

Barrier Creams: Facts and Controversies

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Barrier creams (BCs) represent devices aiming to protect the skin from contact with exogenous hazardous substances, especially under working conditions. By preventing penetration and absorption of contaminants, BCs are designed to reduce the risk of developing both irritant and allergic contact dermatitis. In fact, BCs should improve stratum corneum hydration as well as provide emolliency to maintain skin integrity and to restore and repair the epidermis barrier function. The formulation and ingredients of the available BCs vary widely, and thus the choice of a BC should depend on the kind of contaminants, occupational conditions, and skin dysfunction. Although BCs are commonly recommended to prevent occupational contact dermatitis, their real benefit remains controversial. The aims of this review are to help the choice of appropriate BCs and to analyze the actual effectiveness in maintaining an intact skin barrier, preventing contact dermatitis, and speeding up the healing of barrier-impaired skin.

The stratum corneum (SC) is the first line of defense against external agents. Corneocytes are connected by corneodesmosomes and embedded in an extracellular lipid matrix organized as lamellar lipid layers. The lipids of the SC consist in a mixture of nonpolar lipids including ceramides (50%), free sterols, essential and nonessential free fatty acids (10%-20%), and cholesterol (25%).^{1,2}

The water content of SC is made up of both transepidermal water and retained “static” water located between the lipid bilayers and inside the corneocytes.^{3,4}

The corneocytes contain a number of water-retaining substances, the most important of which is a mix of hygroscopic water-soluble and water-binding fractions of low molecular weight that are generated by filaggrin hydrolysis and termed *natural moisturizing factor*.^{1,5,6} Natural moisturizing factor accounts for about 20% of the total weight of the SC and acts as a very efficient humectant and plasticizer.^{5,7-9} The SC requires a water content of 10% to 13% to maintain its biomechanical properties.¹⁰

The integrity of the SC has a crucial role in preventing contact dermatitis, and many studies have shown that depletion of intercellular lipids and dehydration are the initial step in the development of both irritant contact dermatitis (ICD) and allergic contact dermatitis (ACD).¹¹⁻¹⁵

A complete skin barrier restoration represents an essential strategy in preventing and treating contact dermatitis (CD). Although ICD and ACD differ in their pathogenesis, it is thought that the

incidence of both is reduced through the use of emollients, mild skin cleansing agents, gloves, and barrier creams (BCs). Gloves represent the most effective defense against hand eczema.¹⁶ When gloves cannot be worn for safety reasons, inhibited dexterity, and so forth, BCs may be an alternative.¹⁷

The aims of this review were to (1) analyze physical and chemical characteristics of BCs, (2) guide in the choice of BCs, and (3) evaluated efficacy and safety of BCs.

Barrier Creams: What Are?

There is no a codified definition for BCs. Barrier creams may be intended as a “shelter” that may prevent penetration of hazardous materials such as allergens and irritants. From a practical point of view, the definitions of “barrier cream,” “invisible gloves,” or “prework cream” may be misleading as these products do not provide a real barrier against all noxious agents. The term *skin protective creams*, although less used, may be considered more appropriate.¹⁸

Barrier creams may also be intended as products that may restore a damaged SC, the physiological skin barrier. In this sense, any emollient and moisturizing product can be considered a potential skin barrier improver. The emollients, lipophilic compounds, increase softness and the moisture content of the SC providing an occlusive oily film on the skin surface to reduce Transepidermal Water Loss (TEWL). Moisturizers, being hydrophilic molecules, attract water from the deep dermis and improve hydration of the SC.^{5,6}

It could be advisable to use the term *barrier creams* for products that primarily act against exogenous substances while using the term *barrier repair creams* for products intended to repair the skin's natural barrier.

