protecting the integrity of the skin barrier. Penetration enhancers composed of short chain fatty acids, such as propylene glycol, are thought to integrate into the hydrophilic regions of the packed SC lipids and increase the solubility of this domain for the permeant [41], yet at high concentrations (above 10%) they can irritate the skin [41, 57, 58]. In contrast, penetration enhancers composed of long chain fatty acids like oleic acid insert themselves between the hydrophobic lipid tails to increase the fluidity of the SC lipid bilayers [41].

2.1.4.2 Preservatives

Preservatives are essential components of water-based topical moisturiser formulations and skincare products in general, as they protect products from potentially harmful bacteria. Without preservatives, water-based products would have a very short shelf life and would, for the most part, have to be stored at lower temperatures [59, 60]. Parabens such as methylparaben and propylparaben are arguably the most commonly used preservative ingredients. They have antimicrobial efficacy against a broad spectrum of yeasts, moulds and bacteria, although they are most effective against gram-positive organisms such as *S. aureus* [61]. While parabens exact mechanism of action is not well understood, it is thought to involve the disruption of a pathogen's cell membrane transport processes [62] and the inhibition of DNA/RNA synthesis [63] but it is generally believed that their inhibitory effects on membrane transport and mitochondrial functional processes are key to their antimicrobial actions [64]. The popularity of parabens is based on several advantages when compared to alternative preservatives, including their broad spectrum of antimicrobial activity, stability over a wide temperature and pH range, low degree of systemic toxicity, low frequency of sensitisation, sufficient water solubility, well documented safety record and their lack of odour, taste or colour [59, 60].

2.1.4.3 pH adjusters

In addition to the chemical stability of the ingredients and the formulation itself, pH is a crucial consideration for topical moisturisers. Not only is the absolute pH value important, but the buffer capacity is also crucial to the skin's natural acid mantle. The buffer capacity describes the ability of a formulation to keep the pH value almost constant or as close to the skin's natural pH as possible [65, 66]. This can be achieved by adding pH adjusters to the formulation [66]. The natural pH of the skin surface of most parts of the body is slightly acidic and in the range of pH 4.1–5.8 [66], a feature that can have significant impacts on how the skin reacts to the product. It is a generally accepted fact that the use of alkaline or non pH-balanced products such as soaps, cleansers and creams will lead to skin barrier impairment with a concomitant pH increase in both healthy and diseased skin. The duration of this increase in skin pH depends on skin condition, frequency of application and the composition of the product. Therefore, every skincare product is a potential skin surface pH modifier

and the pH of such products must be adjusted to a physiological pH during its development [67]. Some of the most commonly used pH adjusters for topical moisturisers include aminomethyl propanol and citric acid. Aminomethyl propanol is a synthetically produced pH adjuster that is classed as an aliphatic alcohol. It is commonly used in topical formulations due to its safety profile when used in low concentrations [68, 69]. Citric acid is a weak alpha hydroxy acid (AHA) that is naturally occurring in plants and animals. The majority of citric acid comes from citrus fruits, like oranges, lemons, grapefruit and limes. When used and applied in small amounts, it serves as an effective pH adjuster [70].

2.2 Specialty/complimentary ingredients

The newest generation of topical moisturisers for psoriasis also routinely contains specialty or complimentary ingredients in addition to the fundamental moisturiser components detailed in Section 2.1. Common examples of such ingredients include: (1) ceramides that help to replenish the deficient lipids in psoriatic skin [71], (2) the versatile Panthenol (Pro-vitamin B5), which is a skin protectant with moisturising and anti-inflammatory properties [72, 73] and (3) the 'wonder molecule' nicotinamide (also known as niacinamide and Vitamin B3), which is one of the most widely used complimentary ingredients in topical moisturisers [74, 75].

2.2.1 Ceramides

Ceramides, alongside cholesterol and free fatty acids, are the predominant components of the SC and comprise 30–40% of the SC lipid matrix by mass. They are composed of long chain sphingoid bases (e.g., sphingosine) which are linked to long chain free fatty acids. Incorporating the skin's naturally occurring ceramides such as ceramide I (ceramide EOP) and ceramide III (ceramide NP) in topical moisturisers can help to improve both healthy and psoriatic skin by replacing decreased or even depleted ceramide levels [76]. A functional SC plays an indispensable role in ensuring the skin's flexibility and structural integrity. The ordered alignment and organisation of the lipid bilayers within the SC forms a closed system to prevent TEWL in psoriatic plaques and makes the SC more impermeable. Therefore, even a subtle change or disturbance in the amount, physicochemical characteristics and organisation of the SC ceramides can potentially initiate and/or exacerbate psoriasis [71, 77].

2.2.2 Panthenol

Panthenol is a biologically active component of the B vitamin-complex, which is a basic component of the skin, hair and nails. When applied topically, Panthenol is efficiently absorbed into the epidermis and quickly converted into pantothenic acid, which is then converted to Acetyl Coenzyme-A (Acetyl CoA). Acetyl CoA is an essential mediator of many biochemical reactions within skin cells, and is necessary for optimal energy levels, barrier function, moisturisation, elasticity and strength [72, 73]. Furthermore, Panthenol can act as both an emollient and a humectant. As an emollient, it can help seal cracks in the skin, keeping water locked in, which in turn contributes to skin softness and smoothness. As a humectant, it can bind to and hold water effectively, reducing the amount of TEWL through the skin and helping it maintain moisture, softness and elasticity [72, 73, 78].

