

Review Article

Elucidating the role of zinc oxide in dermatitis of varied etiology across the age spectrum: a comprehensive review

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ABSTRACT

Zinc oxide (ZnO) is widely used in dermatology for its protective, antimicrobial, anti-inflammatory, and wound-healing properties. This comprehensive secondary review evaluates the efficacy of ZnO in preventing and managing skin rashes across pediatric and adult populations, including those caused by tight clothing, frictional dermatoses, sanitary pad dermatitis, diaper dermatitis (DD), contact dermatitis, and anti-chafing conditions. ZnO plays a crucial role in skin barrier repair, hydration, and the treatment of inflammatory conditions, making it particularly beneficial for thick-skin areas. Clinical evidence confirms the efficacy of ZnO in various concentrations, with 5-10% proving effective for mild cases, while higher concentrations or combination therapies with tocopherol and petrolatum enhance therapeutic benefits. Additionally, ZnO has shown effectiveness in wart management, with a 20% ZnO ointment being comparable to a combination of 15% salicylic acid and 15% lactic acid ointment, with half of the patients achieving complete cure within three months without scarring, hypopigmentation, or hyperpigmentation, while another randomized, triple-blinded, placebo-controlled trial found that topical 15% ZnO ointment significantly reduced the median surface area of common warts after four weeks. These findings suggest that ZnO can be used as an adjunctive therapy to enhance the efficacy of other treatments. These findings establish ZnO as a versatile agent in the prevention and treatment of rashes across multiple skin conditions, reinforcing its tolerability, efficacy, and role in maintaining skin health.

Keywords: Diaper dermatitis, Zinc oxide, Barrier creams, Antimicrobial, Anti-inflammatory, Skin healing

INTRODUCTION

Skin rashes and lesions are among the primary concerns prompting individuals to seek medical care. Skin-related conditions are some of the most prevalent health issues in humans, with disorders affecting the skin and subcutaneous tissues being major contributors to the global burden of nonfatal diseases over the past decade.¹ A rash refers to a broad outbreak of skin abnormalities that can differ significantly in appearance.² It may present as red, inflamed, bumpy, dry, itchy, or painful patches on the skin. The primary cause of rashes is dermatitis, which occurs when the skin reacts to allergens or irritants. Other contributing factors include bacterial and viral infections, chronic skin conditions such as eczema, hives, and psoriasis.³ Climate change may influence the temporal

patterns and geographic spread of rashes, with atopic eczema becoming more prevalent in some tropical regions, while people in tropical and subtropical climates often experience a high incidence of rashes due to undergarments.⁴⁻⁶ The term dermatitis broadly refers to a group of common conditions characterized by itchy inflammation of the skin. It results from a complex interplay of environmental, immune, and genetic factors. A family history of dermatitis is a significant risk factor, as certain genetic variations may predispose the skin to excessive reactions when exposed to environmental triggers. Dermatitis manifests in various forms, each with distinct characteristics and causes. The most common types include atopic dermatitis, contact dermatitis, chafing, seborrheic dermatitis, and nummular dermatitis.⁷ Atopic dermatitis is characterized by dry skin,

itching, and excoriations, sometimes affecting the diaper area, where infants may scratch the affected skin, requiring long-term management. Seborrheic dermatitis appears as a red, scaly rash in the diaper area and may extend to the scalp, face, and neck, though the child often remains symptom-free despite its inflamed appearance.⁸ Nummular dermatitis presents as round, inflamed, and intensely itchy patches, commonly affecting the arms, legs, and torso, with dry skin and environmental factors acting as triggers.⁷ Chafing dermatitis, one of the most common diaper rashes, occurs in high-friction areas, presenting with mild redness and papules on a shiny surface.⁸ Contact dermatitis results from exposure to irritants or allergens and is classified into two types: irritant contact dermatitis, caused by harsh substances, and allergic contact dermatitis, triggered by an immune response to allergens like nickel, fragrances, or latex.⁷ Topical preparations containing ZnO are widely used for photoprotection, soothing effects, and as active ingredients in antidandruff shampoos. Their applications have expanded to various dermatological conditions, including infections, inflammatory dermatoses, pigmentary disorders, and certain neoplasias.^{4,5} Understanding the causes, risk factors, and different types of dermatitis is crucial for accurate diagnosis and effective management. With appropriate treatment strategies and preventive measures, the adverse impact of rashes and dermatitis on an individual's quality of life can be minimized.⁷