The US Food and Drug Administration has included BCs among medical devices (MDs) for their proven ability in improving skin

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hydration and decreasing TEWL. These products are not drugs but must be obtained with a medical prescription.¹⁹

In Europe, BCs are both cosmetic formulations and MDs, obtainable without prescription, depending on the market objective of the manufacturer. When registered as MDs, BCs are included in the borderline category of MDs. According to European legislation (Article 1 of the Directive 93/42/EEC),²⁰ MDs must be intended to be “used for human beings for the purpose of: ...diagnosis, prevention, monitoring, treatment, or alleviation of disease.” Evidences for these claims must be provided and proven. If manufacturers register a BC as a cosmetic, no emphasis on disease alleviation must be claimed. However, based on Article 20 of the new Cosmetic Products Regulation (EC) N°1223/2009, applied since July 2013,²¹ the manufacturer must justify all claims for cosmetic products with instrumental or biochemical standards too.²²

Barrier Creams: Which Formulation?

Barrier creams are usually but not necessarily formulated as “creams.” In fact, these products may also be formulated as ointments, pastes, gels, and even foams, in consideration of the chemical nature of occupational hazards.²³ Creams are emulsions of immiscible phases: lipids and water. Oil-in-water (O/W) emulsions are cooling, soothing, light, and easy to apply. Water-in-oil emulsions are emollient, mildly occlusive, and persistent; in the past, they were heavy and sticky, but now they are cosmetically elegant.²⁴ Because of the biphasic nature of creams, both lipophilic and lipophobic actives can be added for achieving a barrier activity.

Ointments are semisolid preparations with a high percentage of oils or fats (80%). They require fewer preservatives because they contain no water and do not sustain microorganism growth. Because of their occlusive nature, ointments form both a protective and lubricating film and generally provide better persistence and penetration of incorporated lipophilic actives than creams. Being insoluble in water, they are difficult to wash off and less cosmetically acceptable than creams or gels but suitable against lipophilic irritants.²⁴

Pastes are formulated with oil, water, and at least 20% to 50% of fine solid materials, the suspended powder, which acts both to absorb water and to hold irritants.²⁵ Pastes are messy, occlusive, protective, and generally difficult to apply and remove.²⁴ Gels are either transparent nonfluid networks or polymer networks, whereas hydrogels contain natural or synthetic hydrophilic polymers in water. Although having the advantage of being water washable, nongreasy, and pleasant, gels have the disadvantages of being removed by perspiration, and they lack emollient properties.²⁴ To exert protective properties, gels must be formulated with specific film-forming polymers.

Foams are colloids composed of 2 or 3 distinct phases: a hydrophilic liquid continuous phase with a foaming agent (amphiphilic substance) in which a gaseous dispersion phase is distributed. A third hydrophobic dispersed phase may be present. Both water-repellent and oil-repellent actives can be included in the foams. The product

dispenser is essential to the creation of the foam. These products are easy to apply; they leave minimal residues because they are created at the time of use but exist only briefly.²⁶

Barrier Creams: Which Ingredients?

Although a univocal definition for BC composition does not exist, in 2003, the Federal Register of the Food and Drug Administration supplied a series of allowable active ingredients and their percentage range of use approved for barrier protective formulation.²⁷ Commercially available BCs contain a combination of ingredients classified as emollients, humectants, and hydrating agents, all central for maintaining SC integrity.^{3,24}

Emollients

Emollients are mainly lipids and oils. They reduce TEWL by creating a hydrophobic barrier over the skin and contributing to the lipidic matrix.^{6,28}

The percentage and type of lipids in the cream are crucial in recovering experimentally damaged skin.^{29,30} A lipid mixture reproducing the intercorneocyte lipids was seen to improve skin barrier function.^{31–34}

Petrolatum (paraffinum liquidum, mineral oil), the oldest barrier product, is a fluid mixture of hydrocarbons with different viscosity. It is highly occlusive and is a standard ingredient of BCs with water-repellent properties. Other occlusive agents are lanolin and paraffin waxes. Lanolin is a mixture of sterols, fatty alcohols, and fatty acids; its precise composition varies qualitatively and quantitatively with humidity, temperature, and method of collection. Paraffin waxes (petrolatum jelly, white petrolatum) are white semisolids derived from petroleum that consists of a mixture of hydrocarbons with greater molecular weights than paraffinum liquidum.⁴ Lanolin and paraffin waxes are used in low concentrations in modern formulations, replaced by synthetic and semisynthetic lipids. These more recent substances are less occlusive and more pleasant. An alternative to these lipids are silicone oils, in particular dimethicone, a liquid, odorless, colorless, nontoxic substance insoluble in water; they are used in water-resistant creams and foams. The silicone oils are less greasy than petrolatum and possess better aesthetic function but are not as effective as petrolatum in reducing TEWL.³⁵