2.2.3 Nicotinamide

Nicotinamide, which easily penetrates the skin, is fast becoming a ubiquitous topical skincare ingredient in a range of moisturiser formulations. A number of clinical trials [79–81] show that the concentration of topical nicotinamide products can go up to 10%, but desired effects can be achieved with concentrations as low as 2–5% [79]. Nicotinamide provides a long list of skin care benefits with its use, including its ability to: (1) support the skin barrier structure and function by facilitating the formation of ceramides and keratin [74, 75]; (2) improve the skin's tone and texture [82]; and (3) boost the effectiveness of moisturisers in general [75]. For example, when formulated in a combination with glycerin, a nicotinamide-containing moisturiser can very effectively improve the integrity of the SC and thus reduce skin dryness over time [75, 83]. In addition, nicotinamide has also been shown to have anti-inflammatory and antioxidant properties, the latter of which may help to reduce the harmful effects of UV radiation, photoageing and oxidative stress [84]. The appropriate concentration of topical nicotinamide for each individual may depend on their skin type and condition, keeping in mind that in some instances, high levels of nicotinamide can cause an allergic reaction for people susceptible to skin allergies [85].

2.3 Active ingredients

Alongside moisturisers, topical therapeutic products for psoriasis that contain active ingredients can also utilise both the fundamental (Section 2.1) and specialty (Section 2.2) ingredients to compliment the active component of the product or provide additional skin conditioning benefits. Common examples of actives indicated for the management of psoriasis include corticosteroids (e.g., hydrocortisone, clobetasone butyrate, mometasone furoate) (Section 2.3.1), tar-based actives (e.g., coal tar, pine tar) (Section 2.3.2) and keratolytics (e.g., salicylic acid) (Section 2.3.3). While these active ingredients are included to treat specific symptoms or characteristics of psoriasis such as inflammation, itch and plaque build-up, the use of a moisturising base can help to dramatically improve patient outcomes [6, 35]. While non-active moisturisers containing only fundamental ingredients are an important adjuvant therapy of classical psoriasis treatment modalities and used as supportive treatment in relapse-free phases [6, 35, 50], a moisturising base containing a topical corticosteroid will be able to not only manage the inflammation associated with psoriasis but also reduce the dryness and itch, and the accompanying scratch response that can significantly worsen disease morbidity [86].

2.3.1 Corticosteroids

Corticosteroids play a key role in the management of psoriasis. In this context, their mechanism of action involves the reduction of skin redness and the expression of anti-inflammatory mediators, as well as achieving an improvement and/or clearance of psoriatic plaques (**Figure 4**) [87]. These effects are exerted via intracellular corticosteroid receptors, which regulate gene transcription, including several that code for pro-inflammatory mediators. Topical corticosteroids are classified based on their skin vasoconstrictive activity, ranging in strength (potency): (a) super potent/ultrahigh (e.g., clobetasol propionate 0.05%); (b) high (e.g., mometasone furoate 0.1%); (c) moderate (medium) (e.g., betamethasone valerate 0.1%) [43, 86] and (d) low (e.g., hydrocortisone 1.0%) [43]. Choosing a corticosteroid with appropriate

Figure 4. The choice of management strategy for psoriasis is driven by the skin’s dryness and itchiness; inflammation and redness; scaliness and thickness [6, 35, 45, 86, 87, 91, 99].

potency plus the appropriate topical formulation should be based on the disease severity and area affected, and the patient’s preference and age [88]. Lower potency corticosteroids such as hydrocortisone should be used on the face, intertriginous areas, and areas that are susceptible to steroid atrophy (e.g., forearms) [88, 89]. In adults, higher potency corticosteroids such as clobetasone butyrate and mometasone furoate are generally recommended as initial therapy [86, 88, 90]. Areas with thick, chronic plaques often require management with ultrahigh-potency corticosteroids. In numerous randomised clinical trials [4, 91–94], different potency topical corticosteroids were effective and safe at 2 to 4 weeks in the management of mild to severe plaque psoriasis. Evidence on the efficacy of topical corticosteroids for the management of psoriasis varies greatly due to the differences in study designs, patient populations, corticosteroid class and concentration, adverse effects and outcomes [86].

2.3.2 Tar-based actives

Tars represent one of the first therapies developed in the history of psoriasis [87]. In fact, pine tar has probably been produced in Scandinavia since the Iron Age and its use in medicine was first described by Hippocrates more than 2000 years ago in ancient Greece to treat a range of skin conditions because of its soothing and anti-septic properties [95]. Pine tar should not be confused with coal tar, which has been produced from coal for approximately a 100 years. Today, it is available in various formulations, from gels, to lotions and soap-free bars [96]. As an effective anti-inflammatory, antibacterial and antifungal substance, topical pine tar has been used in topical formulations for a long time to relieve itchiness and inflammation associated with a range of dry, itchy, flaky or inflamed skin conditions (Figure 4), particularly eczema and psoriasis, with minimal safety risk [96]. Furthermore, both coal tar and wood tars such as birch and beech are also available as topical anti-psoriatic ingredients in different topical formulations [87, 97]. Due to its inherent chemical composition and complexity [98], the mechanism of action of coal tar is not well understood, but it likely suppresses DNA synthesis and reduces keratinocyte proliferation. Coal tar is often used as either a monotherapy or in combination with other management strategies [87, 97]. Pine tar is thought to exert its effect by reducing DNA synthesis and mitotic (cell division) activity, which promotes a return to normal keratin development [96]. Tar-based formulations are indicated for the management of chronic, stable forms of plaque-type psoriasis and scalp psoriasis, whereas their use might be limited in sensitive areas such as around the genitals due to their irritation potential [87].