DIAPER DERMATITIS: A COMMON CONCERN ACROSS AGES

Diaper dermatitis (DD), also known as napkin dermatitis or diaper rash, is a common inflammatory condition affecting the skin in the diaper region.⁹ Diaper rash primarily involves areas such as the buttocks, perianal region, genitals, inner thighs, and waistline.¹⁰ This condition is particularly common in neonates and infants particularly between 9 and 12 months of age, affecting approximately 7% to 50% of the general population, with no significant ethnic variations.¹¹ Additionally, it is prevalent among elderly individuals, especially those with urinary incontinence or who are bedridden, with reported cases ranging from 5.6% to 50%.^{2,9} The Diaper rash typically begins as mild erythema with minimal scaling but can progress to more severe forms, including the development of papules, pustules, and erosions, which can cause significant discomfort and pain. If left untreated, diaper rash can worsen over time and may persist until diaper use is discontinued.¹⁰ The barrier creams, ointments, and pastes are widely recommended as the first-line treatment and preventive measure for managing diaper rash, given that avoiding diaper use is often impractical.¹⁰ Regular application of these formulations during diaper changes helps to protect the skin by forming a protective lipid barrier, preventing direct contact with moisture and irritants. Most effective barrier creams contain ZnO, petrolatum, or a combination of both as active ingredients.¹⁰ ZnO, a naturally occurring mineral compound, is known for its anti-inflammatory,

antimicrobial, and protective properties. It serves as a physical barrier against excessive moisture absorption and reduces the risk of secondary bacterial infections by preventing microbial adhesion and penetration.¹¹ The recurrence of diaper rash is often linked to infrequent diaper changes and inconsistent use of barrier creams.¹⁰ This manuscript aims to establish the role of ZnO in preventing and managing skin rashes across all age groups. It highlights ZnO's protective, anti-inflammatory, and antimicrobial properties, emphasizing its effectiveness in reducing severity, preventing recurrence, and supporting skin health.

ETIOLOGICAL INSIGHTS INTO SKIN RASHES ACROSS DIFFERENT AGES AND GENDERS

In pediatrics: Diaper rash in children is a broad condition with multiple underlying causes, with differential diagnoses revealing over 20 potential factors.⁸ The most common cause of diaper rash in children is irritant contact dermatitis, which occurs due to compromised skin integrity and barrier function. This primarily results from increased moisture within occlusive diaper environment, in combination with urine and fecal waste, as well as elevated skin pH caused by enhanced protease and lipase activity.¹³ In addition to irritant diaper rash, other skin conditions such as seborrheic dermatitis, chafing, atopic dermatitis, psoriasis vulgaris, and infections like candidiasis, scabies, bullous impetigo, and tinea cruris may present with similar symptoms. Less common causes include Langerhans cell histiocytosis, congenital syphilis, child abuse, and acrodermatitis enteropathica.¹¹

In elderly adults: Diaper rash is a prevalent skin disorder among the elderly, particularly in bedridden patients, and is a frequent reason for dermatological consultations. In elderly individuals, various skin conditions can manifest in the diaper area, including psoriasis, contact dermatitis, pemphigoid, and infectious diseases.¹² Ulcer development in elderly patients, especially pressure ulcers, is often linked to incontinence, requiring diaper use. Prolonged moisture exposure, friction, and factors like ischemia, sensory impairment, and reduced mobility increase ulcer risk. Differentiating between mild and moderate ulcers is challenging, as both present as erythema, but their causes differ, pressure ulcers form over bony prominences due to ischemic damage, while incontinence-associated dermatitis affects moisture-exposed areas like the perineum and buttocks. Unlike pressure ulcers, diaper-related erythema is diffuse and linked to irritant exposure, aligning more with DD than true pressure ulcers.¹³