Ceramides, functional lipid agents frequently found in BCs, are characterized by a polar head group and hydrocarbon chain. Twelve classes of ceramides, corresponding to over 340 ceramide species, have been identified in human skin, and many are chemically synthesized for inclusion in BCs.³¹ In vivo studies have demonstrated that ceramide synthesis is the first step in healing a damaged skin barrier.^{31–34,36} Palmitoyl ethanolamide (palmitamide MEA) is another lipidic active ingredient that decreases itching. It is a derivative of fatty acids, deficient in atopic skin.⁴

Humectants

Humectants are low molecular weight compounds with high affinity to water (hygroscopicity). The most widely used humectants

in BCs are glycerine (glycerol), propylene glycol, or 70% sorbitol solution; among these, the most effective is the trihydroxylated molecule glycerine.^{6,37,38} Humectants play a passive role being able to attract water from 2 sources; they enhance water absorption from the dermis into the epidermis, and in humid conditions (humidity at least 80%), they also help the SC to absorb water from the external environment.³⁸ However, when humidity decreases, they can take water from the deeper epidermis, resulting in increased skin dryness. Any humectants have this potential if used alone, so they need to be used in combination with occlusive emollient ingredients.

Hydrating Agents

Hydrating agents actively maintain the water balance both supplying and maintaining the water of the SC. Urea and allantoin, a heterocyclic ureidic derivative, have moisturizing and keratolytic effects.³⁹ Another moisturizing agent present in BCs is reconstructed natural moisturizing factor, a highly hygroscopic mixture of amino acids, salts, sodium lactate, urea, and PCA (2-pyrrolidone 5-carboxylic acid).⁴⁰ Hyaluronic acid, a component of the extracellular matrix, maintains skin hydration acting as a sponge that attracts and holds water.⁴

The formulation of hydrogels includes some film-forming polymers soluble or dispersible in water such as the oldest PVP (polyvinylpyrrolidone) and VP/VA copolymer (polyvinylpyrrolidone vinyl acetate copolymer) and the newest VP/eicosene copolymer and ammonium acryloyldimethyltaurate/VP copolymer. They are rheological agents that both make gels adherent to skin when applied and thicken gels, either alone or in addition to natural polymers such as cellulose derivatives or gums.⁴¹ Polymers have excellent wetting and film-forming properties and have shown to significantly affect the skin protective efficacy of barrier formulations.⁴² The newest polymers are also water repellent.⁴¹

Numerous other substances are commonly found in BCs with the aim to enhance protection against irritants and skin health. Important chemical compounds in BCs are polyperfluoromethylisopropyl ether, FOMBLIN HC(R), obtained by UV polymerization of tetrafluoroethylene with oxygen. Fomblin HCs are synthetic polymer consisting only of fluorine, carbon, and oxygen. They are transparent liquids, odorless and colorless, water-repellent and oil-repellent, insoluble in all organic solvents, and polar and not polar. Fomblin HCs are chemically and thermally stable but permeable to water vapor, biologically inert, toxicologically safe, noncomedogenic, and gentle. Fomblin HCs form a thin film that does not occlude the pores, and they protect the skin with a dose-related effect.^{43,44} Fomblin HC can be incorporated into almost any cosmetic technical form; in the case of emulsions, they may be dispersed by vigorous stirring either in the oily or in the aqueous phase before emulsification. Being insoluble, Fomblin HCs build up a third phase that helps to stabilize the system.