2.3.3 Keratolytics

Keratolytics (**Figure 4**) such as salicylic acid are readily used as active ingredients in many topical formulations, but may have particular utility when it comes to psoriasis as the disease is characterised by a build-up of keratinocytes on the skin. Keratolytics promote the physiologic skin shedding process and also decrease cell-to-cell cohesion in the SC, in effect loosening the glue that keeps keratinocytes together [87, 99]. Salicylic acid has been shown to aid in the removal of excessive keratin in psoriatic plaques and to produce desquamation of the SC while being safe to use and not effecting qualitative or quantitative changes in the structure of the viable epidermis [100]. It is often used as either monotherapy or as part of combination therapy to reduce the size and scale of psoriatic plaques [15, 100]. Keratolytics have proven to be particularly effective in reducing psoriatic plaque thickness if prescribed several days prior starting a first-line treatment (i.e., corticosteroids) for localised psoriasis or in specific areas such as the scalp [87, 99].

3. The necessity of topical moisturiser formulation modality: lotion, gel, cream and ointment

While the specific ingredients used in topical moisturisers or active therapeutics containing moisturising ingredients are important to effectively manage psoriasis, it is equally important to consider the base used to ensure that the product functions as intended. The most common bases include lotions, gels, creams and ointments, and each is distinguished by unique composition and properties that can have significant impact on the cosmetic and/or therapeutic effects they exert on psoriatic skin (**Figure 5**). An important initial factor to consider is the skin's dryness. Very dry skin will likely benefit from an occlusive ointment or cream to trap in moisture, often at the expense of product feel (and as a result, patient compliance) whereas mild to moderately dry skin can often be managed with a lotion or cream, which tend to be more appealing and thus may make for a product that is more readily used. In reality, patients often require more than one topical moisturiser formulation; a less greasy, cosmetically-acceptable product such as a lotion or light cream for use during the day and a heavier or greasier formulation such as an ointment or gel for night-time use [6, 35, 36].

3.1 Combination of basic blend and tailored blend topical moisturisers for the management of psoriasis

The commonly used topical formulation blends, either basic or tailored (**Figure 5**), can provide efficacy through divergent pathways. As these formulation blends contain a unique combination of ingredients (Section 2) they can potentially act through different mechanisms. As a result, there is a scientific rationale for their use in the management of psoriasis, either individually or in combination. This rationale assumes that such formulation blends are selected on the basis of their individual mechanism of action and the biophysical effects they exert on psoriatic skin, which may offer the possibility of synergistic efficacy as well as a reduction in the occurrence of cosmetic problems and side effects (**Figure 6**) [99].

Topical moisturiser formulation blends and topical therapeutics with moisturising bases (**Figure 5**) can be used in a deliberate sequence individually or in combination

Figure 5. A range of basic blend and tailored blend topical moisturiser formulations: Lotions, gels, creams and ointments, each distinguished by its unique composition, ingredient combination, and cosmetic and/or therapeutic effects they exert on psoriatic skin, resulting in a range of skin benefits.

	ACTIVE	EFFICACY	RELAPSE RATE	SIDE EFFECTS	COSMETIC PROBLEMS
BASIC BLEND MOISTURISER	-	1	1	0	1
TAILORED BLEND MOISTURISER	Keratolytics	1	1	1	1
	Coal tar/Pine tar	2	1	1	2
	Corticosteroids	3	2	2	0

Figure 6. Efficacy, relapse rate, side effects and cosmetic problems associated with the use of basic blend moisturisers that contain no actives, tailored blend moisturisers that contain actives such as keratolytics and tar-based actives (coal tar and/or pine tar), and therapeutics with moisturising ingredients and actives such as corticosteroids in the management of psoriasis. Scored on a scale from zero (0) to three (3): 0 denotes little or no change/effect; 3 denotes great and frequent change/effect [102].

(and even with other management options such as phototherapy and systemic medications) with the aim of achieving initial efficacy for the management of psoriasis followed by a safe maintenance regimen. This management strategy maximises the efficacy of each product while helping to minimise relapse rate, cosmetic problems and long term side effects (Figure 6) [99, 101, 102].

Now, when we are familiar with a range of basic blend and tailored blend topical moisturiser formulations and their unique composition and ingredient combination (as explained above) (Figure 5), an example of a management strategy for psoriasis would be as follows: first, the use of a topical therapeutic with a moisturising base

containing a topical steroid potent enough for the severity of the disease (e.g., hydrocortisone for mild, mometasone furoate for moderate to severe) or pine-tar active, at the maximum therapeutic dose, with the main aim of promptly controlling psoriasis flare-ups accompanied by redness and inflammation. This first step can then be followed by the use of a topical moisturiser formulation blend in which a well-tolerated ingredient such as a keratolytic is introduced to reduce psoriatic plaque thickness and scaling. Finally, by using a cosmetically beneficial basic topical moisturiser formulation, the patient can remain indefinitely on a maintenance regimen that aims for continuous hydration of the skin as well as improvements in skin suppleness, flexibility and strength, and the minimisation of dryness and itchiness (**Figure 4**).

While moisturisers are important tools in the management of psoriasis, their use comes with some challenges such as patient perspectives [10] as described in Section 1.4, and some general and more specific concerns regarding the development, uses and regulations of novel anti-psoriatic topical formulations [99]. These include the following amongst many others: (1) heterogeneity in psoriatic plaque thickness, (2) management of psoriasis in different groups of patients (e.g., elderly, pregnant women, children, immuno-compromised patients) requires a few specific care factors and considerations (e.g., prolonged use of topical corticosteroids may lead to thinning of the skin in elderly patients) [10], (3) the safety and efficacy of novel moisturisers when used in combination with existing and established therapies [99] and (4) regulatory requirements and classifications of topical moisturisers, be they cosmetic or therapeutic [103, 104].