Influence of skin structure variations in men vs women

Men have higher stratum corneum hydration in youth, but it declines after 40, while women's hydration remains stable or increases. Trans-epidermal water loss (TEWL) is lower in men but equalizes with age, except on the forearm. Sebum production is higher and stable in men, whereas it declines in women, leading to impaired barrier function. Male skin is thicker but thins from age 20, while

female skin remains stable until menopause, after which collagen loss causes thinning.¹⁹ Men generally have a lower skin pH, though some studies show no sex-related differences; male pH increases with age, while female pH stays above 5 except on forehead. Women have higher skin elasticity and better recovery after stretching, though aging affects elasticity differently in each sex. Skin friction coefficients are higher in women, especially around 40, correlating with hydration, with female skin also being scalier.^{14,15} Additionally, women are more affected by skin diseases than men, with seasonal variations playing a role. Studies indicate that 8.8% of males, 13.6% of females are more prone to skin diseases during summer, highlighting sex-related vulnerability. These variations in skin physiology shows impact of age, hormones, environmental factors and seasonal influences on skin health.¹⁶

Frictional and contact dermatosis in women

Frictional dermatosis and contact dermatitis are skin conditions that are more common in women than in men and arise due to external factors affecting the skin barrier.^{17,18} Frictional dermatosis occurs when repeated friction between two surfaces leads to skin irritation or injury. This condition results from an imbalance in frictional forces and is influenced by factors such as temperature, tight clothing, sweating, and repetitive activities. People involved in professions like sports, music, computer work, and healthcare are more vulnerable due to constant rubbing and microtrauma. Women are at a higher risk than men, as household activities often expose them to increased friction.²¹

Sanitary pad dermatosis

Sanitary pad dermatitis in women is primarily caused by prolonged moisture exposure, friction, and irritants present in sanitary products.¹⁹ According to the national family health survey-5 (NFHS-5), 77.3% of women use hygienic menstrual protection methods, with sanitary napkin usage ranging from 42% to 60%.²⁰ Fragrances in pads and methylidibromo glutaronitrile in adhesives have been identified as allergens, leading to irritation and dermatitis.²¹ The thin stratum corneum of the vulvar skin, with higher water content and friction, makes it highly susceptible to contact dermatitis. The persistently wet condition under sanitary napkins promotes microbial proliferation, releasing irritants that penetrate the skin.²² Unlike other body areas, the vulvar skin has lower resistance to mechanical stimulation, increasing inflammation risk. Symptoms include erythema, itching, swelling, and, in severe cases, ulcers. Poor hygiene, excessive soap use, and prolonged dampness worsen irritation.²³ Patch testing modifications are necessary to assess the true irritant potential of sanitary pads.²⁴

Rash due to tight clothing and anti-chafing strategies

Chafing is a skin irritation caused by repeated friction includes exercise, tight clothing, ill-fitting shoes, body

weight, breastfeeding, diapers, and hot, humid weather, often worsened by moisture. It commonly affects areas like inner thighs, groin, buttocks, armpits, and under the breasts. Though painful, it is usually mild and easily treatable. Chafing occurs in skin folds and areas where body parts/clothing repeatedly rub against skin.^{8,23} Mild symptoms of chafing include redness, raised bumps, warmth in the affected area, burning or stinging sensation, itching, irritation, tenderness, and dry, flaky skin. Stop any activity that causes chafing to prevent further irritation. Wear loose-fitting, 100% cotton clothing and keep it clean and dry. Use anti-chafing creams, moisture-wicking socks, and protective bandages to min friction and discomfort.²³

UNDERSTANDING PATHOPHYSIOLOGY OF DIAPER RASH

The pathophysiology of diaper rash is multifactorial, influenced by both intrinsic and extrinsic factors.⁹ In newborns, the skin is immature and more susceptible to barrier disruption, leading to increased percutaneous absorption.¹⁴ In contrast, aging skin in elderly patients undergoes structural and functional changes due to genetic factors and environmental influences such as UV exposure and smoking. Thinning of the epidermis, reduced cell regeneration, and a weakened lipid barrier make the skin more vulnerable to damage and delayed healing. Additionally, decreased collagen, micro-vascularization, and sensory function contribute to dryness, wrinkles, and reduced elasticity.¹⁷ Excess moisture in the diaper area contributes to the breakdown of the stratum corneum, weakening its “brick and mortar” structure and impairing barrier function.⁹ An acidic skin surface is crucial for preserving the normal skin microbiota, offering natural protection against harmful bacteria and yeasts, while also regulating enzymatic activity necessary for maintaining the stratum corneum. Disruption of the acid-mantle can impair both functions.²⁵ Urine contains urea, which is converted to ammonia by fecal bacteria with urease activity as shown in Figure 1. This, along with proteolytic enzymes in feces, contributes to irritant dermatitis.¹² Prolonged exposure to urine and feces increases skin pH, leading to microbial colonization, activation of fecal protease and lipase enzymes, and further impairment of the stratum corneum. These factors create a favorable environment for microbial invasion and inflammation, with *Candida albicans*, *Staphylococcus aureus*, *Streptococcus* spp., *Escherichia coli*, and *Bacteroides* spp. commonly implicated in DD.⁹