Plant derivatives or botanical extracts are frequently found in BCs. Glycyrrhetic acid (a root licorice extract), bisabolol (derived from chamomile), and *Butyrospermum parkii* butter (shea butter) can serve as lenitive and anti-inflammatory ingredients. Other

botanicals such as *Vitis vinifera* extract (derived from grapes) and *Rosa canina* fruit extract serve as antioxidant ingredients.⁴

Sodium bischlorophenyl sulfamine and aluminum chlorohydrate make the SC less permeable forming a “plug” at the follicular infundibulum and preventing the skin penetration of harmful substances. Because of their antimicrobial and astringent properties, they can reduce the use of preservatives in the formulation.⁴⁵

Acting as a protective physical layer on the skin, several solid inorganic substances, such as talc, zinc oxide, kaolin, and more recently the organoclay quaternium-18 bentonite, are ingredients of BCs with proven efficacy.^{25,35}

With the aim to prevent absorption of nickel, chromium, and copper, metal chelants such as EDTA (disodium ethylenediaminetetracetic acid) and pentetic acid (diethylenetriamine pentacetic acid) were introduced in BCs.⁴⁶

How a Barrier Cream Should Be Chosen and Used?

It is not realistic that a universal BC, appropriate for all the environmental stressors, may exist. The physical-biochemical-molecular characteristics of the commonest offending agents in work places should guide in the selection and formulation of specific BCs. The general rule is that water-in-oil emulsions are effective against aqueous solutions of irritants, and O/W emulsions are effective against lipophilic materials, but some exceptions have been reported.⁴⁷ Water-repellent BCs should be used to protect against acids, alkalies, soaps, water-soluble irritants, and detergents (Fig. 1). Therefore, formulations containing hydrophobic (lipophilic) substances should be used. An oil-repellent type should protect against oils, varnishes, and organic solvents. Therefore, creams containing hydrophilic (lipophobic) ingredients may be suggested (Fig. 1).^{17,18}

The protective efficacy of a BC depends on its application and dose. Barrier creams must be applied in adequate amounts and must cover the entire skin surface, paying special attention to cutaneous folds, cuticles, and the skin under nails. Using a Wood's lamp, it was evidenced that after application of BCs, the dorsum of the hands and the interdigital spaces, excluding the space between the index finger and thumb, were frequently missed.¹⁶

It has been found that skin irritation may be reduced by BCs in a dose-dependent manner; the protective function of different BCs depends on the amount of product applied per unit of skin surface area.⁴⁸ Under routine working conditions, less than 1 mg of BC/cm² of skin is generally applied; this is much lower than the amounts that have been used in experimental efficacy studies, ranging from 4 to 25 mg/cm².⁴⁹ It is possible that the doses used in trials in the past were unrealistically high, leading to overestimation of the efficacy of some BCs. In clinical practice, a dose of 2 mg product/cm², used by COLIPA (now Cosmetic Europe) for assessment of the sun protection factor skin, should be encouraged.⁴⁸ As the area of 1 hand is estimated to be about 2.5% of the total body surface area, corresponding to about 400 to 500 cm², both hands require about 2 grams of BC for each application (Table 1). If applied sufficiently, BCs are