4. Conclusions

Psoriasis is a chronic skin condition characterised primarily by dysfunctional skin barrier integrity, dry and itchy skin, and the development of scaly plaques. Being defined as a multifactorial skin condition caused by an interaction between various genetic and environmental factors, psoriasis requires a 1-2-3 step-ladder combination approach of therapeutics to treat the condition and topical moisturisers to alleviate the symptoms.

Therapeutics like topical corticosteroids are not moisturisers themselves, but benefit from having a moisturising base and fundamental and complimentary moisturising ingredients. Therefore, understanding the interplay and synergism amongst different ingredients as well as being familiar with their advantageous biophysical effects and potential adverse effects is essential to get a range of cosmetically acceptable and/or therapeutically stable products with desired impact on both healthy and psoriatic skin.

Topical moisturisers are a key part of psoriasis management and come in various formulations such as lotions, gels, creams and ointments. By using such formulations readily and frequently, the patient can remain on a daily maintenance regimen that aims for continuous hydration of the skin as well as improvements in skin's functionality, structural strength, visual and tactile attributes as well as minimisation of dryness and itchiness.

Conflict of interest

The authors declare no conflict of interest.

IntechOpen

IntechOpen

Author details

Dalibor Mijaljica, Fabrizio Spada and Ian P. Harrison*
Department of Scientific Affairs, Ego Pharmaceuticals Pty Ltd, Braeside, Victoria,
Australia

*Address all correspondence to: ian.harrison@egopharm.com

IntechOpen

© 2022 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

References

- [1] Augustin M, Alvaro-Gracia JM, Bagot M, Hillmann O, van de Kerkhof PC, Kobelt G, et al. A framework for improving the quality of care for people with psoriasis. *Journal of the European Academy of Dermatology and Venereology*. 2012;**26**(4):1-16. DOI: 10.1111/j.1468-3083.2012.04576.x
- [2] Maroto-Morales D, Montero-Vilchez T, Arias-Santiago S. Study of skin barrier function in psoriasis: The impact of emollients. *Life (Basel)*. 2021;**11**(7):651. DOI: 10.3390/life11070651
- [3] Rendon A, Schäkel K. Psoriasis pathogenesis and treatment. *International Journal of Molecular Sciences*. 2019;**20**(6):1475. DOI: 10.3390/ijms20061475
- [4] Segaert S, Calzavara-Pinton P, de la Cueva P, Jalili A, Lons Danic D, Pink AE, et al. Long-term topical management of psoriasis: The road ahead. *The Journal of Dermatological Treatment*. 2020:1-10. DOI: 10.1080/09546634.2020.1729335 [Ahead-of-print]
- [5] Lodén M. Barrier recovery and influence of irritant stimuli in skin treated with a moisturizing cream. *Contact Dermatitis*. 1997;**36**(5):256-260. DOI: 10.1111/j.1600-0536.1997.tb00213.x
- [6] Lodén M. Role of topical emollients and moisturizers in the treatment of dry skin barrier disorders. *American Journal of Clinical Dermatology*. 2003;**4**(11):771-788. DOI: 10.2165/00128071-200304110-00005
- [7] Buraczewska I, Berne B, Lindberg M, Törmä H, Lodén M. Changes in skin barrier function following long-term treatment with moisturizers, a randomized controlled trial. *The British Journal of Dermatology*. 2007;**156**(3):492-498. DOI: 10.1111/j.1365-2133.2006.07685.x
- [8] Griffiths CEM, Armstrong AW, Gudjonsson JE, Barker JNWN. Psoriasis. *Lancet*. 2021;**397**(10281):1301-1315. DOI: 10.1016/S0140-6736(20)32549-6
- [9] Griffiths CE, Barker JN. Pathogenesis and clinical features of psoriasis. *Lancet*. 2007;**370**(9583):263-271. DOI: 10.1016/S0140-6736(07)61128-3
- [10] Bakshi H, Nagpal M, Singh M, Dhingra GA, Aggarwal G. Treatment of psoriasis: A comprehensive review of entire therapies. *Current Drug Safety*. 2020;**15**(2):82-104. DOI: 10.2174/1574886315666200128095958
- [11] Gupta R, Debbaneh MG, Liao W. Genetic epidemiology of psoriasis. *Current Dermatology Reports*. 2014;**3**(1):61-78. DOI: 10.1007/s13671-013-0066-6
- [12] Dand N, Mahil SK, Capon F, Smith CH, Simpson MA, Barker JN. Psoriasis and genetics. *Acta Dermato-Venereologica*. 2020;**100**(3):adv00030. DOI: 10.2340/00015555-3384
- [13] Raharja A, Mahil SK, Barker JN. Psoriasis: A brief overview. *Clinical Medicine (London, England)*. 2021;**21**(3):170-173. DOI: 10.7861/clinmed.2021-0257
- [14] Kuchekar AB, Pujari RR, Kuchekar SB, Dhole SN, Mule PM. Psoriasis: A comprehensive review. *International Journal of Pharmaceutical and Life Sciences*. 2011;**2**(6):857-877
- [15] Kim WB, Jerome D, Yeung J. Diagnosis and management of psoriasis. *Canadian Family Physician*. 2017;**63**(4):278-285