Several factors may exacerbate or prolong diaper rash, including frequent urination and defecation, hygiene practices, cleansing routines, the type of diaper used, frequency of diaper changes, diet, medications, and gastrointestinal illnesses.⁹ Although diaper rash typically resolves quickly, it can lead to significant discomfort for both infants and adults when it persists.²⁶ Addressing these contributing factors is crucial in managing and preventing DD.

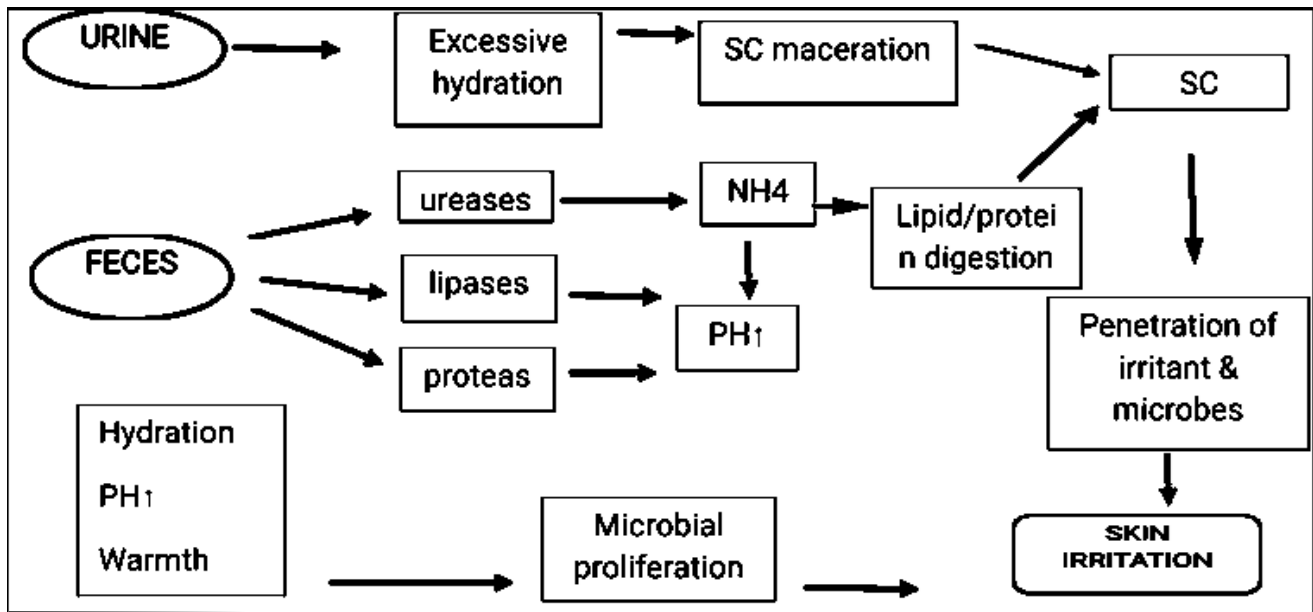


Figure 1: Physical and biochemical factors involved in the pathophysiology of diaper rash.¹⁰

SC: stratum corneum.