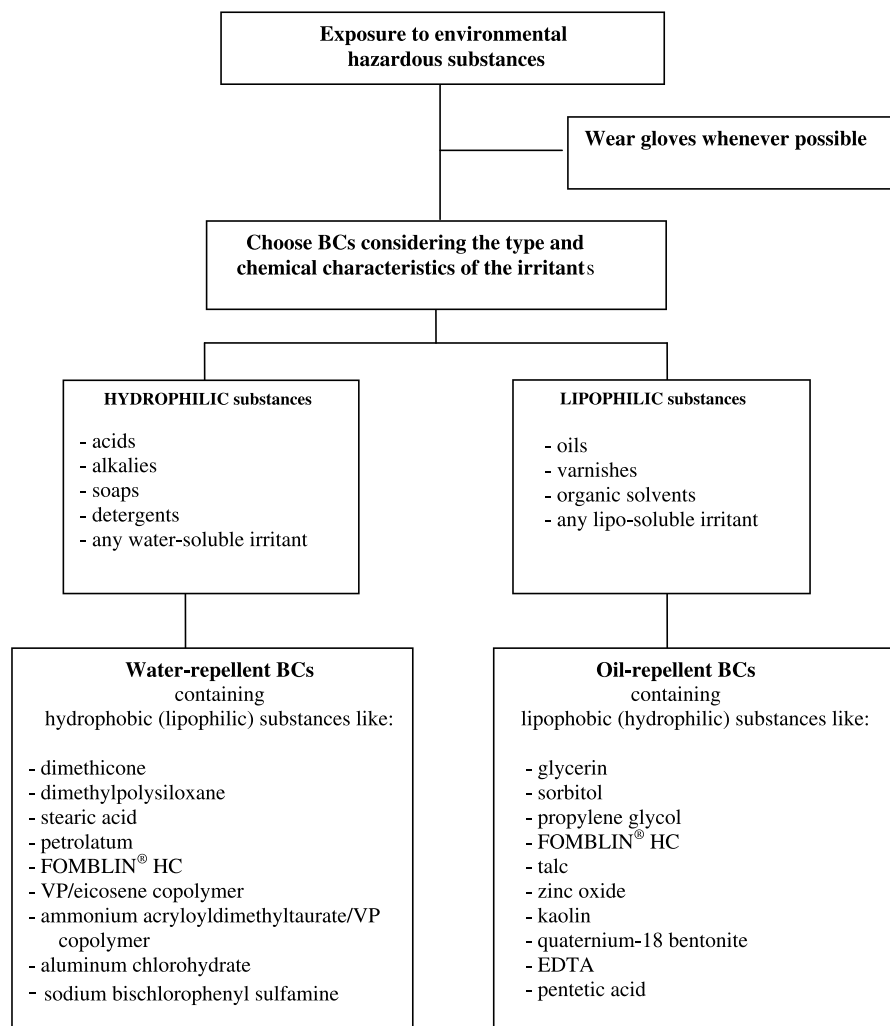


Figure 1. Flow chart for an appropriate choice of BCs.

expected to remain effective for 3 or 4 hours.¹⁶ Therefore, BCs must be reapplied regularly on a 3- to 4-hour period and after every hand washing (Table 1). The effectiveness of BCs may also increase with education of workers and periodic checks.⁵⁰

Are Barrier Creams Really Effective?

Although BCs are commonly recommended to prevent occupational CD, their real benefit at the workplace remains controversial. In an international survey of expert dermatologists, 98% of those interviewed considered BCs to be no more effective than bland emollients in the prevention of CD.^{45,51}

Different commercially available emollients and moisturizers have been proven not only to prevent but also to treat ICD.^{52–55} Moisturizers (especially with high lipid content) were found to accelerate regeneration of the skin barrier function when compared with sodium lauryl sulfate (SLS)-irritated nontreated skin.^{30,56} Repairing the barrier or preventing barrier dysfunction are important strategies for reducing the risks of dermatitis and

prolonging the time to relapse of dermatitis.^{57,58} The actual advantage of BCs over bland emollients for skin protection is still hotly discussed. Some studies have shown improvement of clinical skin status and SC hydration without significant differences between BCs and their moisturizing vehicle or other emollients; all were effective as protective measures against occupational CD in health care workers and apprentice hairdressers.^{45,59,60} Effectiveness was evaluated both clinically and by means of bioengineering parameters.

TABLE 1. Instructions for BCs Use

- Wash and dry your hands
- Apply proper quantity of BCs (about 1 gram for hand)
- Spread a thin layer over the entire hand area, paying special attention to cuticles, skin under nails, and between fingers
- Wait for 1 to 3 minutes before starting work
- Reapply every 3 to 4 hours and after every hand washing

Various clinical and experimental studies have been conducted to determine efficacy of BCs. However, many test models supplied by manufacturers investigate acute toxicity instead of evaluating the effects of repeated exposure. International guidelines recommend human repetitive irritation test to assess real efficacy in occupational environmental conditions.⁶¹

The efficacy of different kinds of BCs was studied by many authors using the repetitive irritation test.^{18,62,63} The benefits of BCs against detergents, such as SLS, and hydrophilic substances, such as NaOH, in wet work have been proven.^{64–67} Protection against lipophilic substances, such as solvents and oils, frequently claimed by manufacturers, is more debatable. None of 4 evaluated BCs gave protection against toluene.⁶⁶ In a recent trial, none of 6 commercially available BCs offered protection against relevant irritant model solvents (n-octane and cumene).⁶¹ Barrier creams did not seem to have any significant effect against cutting oil dermatitis in exposed workers.⁶⁸