- [16] Patel RV, Tsui CL. Evaluating psoriasis: A review of the assessments most commonly used in clinical trials. *Journal of Psoriasis and Psoriatic Arthritis*;17(4):259-266. DOI: 10.1177/247553031117a00403
- [17] Takeshita J, Grewal S, Langan SM, Mehta NN, Ogdie A, Van Voorhees AS, et al. Psoriasis and comorbid diseases: Epidemiology. *Journal of the American Academy of Dermatology*. 2017;76(3):377-390. DOI: 10.1016/j.jaad.2016.07.064
- [18] Elias PM. Stratum corneum defensive functions: An integrated view. *The Journal of Investigative Dermatology*. 2005;125(2):183-200. DOI: 10.1111/j.0022-202X.2005.23668.x
- [19] Lee SH, Jeong SK, Ahn SK. An update of the defensive barrier function of skin. *Yonsei Medical Journal*. 2006;47(3):293-306. DOI: 10.3349/ymj.2006.47.3.293
- [20] Roure R, Lanctin M, Nollent V, Bertin C. Methods to assess the protective efficacy of emollients against climatic and chemical aggressors. *Dermatology Research and Practice*. 2012;2012:864734. DOI: 10.1155/2012/864734
- [21] Évora AS, Adams MJ, Johnson SA, Zhang Z. Corneocytes: Relationship between structural and biomechanical properties. *Skin Pharmacology and Physiology*. 2021;34(3):146-161. DOI: 10.1159/000513054
- [22] Cork MJ, Danby S. Skin barrier breakdown: A renaissance in emollient therapy. *The British Journal of Nursing*. 2009;18(14):872, 874, 876-7. DOI: 10.12968/bjon.2009.18.14.43356.
- [23] Agrawal R, Woodfolk JA. Skin barrier defects in atopic dermatitis. *Current Allergy and Asthma Reports*. 2014;14(5):433. DOI: 10.1007/s11882-014-0433-9
- [24] Elias PM. Skin barrier function. *Current Allergy and Asthma Reports*. 2008;8(4):299-305. DOI: 10.1007/s11882-008-0048-0
- [25] Lawton S. Skin 1: The structure and functions of the skin. *Nursing Times*. 2019;115(12):30-33
- [26] Ortonne JP. Aetiology and pathogenesis of psoriasis. *The British Journal of Dermatology*. 1996;135(49):1-5. DOI: 10.1111/j.1365-2133.1996.tb15660.x
- [27] Robert C, Kupper TS. Inflammatory skin diseases, T cells, and immune surveillance. *The New England Journal of Medicine*. 1999;341(24):1817-1828. DOI: 10.1056/NEJM199912093412407
- [28] Benhadou F, Mintoff D, Del Marmol V. Psoriasis: Keratinocytes or immune cells—Which is the trigger? *Dermatology*. 2019;235(2):91-100. DOI: 10.1159/000495291
- [29] Strober BE, van der Walt JM, Armstrong AW, Bourcier M, Carvalho AVE, Chouela E, et al. Clinical goals and barriers to effective psoriasis care. *Dermatol Ther (Heidelb)*. 2019;9(1):5-18. DOI: 10.1007/s13555-018-0279-5
- [30] Samarasekera EJ, Smith CH. National Institute of Health and Care Excellence; Royal College of Physicians. Psoriasis: Guidance on assessment and referral. *Clinical Medicine (London, England)*. 2014;14(2):178-182. DOI: 10.7861/clinmedicine.14-2-178
- [31] Wong T, Hsu L, Liao W. Phototherapy in psoriasis: A review of mechanisms of action. *Journal of Cutaneous Medicine and Surgery*. 2013;17(1):6-12. DOI: 10.2310/7750.2012.11124
- [32] Zhang P, Wu MX. A clinical review of phototherapy for psoriasis. *Lasers in*

- Medical Science. 2018;**33**(1):173-180.
DOI: 10.1007/s10103-017-2360-1
- [33] Gisondi P, Del Giglio M, Girolomoni G. Treatment approaches to moderate to severe psoriasis. *International Journal of Molecular Sciences*. 2017;**18**(11):2427. DOI: 10.3390/ijms18112427
- [34] Lofholm PW. The psoriasis treatment ladder: A clinical overview. *Journal of Modern Pharmacy*. 2001;**8**(11):12-15. DOI: 10520/AJA16836707_1241
- [35] Lodén M. Do moisturizers work? *Journal of Cosmetic Dermatology*. 2003;**2**(3-4):141-149. DOI: 10.1111/j.1473-2130.2004.00062.x
- [36] Kraft JN, Lynde CW. Moisturizers: What they are and a practical approach to product selection. *Skin Therapy Letter*. 2005;**10**(5):1-8
- [37] Feldman SR, Goffe B, Rice G, Mitchell M, Kaur M, Robertson D, et al. The challenge of managing psoriasis: Unmet medical needs and stakeholder perspectives. *American Health & Drug Benefits*. 2016;**9**(9):504-513
- [38] Lynde CW. Moisturizers: What they are and how they work. *Skin Therapy Letter*. 2001;**6**(13):3-5
- [39] Shi VY, Tran K, Lio PA. A comparison of physicochemical properties of a selection of modern moisturizers: Hydrophilic index and pH. *Journal of Drugs in Dermatology*. 2012;**11**(5):633-636
- [40] Mayba JN, Gooderham MJ. A guide to topical vehicle formulations. *Journal of Cutaneous Medicine and Surgery*. 2018;**22**(2):207-212. DOI: 10.1177/1203475417743234
- [41] Danby SG, Draelos ZD, Gold LFS, Cha A, Vlahos B, Aikman L, et al. Vehicles for atopic dermatitis therapies: More than just a placebo. *The Journal of Dermatological Treatment*. 2020;11-14. DOI: 10.1080/09546634.2020.1789050 [Ahead-of-print]
- [42] Nolan K, Marmur E. Moisturizers: Reality and the skin benefits. *Dermatologic Therapy*. 2012;**25**(3):229-233. DOI: 10.1111/j.1529-8019.2012.01504.x
- [43] Uva L, Miguel D, Pinheiro C, Antunes J, Cruz D, Ferreira J, et al. Mechanisms of action of topical corticosteroids in psoriasis. *International Journal of Endocrinology*. 2012;**2012**:561018. DOI: 10.1155/2012/561018
- [44] Reid C, Griffiths CEM. Psoriasis and treatment: Past, present and future aspects. *Acta Dermato-Venereologica*. 2020;**100**(3):adv00032. DOI: 10.2340/00015555-3386
- [45] Purnamawati S, Indrastuti N, Danarti R, Saefudin T. The role of moisturizers in addressing various kinds of dermatitis: A review. *Clinical Medicine & Research*. 2017;**15**(3-4):75-87. DOI: 10.3121/cmr.2017.1363
- [46] Baumann L. Understanding and treating various skin types: The Baumann skin type indicator. *Dermatologic Clinics*. 2008;**26**(3):359-373. DOI: 10.1016/j.det.2008.03.007
- [47] Greive K. Cleansers and moisturisers: The basics. *Wound Practice and Research*. 2015;**23**(2):76-81
- [48] Nair B. Cosmetic ingredients review expert panel. Final report on the safety assessment of stearoxy dimethicone, dimethicone, methicone, amino bispropyl dimethicone, aminopropyl dimethicone, amodimethicone, amodimethicone hydroxystearate,