MANAGEMENT AND TREATMENT STRATEGIES

General care and preventive measures

The most effective approach to managing diaper rash is prevention. To prevent diaper rash, proper skin care should aim to strengthen the skin barrier, keep the area dry, reduce friction, and minimize contact with irritants such as urine and feces.⁹

Formulated for protection: must-have properties in rash treatments

An ideal rash formulation requires an optimal hydrophilic-lipophilic balance (HLB) to ensure stable emulsification, enhancing spreadability and active ingredient absorption. The right emulsifier lowers surface tension, aiding in uniform application and effectiveness. Droplet size and zeta potential are critical for stability, preventing aggregation and ensuring uniform dispersion. Optimized rheology is essential, as suitable viscosity enhances product stability, smooth application, and skin adherence, improving user experience.²⁴ The formulation must maintain an acidic pH (4-6) to support stratum corneum homeostasis and barrier permeability, ensuring skin protection.²⁷ Rash creams work by forming a protective lipid barrier that shields the skin from irritants and prevents excessive wetness exposure. They are biocompatible and non-toxic application. Additionally, they do not penetrate normal or damaged human skin, minimizing the risk of systemic exposure. Ensuring a well-assessed therapeutic margin is crucial to prevent excessive absorption of active ingredients, considering molecular weight, hydrophilicity, and barrier integrity.²⁸ Pediatric formulations should be

tailored to lesion characteristics, patient needs, and drug properties, as commercial options are limited. Customized compounding offers a viable alternative, ensuring tolerability and efficacy.²⁹ The formulation should comply with microbiological standards, preventing harmful microbial growth while maintaining stability in terms of appearance, color, pH, and viscosity. Water/oil emulsions carrying the oil phase and ZnO have shown superior results. The formulation's overall efficacy depends on pH balance, viscosity control, HLB optimization, and microbiological tolerability, making it suitable for infant skin protection.³⁰

Role of barrier creams and ointments

Barrier creams are formulated to protect the skin from harmful external factors by creating a diffusion barrier between the skin and irritants. These creams serve different purposes, including medical applications for diaper rash, industrial protection for workers, and sports applications for athletes. Skin barrier function is assessed by measuring TEWL, stratum corneum hydration, and skin surface pH.²⁸ Barrier preparations have long been used in skincare to enhance skin barrier function and aid in the prevention and treatment of DD.^{9,31} It helps to protect the diaper area by forming a protective layer on the skin's surface while delivering essential lipids like cholesterol, free fatty acids, and ceramides.³² These lipids penetrate the intercellular spaces of the stratum corneum, preventing exposure to moisture, irritants, and microbial invasion while aiding in skin repair.⁹ By mimicking the skin's natural lipid barrier, they reduce excessive water loss and maintain hydration. A healthy stratum corneum is flexible and plays a key role in minimizing water loss while

blocking harmful substances and microbes. Damage to this barrier increases TEWL and allows harmful molecules and microorganisms to penetrate the skin.^{10,11} Ointments and pastes are generally more effective than oils, creams, and lotions, as they adhere better to damaged skin. Any remaining paste should be left in place and gently removed from irritated areas only after defecation. It is important to reapply the paste generously with each diaper change to ensure continuous protection.¹⁰ Research has shown that consistently applying a water-in-oil emollient significantly reduces dermatitis in neonates, leading to a shift in the understanding of diaper rash prevention.¹¹ The association of women's health, obstetric and neonatal nurses, along with the national association of neonatal nurses, have established skincare guidelines recommending that infants be bathed without soap and a barrier ointment be applied daily. A study found that implementing these guidelines in neonatal intensive and special care units led to improved skin health, with increased emollient use and reduced soap exposure resulting in less dryness, redness, and skin damage.¹¹ Barrier preparations commonly contain ZnO and petrolatum, while other ingredients such as Titanium oxide, white soft-paraffin, dimethicone, or other silicones are also used for their water-repellent properties.¹⁰ ZnO is well known for its shielding effect and is widely used in sunscreens and barrier creams to protect the skin from moisture, irritants, and external aggressors.³³ Certain over-the-counter products marketed for diaper area care include preservatives, fragrances, and additives like vitamins, aloe, or herbal extracts, which may cause irritation or allergic contact sensitization.¹⁰ As a result, barrier preparations, should be formulated to minimize TEWL and maintain it at levels close to normal.¹¹