Three BCs, commercialized as effective against lipophilic and hydrophilic substances, showed different efficacy in an in vivo method to measure effectiveness against methylene blue in water and oil red O in ethanol, dyes chosen as representative of hydrophilic and lipophilic substances, respectively.⁶⁹

Laser-induced breakdown spectroscopy was used to evaluate the effect of 3 commercial BCs on human skin; all products, advertised as effective against lipophilic and hydrophilic substances, provided an appreciable protection against zinc ion penetration into the skin.⁷⁰

Perfluoropolyethers, nonreactive perfluorinated liquid polymers, widely used in BCs, at a 4% concentration in O/W emulsion, significantly inhibited irritation caused by numerous lipophilic and hydrophilic irritants in a human cumulative irritancy model.⁴⁴ The same products gave a statistically significant higher cure versus base in patients affected by chronic irritant dermatitis.⁷¹

Glove-induced irritant CD was significantly reduced in 2 different studies in which 2 BCs, a lipid emulsion and a zinc gel, were evaluated.^{72,73}

A unique definitive conclusion on BC efficacy cannot be drawn due to scarcely comparable studies (different BCs, different hazardous substances tested in different study populations, and different methodological studies design). The concept that BCs are always protective against skin contactants is attractive but not always applicable in work environments. However, a general impression of utility on skin protection and improvement is deducible from literature.

Are Barrier Creams Always Safe?

There have been reports of exacerbations of CD with the use of BCs. It has been suggested that certain irritants may be concentrated or trapped on the skin in the presence of BCs, increasing the likelihood that dermatitis may develop.^{16–18,48,66}

Paradoxically, moisturizer-treated skin has shown greater susceptibility to SLS-irritating potential than untreated skin. The

authors explain this phenomenon saying that a fully hydrated SC becomes more permeable to hydrophilic substances such as SLS. Furthermore, BCs can modify the composition of the lipid bilayer of SC increasing or modifying penetration of molecules.⁷⁴

Moreover, chemical reactions may happen between some BC constituents and hazardous molecules used during work enhancing irritation. In 1 study, stearic acid contained in a BC reacted with NaOH, a standard alkali irritant tester, inducing sodium stearate precipitation, a known irritant soap.⁴⁷

The BCs themselves may potentially cause ICD or ACD because they contain various fragrances, preservatives, and emulsifiers that could induce or elicit sensitization. Petrolatum and some oil-based agents may cause rubber and latex glove deterioration and may increase the transfer of protein latex allergens. Workers who concomitantly use BCs and gloves should pay attention when selecting hand care products and gloves.^{60,75} Another occupational risk may exist for those who believe that the BCs offer more protection than they actually do. This false sense of protection may prolong exposure to various irritants or allergens, with dangerous consequences.

Which Is the Ideal Barrier Cream?

Ideally, BCs should improve SC hydration as well as provide emolliency to maintain skin integrity, retain or increase skin water content, and restore and repair the epidermal barrier function to target the objective to reduce the risk of CD. Barrier creams should also be cosmetically elegant and acceptable, odorless, and without greasy compositions that could interfere with the users' dexterity. Moreover, BCs should be absorbed rapidly and be long lasting, possibly resisting being washed off. To be suitable for use on damaged skin, an ideal BC should be formulated as hypoallergenic, nonsensitizing, fragrance-free, alcohol-free, and noncomedogenic. These aspects are relevant for improving patient adherence to constant BC use. For the same reason, BC should be inexpensive or cost-effective.

CONCLUSIONS

Barrier creams may be considered among the prophylactic measures to reduce the risk of developing CD. Barrier creams may be recommended in the presence of low-grade irritants found in the working environment, improving the "outside-inside" barrier against certain chemicals. They should be selected considering both the formulation and the ingredients. A regular, frequent, and correct application of the product must be encouraged in order for it to be effective. The effectiveness of BCs remains controversial and is an important issue for further studies and evaluation.

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