behenoxy dimethicone, C24-28 alkyl methicone, C30-45 alkyl methicone, C30-45 alkyl dimethicone, cetearyl methicone, cetyl dimethicone, dimethoxysilyl ethylenediaminopropyl dimethicone, hexyl methicone, hydroxypropyldimethicone, stearamidopropyl dimethicone, stearyl dimethicone, stearyl methicone, and vinyl dimethicone. *International Journal of Toxicology*. 2003;22(2):11-35. DOI: 10.1080/10915810390204854

[49] Maxon B, Michael SM. Formulating skin care products with silicones: Approaches and strategies. In: Dayan N, editor. *Handbook of Formulating Dermal Applications: A Definitive Practical Guide*. New Jersey: Wiley and Sons Inc.; 2017. pp. 59-114. DOI: 10.1002/9781119364221.ch4

[50] Fluhr JW, Darlenski R, Surber C. Glycerol and the skin: Holistic approach to its origin and functions. *The British Journal of Dermatology*. 2008;159(1):23-34. DOI: 10.1111/j.1365-2133.2008.08643.x

[51] Caussin J, Rozema E, Gooris GS, Wiechers JW, Pavel S, Bouwstra JA. Hydrophilic and lipophilic moisturisers have similar penetration profiles but different effects on SC water distribution *in vivo*. *Experimental Dermatology*. 2009;18(11):954-961. DOI: 10.1111/j.1600-0625.2009.00881.x

[52] Margolis DJ, Kim B, Apter AJ. Thymic stromal lymphopoietin variation, filaggrin loss of function, and the persistence of atopic dermatitis. *AMA Dermatology*. 2014;150(3):254-259. DOI: 10.1001/jamadermatol.2013.7954

[53] Rawlings AV, Lombard KJ. A review on the extensive skin benefits of mineral oil. *International Journal of Cosmetic Science*. 2012;34(6):511-518. DOI: 10.1111/j.1468-2494.2012.00752.x

[54] Czarnowicki T, Malajian D, Khattri S, Correa da Rosa J, Dutt R, Finney R, et al. Petrolatum: Barrier repair and antimicrobial responses underlying this “inert” moisturizer. *The Journal of Allergy and Clinical Immunology*. 2016;137(4):1091-1102. DOI: 10.1016/j.jaci.2015.08.013

[55] Brown MB, Turner M, Lim ST. Topical product formulation development. In: Benson HAE, Watkinson A, editors. *Transdermal and Topical Drug Delivery: Principles and Practice*. 1st ed. Hoboken, NJ: Wiley and Sons Inc.; 2012. pp. 255-286. DOI: 10.1002/9781118140505

[56] Parhi R, Suresh P, Mondal S, Kumar PM. Novel penetration enhancers for skin applications: A review. *Current Drug Delivery*. 2012;9(2):219-230. DOI: 10.2174/156720112800234585

[57] Lessmann H, Schnuch A, Geier J, Uter W. Skin-sensitizing and irritant properties of propylene glycol. *Contact Dermatitis*. 2005;53(5):247-259. DOI: 10.1111/j.0105-1873.2005.00693.x

[58] Trommer H, Neubert RHH. Overcoming the stratum corneum: The modulation of skin penetration. A review. *Skin Pharmacology and Applied Skin Physiology*. 2006;19(2):106-121. DOI: 10.1159/000091978

[59] Francisco A, Fonseca AP. Parabens paradoxes in cosmetic formulations; a review. *International Journal of Medical Research and Pharmaceutical Sciences*. 2016;3(8):1-11. DOI: 10.5281/zenodo.61076

[60] Lincho J, Martins RC, Gomes J. Paraben compounds-Part I: An overview of their characteristics, detection, and impacts. *Applied Sciences*. 2021;11(5):2307. DOI: 10.3390/app11052307

