

Chapter 1

Anti-Irritants Agents

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1. Introduction

Anti-irritants agents counteract or suppress *irritation* responses. These agents/ingredients, regardless of whether naturally occurring or man-made, used alone or in formulations, possess the capacity to reduce irritation caused by acute and chronic exposure to irritants.¹

Irritant contact dermatitis (ICD) is common in the workplace and at home.² During daily activities, human skin may be exposed to potential irritants (for example, surfactants, cutting oils, etc.) that might result in ICD.^{3,4} Minimizing exposure to such harmful substances is recommended but often not practical since in many occupations (for instance, farmers, forest fire-fighters, outdoor activities, hospitals and even households), such encounters are ubiquitous.

To prevent or reduce the risk of developing ICD, anti-irritants agents/substances (including barrier creams (BC) and moisturizers) are widely utilized.⁵⁻¹⁰ Though BC and moisturizers are not identical, due to their ambiguous definitions, the terms BC and moisturizers are often used interchangeably in literature and marketplace. The BC target is in the prevention of external noxious substances penetrating skin, used usually in occupational setting^{6, 8, 9, 10} and moisturizers are frequently used for “dry” skin conditions as well as to maintain healthy skin.^{5, 7, 10-13} However, moisturizers and BC may share characteristics⁵; to strictly distinguish between them may be difficult. Therefore, standardized terminology of skin protection is suggested.¹⁴

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Table 1. Common terms and definitions of skin protection

Term	Definition
Barrier creams (BC)	Topical products are used to prevent or reduce the penetration and absorption of external noxious substances penetrating into skin, are used usually in occupational setting.
Moisturizers	Topical products are used to alleviate or improve “dry” skin conditions and maintain healthy skin, are often used in both workplace and daily life.
Anti-irritants	Agents are used to reduce the irritation potential of other more irritating ingredients in the same product or reduce existing skin irritation.
Occupational skin protection	It is a complex term of protective measures that protect the skin against hazards from the workplace by using protective measures, including personal protective equipment, engineering controls or work practices improvement, which may include the use of protective gloves or chemical protective clothing, and/or the application of BC, moisturizers, and anti-irritant agents.
Occupational dermatologic products	Dermatologic products are employed for industrial skin protection, systematic skin protection or skin care programs (e.g. hygienic practices) against hazards from the workplace, and typically consist of three components: skin protection products; skin cleansers; skin conditioning/regeneration products.
Skin protection products	Topical products are used to apply on the skin before contact with hazardous or skin impairing substances to prevent/minimize skin damage or skin diseases, which may include BC, moisturizers, and anti-irritant agents.
Skin cleansers	Topical products are used for the removal of undesirable materials and particles from the skin surface.
Skin conditioning products	Topical products are used after work or during longer work interruptions to increase moisture and smoothness of the skin.
Skin regeneration products	Topical products are used to restore the natural barrier function of the skin.

We summarize the common terms and definitions in this field, as listed in **Table 1**. Numerous ingredients have been formulated into the skin protection products in the marketplace. Nevertheless, the US Food and Drug Administration (FDA) only endorsed 13 skin protectants for over-the-counter (OTC) products.¹⁵ Based on extensive literature review, the current chapter summarizes related studies and data of the efficacy of proposed anti-irritants agents/substances in reducing ICD in man. However, studies and data were excluded if they were not conducted in man.

1.1. Method

We performed a literature search using PubMed, EMBASE, and Scopus via the library at University of California San Francisco, and a hand search in an attempt to investigate products that can be considered anti-irritants in either prevention or treatment.

1.2. Study Selection

Emphasis was placed on studies that included quantitative and qualitative results and that followed evidence-based dermatological guidelines. We defined an anti-irritant as a moiety that either inhibits (prevents) or treats ICD. For the purposes of this review we focused on clinical markers of irritation, that is, edema, erythema, vesiculation, and diminished barrier function, as these are more readily and objectively assessed via visual scoring criteria, bioengineering measurements.

1.3. Irritant Reaction

ICD is the result of an unspecific damage due to contact to chemical substances that cause an inflammatory skin reaction.²⁻⁴ Human exposure to irritants such as solvents, detergents,

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and even water¹⁶ at home and at work, leads to damage to the stratum corneum and skin barrier impairment.⁵ The exact mechanisms of irritant action are not completely understood, but it seems likely that there is an “immunologic-like” component to the irritant response.⁴ The clinical appearance of ICD varies depending on multiple external and internal factors.^{3,4} Airborne ICD may develop in uncovered skin areas, mostly in the face and neck after exposure to volatile irritants or vapor. Avoidance of these irritants may not be practical for persons whose occupation or daily activities require them. Prophylactic measures reduce the risk of developing ICD: BC and moisturizers as well as anti-irritant agents may play a key role in this strategy.

2. Barrier Cream (BC) Efficacy

Lupulescu and Birmingham¹⁷ observed the ultrastructural and relief changes of human epidermis following exposure to a protective gel and acetone and kerosene on humans. Unprotected skin showed cell damage and a disorganized pattern in the upper layers of epidermis. Protective agent applied prior to solvent exposure substantially reduced the ultrastructural and relief changes of epidermis cells.

Grunewald et al.¹⁸ evaluated BC protective effects by measuring with bioengineering techniques utilizing a sodium lauryl sulfate (SLS) repetitive washing model on 15 human volunteers. All BC reduced the deterioration of skin functions following one week repetitive washing. Subsequently, they found urea and glycerol oil-in-water emulsions provided a greater protection than three tested commercially BC against a lipophilic irritant (toluene) after seven days of repetitive irritation.¹⁹

We²⁰ measured the effectiveness of BC on human subjects against dye indicator solutions: methylene blue in water and oil red O in ethanol, representative of model hydrophilic and lipophilic compounds. 5% of each solution was applied to untreated and BC-pretreated skin with the aid of aluminum occlusive chambers for 0 h and 4 h. Post application time, materials were removed and consecutive skin surface biopsies (SSBs) obtained. The amount of dye penetrating into each strip was determined colorimetrically. Two model creams exhibited effectiveness, but one enhanced the cumulated amount of dye.

Schlüter-Wigger and Elsner²¹ assessed four commercially available BC against four standard irritants: 10% SLS, 1% sodium hydroxide (NaOH), 30% lactic acid (LA), and undiluted toluene (TOL) in the repetitive irritation test (RIT) in humans for 12 days. Irritation was assessed by visual scoring, transepidermal water loss (TEWL), and colorimetry. All products were effective against SLS irritation. Nevertheless, no BC provided significant protection against TOL. Three products showed a partially protective effect against all ionic irritants, while the fourth showed less protection against SLS and NaOH, and even amplification of inflammation by TOL.

Wigger-Alberti and Elsner²² evaluated the protective effects of petrolatum utilizing the above model and noted that petrolatum was effective against SLS, NaOH, and LA irritation and also provided a moderate protection against TOL. Subsequently, Wigger-Alberti et al.²³ examined three other BC and petrolatum against 10% SLS, 0.5% NaOH, 15% LA, and undiluted TOL in the RIT in humans for nine days. All BC exhibited a significant protective effect against irritation by SLS, NaOH, and LA. Less efficacy was observed against TOL. In another 12-days RIT study²⁴, white petrolatum provided a significant protective effect against SLS, NaOH, and TOL but with less protective effect against LA irritation.