- [61] Cashman AL, Warshaw EM. Parabens: A review of epidemiology, structure, allergenicity, and hormonal properties. *Dermatitis*. 2005;**16**(2):57-66. DOI: 10.2310/6620.2005.05008
- [62] Freese E, Sheu CW, Galliers E. Function of lipophilic acids as antimicrobial food additives. *Nature*. 1973;**241**(5388):321-325. DOI: 10.1038/241321a0
- [63] Nes IF, Eklund T. The effect of parabens on DNA, RNA and protein synthesis in *Escherichia coli* and *Bacillus subtilis*. *The Journal of Applied Bacteriology*. 1983;**54**(2):237-242. DOI: 10.1111/j.1365-2672.1983.tb02612.x
- [64] Tade RS, More MP, Chatap VK, Deshmukh PK, Patil PO. Safety and toxicity assessment of parabens in pharmaceutical and food products. *Inventi Rapid: Pharmacy Practice*. 2018;**2018**(3):10. DOI: 10.13140/RG.2.2.23621.40161
- [65] Wohlrab J, Gebert A. pH and buffer capacity of topical formulations. *Current Problems in Dermatology*. 2018;**54**:123-131. DOI: 10.1159/000489526
- [66] Schulte de Brinke A, Mehlich A, Doberenz C, Janssens-Böcker C. Acidification of the skin and maintenance of the physiological skin pH value by buffered skin care products formulated around pH 4. *Journal of Cosmetics, Dermatological Sciences and Applications*. 2021;**11**(01):44-57. DOI: 10.4236/jcdsa.2021.111005
- [67] Lukić M, Pantelić I, Savić SD. Towards optimal pH of the skin and topical formulations: From the current state of the art to tailored products. *Cosmetics*. 2021;**8**(3):69. DOI: 10.3390/cosmetics8030069
- [68] Burnett CL, Bergfeld WF, Belsito DV, Klaassen CD, Marks JG Jr, Shank RC, et al. Cosmetic ingredient review expert panel, Andersen FA. Final amended report on safety assessment on aminomethyl propanol and aminomethyl propanediol. *International Journal of Toxicology*. 2009;**28**(6):141S-161S. DOI: 10.1177/1091581809350932
- [69] Becker LC, Bergfeld WF, Belsito DV, Hill RA, Klaassen CD, Liebler DC, et al. Safety assessment of tromethamine, aminomethyl propanediol, and aminoethyl propanediol as used in cosmetics. *International Journal of Toxicology*. 2018;**37**(1):5S-18S. DOI: 10.1177/1091581817738242
- [70] Fiume MM, Heldreth BA, Bergfeld WF, Belsito DV, Hill RA, Klaassen CD, et al. Safety assessment of citric acid, inorganic citrate salts, and alkyl citrate esters as used in cosmetics. *International Journal of Toxicology*. 2014;**33**(2):16S-46S. DOI: 10.1177/1091581814526891
- [71] Kahraman E, Kaykın M, Şahin Bektay H, Güngör S. Recent advances on topical application of ceramides to restore barrier function of skin. *Cosmetics*. 2019;**6**(3):52. DOI: 10.3390/cosmetics6030052
- [72] Camargo FB Jr, Gaspar LR, Maia Campos PMBG. Skin moisturizing effects of panthenol-based formulations. *Journal of Cosmetic Science*. 2011;**62**(4):361-370
- [73] Proksch E, de Bony R, Trapp S, Boudon S. Topical use of dexpanthenol: A 70th anniversary article. *The Journal of Dermatological Treatment*. 2017;**28**(8):766-773. DOI: 10.1080/09546634.2017.1325310
- [74] Gehring W. Nicotinic acid/niacinamide and the skin. *Journal of Cosmetic Dermatology*. 2004;**3**(2):88-93. DOI: 10.1111/j.1473-2130.2004.00115.x

- [75] Christman JC, Fix DK, Lucus SC, Watson D, Desmier E, Wilkerson RJ, et al. Two randomized, controlled, comparative studies of the stratum corneum integrity benefits of two cosmetic niacinamide/glycerin body moisturizers vs. conventional body moisturizers. *Journal of Drugs in Dermatology*. 2012;**11**(1):22-29
- [76] Tessema EN, Gebre-Mariam T, Neubert RHH, Wohlrab J. Potential applications of phyto-derived ceramides in improving epidermal barrier function. *Skin Pharmacology and Physiology*. 2017;**30**(3):115-138. DOI: 10.1159/000464337
- [77] Pietrzak A, Michalak-Stoma A, Chodorowska G, Szepietowski JC. Lipid disturbances in psoriasis: An update. *Mediators of Inflammation*. 2010;**2010**:535612. DOI: 10.1155/2010/535612
- [78] Stettler H, Kurka P, Kandzora J, Pavel V, Breuer M, Macura-Biegun A. A new topical panthenol-containing emollient for maintenance treatment of childhood atopic dermatitis: Results from a multicenter prospective study. *The Journal of Dermatological Treatment*. 2017;**28**(8):774-779. DOI: 10.1080/09546634.2017.1328938
- [79] Levin J, Momin SB. How much do we really know about our favorite cosmeceutical ingredients? *The Journal of Clinical and Aesthetic Dermatology*. 2010;**3**(2):22-41
- [80] Forbat E, Al-Niaimi F, Ali FR. Use of nicotinamide in dermatology. *Clinical and Experimental Dermatology*. 2017;**42**(2):137-144. DOI: 10.1111/ced.13021
- [81] Boo YC. Mechanistic basis and clinical evidence for the applications of nicotinamide (niacinamide) to control skin aging and pigmentation. *Antioxidants (Basel)*. 2021;**10**(8):1315. DOI: 10.3390/antiox10081315
- [82] Bissett DL, Miyamoto K, Sun P, Li J, Berge CA. Topical niacinamide reduces yellowing, wrinkling, red blotchiness, and hyperpigmented spots in aging facial skin. *International Journal of Cosmetic Science*. 2004;**26**(5):231-238. DOI: 10.1111/j.1467-2494.2004.00228.x
- [83] Lichterfeld A, Hauss A, Surber C, Peters T, Blume-Peytavi U, Kottner J. Evidence-based skin care: A systematic literature review and the development of a basic skin care algorithm. *Journal of Wound, Ostomy, and Continence Nursing*. 2015;**42**(5):501-524. DOI: 10.1097/WON.0000000000000162
- [84] Gensler HL. Prevention of photoimmunosuppression and photocarcinogenesis by topical nicotinamide. *Nutrition and Cancer*. 1997;**29**(2):157-162. DOI: 10.1080/01635589709514618
- [85] Tian YJ, Li D, Ma Q, Gu XY, Guo M, Lun YZ, et al. Excess nicotinamide increases plasma serotonin and histamine levels. *Sheng Li Xue Bao*. 2013;**65**(1):33-38
- [86] Elmetts CA, Korman NJ, Prater EF, Wong EB, Rupani RN, Kivelevitch D, et al. Joint AAD-NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures. *Journal of the American Academy of Dermatology*. 2021;**84**(2):432-470. DOI: 10.1016/j.jaad.2020.07.087
- [87] Chiricozzi A, Pimpinelli N, Ricceri F, Bagnoni G, Bartoli L, Bellini M, et al. Treatment of psoriasis with topical agents: Recommendations from a

Tuscany Consensus. Dermatologic Therapy. 2017;**30**(6):e12549.
DOI: 10.1111/dth.12549

[88] Spada F, Barnes TM, Greive KA. Comparative safety and efficacy of topical mometasone furoate with other topical corticosteroids. The Australasian Journal of Dermatology. 2018;**59**(3):e168-e174. DOI: 10.1111/ajd.12762

[89] Greive KA, Barnes TM. Increased bioavailability of hydrocortisone dissolved in a cream base. The Australasian Journal of Dermatology. 2015;**56**(2):e30-e34. DOI: 10.1111/ajd.12128

[90] Ference JD, Last AR. Choosing topical corticosteroids. American Family Physician. 2009;**79**(2):135-140

[91] Castela E, Archier E, Devaux S, Gallini A, Aractingi S, Cribier B, et al. Topical corticosteroids in plaque psoriasis: A systematic review of efficacy and treatment modalities. Journal of the European Academy of Dermatology and Venereology. 2012;**26**(3):36-46. DOI: 10.1111/j.1468-3083.2012.04522.x

[92] Mason AR, Mason J, Cork M, Dooley G, Hancock H. Topical treatments for chronic plaque psoriasis. Cochrane Database of Systematic Reviews. 2013;**3**:CD005028. DOI: 10.1002/14651858.CD005028.pub3

[93] Das A, Panda S. Use of topical corticosteroids in dermatology: An evidence-based approach. Indian Journal of Dermatology. 2017;**62**(3):237-250. DOI: 10.4103/ijid.IJD_169_17

[94] Kleyn EC, Morsman E, Griffin L, Wu JJ, Cm van de Kerkhof P, Gulliver W, et al. Review of international psoriasis guidelines for the treatment of psoriasis: Recommendations for

topical corticosteroid treatments. The Journal of Dermatological Treatment. 2019;**30**(4):311-319. DOI: 10.1080/09546634.2019.1620502

[95] Alqahtani EA, Elagib MFA, Al-Yami RH, Abu Hatlah AS, Faragalla AI, Reddy R. Evaluation of antibacterial activity of pine tar on periodontal pathogenic bacteria: An in vitro study. Ethiopian Journal of Health Sciences. 2020;**30**(6):991-998. DOI: 10.4314/ejhs.v30i6.17

[96] Barnes TM, Greive KA. Topical pine tar: History, properties and use as a treatment for common skin conditions. Australian Journal of Dermatology. 2017;**58**(2):80-85. DOI: 10.1111/ajd.12427

[97] Chiricozzi A, Chimenti S. Effective topical agents and emerging perspectives in the treatment of psoriasis. Expert Review of Dermatology. 2012;**7**(3):283-293. DOI: 10.1586/edm.12.18

[98] Singh RR, Goyal N, Kaur N. Use of coal tar. SSRG International Journal of Civil Engineering. 2015;**2**(3):28-30. DOI: 10.14445/23488352/IJCE-V2I3P108

[99] Mitra A, Atillasoy E. Topical therapies for psoriasis. In: Soung J, Koo B, editors. Psoriasis. Rijeka: Intech Open; 2012. pp. 309-330. DOI: 10.5772/27027

[100] Jacobi A, Mayer A, Augustin M. Keratolytics and emollients and their role in the therapy of psoriasis: A systematic review. Dermatol Ther (Heidelb). 2015;**5**:1-18. DOI: 10.1007/s13555-015-0068-3

[101] Koo J. Systemic sequential therapy of psoriasis: A new paradigm for improved therapeutic results. Journal of the American Academy of Dermatology. 1999;**41**(3 Pt 2):S25-S28. DOI: 10.1016/s0190-9622(99)70363-4

[102] Greaves MW, Weinstein GD. Treatment of psoriasis. The New England Journal of Medicine. 1995;**332**(9):581-589. DOI: 10.1056/NEJM199503023320907

[103] Wohlrab J. Topical preparations and their use in dermatology. Journal der Deutschen Dermatologischen Gesellschaft. 2016;**14**(11):1061-1070. DOI: 10.1111/ddg.13151

[104] Raj RK, Chandrul KK. Regulatory requirements for cosmetics in relation with regulatory authorities in India against US, Europe, Australia and Asean countries. International Journal of Pharma Research and Health Sciences. 2016;**4**(5):1332-1341. DOI: 10.21276/ijprhs.2016.05.01