ZnO: AN ESSENTIAL THERAPEUTIC AGENT IN DIAPER RASH PROTECTION

ZnO based creams, pastes, and ointments have for long been established as effective treatments for diaper rash. These formulations create a protective barrier on the skin, preventing irritation and aiding in skin healing.¹⁰ Additionally, ZnO possesses antimicrobial, anti-inflammatory, and wound-healing properties, making it a widely used ingredient in over-the-counter diaper rash products.^{34,35} American academy of dermatology (AAD) recommends for mild to moderate diaper rash in adults and infants, ZnO cream as diaper rash ointment or cream to be applied liberally to the affected area, 2 to 4 times a day.³⁶

Protective barrier and skin healing

ZnO based diapering products exert their protective and preventive properties by forming a physical barrier on the skin surface.¹⁰ In a study conducted on 36 adults, the overnight use of ZnO containing topical products effectively prevented dye penetration into the treated skin. Additionally, *in vivo* Raman micro-spectroscopy demonstrated that ZnO barrier creams blocked externally applied caffeine penetration, confirming their protective role against skin irritants.¹⁰ ZnO ointments act as a skin-

drying agent and have significant skin-protective capacity.³⁷ The application of ZnO paste fills the hollow skin microrelief, reducing friction between the skin and diapers, which may contribute to its beneficial effects. This feature minimizes epidermal damage and prevents secondary infections, particularly those caused by *Candida* species.³⁸ Research findings have shown that using a diaper infused with a ZnO and petrolatum-based formulation leads to better skin condition in the diaper area compared to standard high-quality diapers. The protective effect is further enhanced by the inclusion of ZnO in the petrolatum-based formulation.³⁹

Antimicrobial and anti-inflammatory properties

ZnO has potent antimicrobial activity. Studies indicate that ZnO exhibits strong antibacterial properties, particularly against *Streptococcus mutans*, by inhibiting bacterial adhesion and penetration.¹⁵ ZnO nanoparticles are known to disrupt bacterial cell membranes and inhibit bacterial cell division by targeting the filamenting temperature-sensitive mutant Z protein, a key component in bacterial cytokinesis. This multi-target bactericidal action makes ZnO effective in reducing the risk of diaper rash-related infections.⁴⁰ Beyond its antimicrobial effects, ZnO possesses anti-inflammatory properties. It inhibits the production of inflammatory mediators like TNF-alpha, IL-6, and nitric oxide, modulates toll-like receptors, and influences dendritic cell function, thus aiding in immune regulation. Furthermore, ZnO maintains macrophage and neutrophil function and stabilizes lysosomal membranes, reinforcing its role in skin repair and immune response.⁴¹

Nutritional zinc deficiency and diaper rash

Nutritional deficiencies can exacerbate DD.³¹ Infants with lower zinc levels tend to have a higher incidence of DD, suggesting that topical ZnO applications may aid in mitigating dermatitis through enhanced skin repair and immune support.¹² *Acrodermatitis enteropathica*, a rare genetic disorder of zinc metabolism, manifests as severe diaper area eruptions, along with irritability, diarrhea, growth failure, and alopecia. This condition highlights the importance of zinc in maintaining healthy skin and immune function.¹⁹

ZnO IN ACTION: CLINICAL PROOF FOR RASH RELIEF

Clinical studies have demonstrated the effectiveness of various concentrations of ZnO in reducing the severity of skin rash and promoting skin healing as shown in Table 1. ZnO 5% is widely recognized for its effectiveness in managing DD, particularly in alleviating symptoms associated with diarrhea-induced skin irritation.¹⁵ A study evaluating the effects of 10% ZnO alone versus a combination of 10% ZnO and tocopherol (Vitamin E) on 88 infants revealed promising results. The combination therapy led to a greater reduction in rash dimensions ($p=0.004$) and a significantly lower severity score on day

five ($p<0.001$). This suggests that tocopherol accelerates healing by enhancing the skin barrier, speeding up recovery, and restoring skin pH, making it a beneficial addition to treatment protocols for DD.⁴² In addition to tocopherol, ZnO's efficacy is further enhanced when combined with other agents. A study comparing diapers with and without a ZnO-infused top-sheet demonstrated that a formulation containing 7.5% or 40% ZnO in a petrolatum/stearyl alcohol base significantly improved skin health by reducing trans-epidermal water loss and erythema. This combination provided better skin barrier protection than petrolatum alone, highlighting the potential for improved outcomes when optimizing ZnO delivery or increasing its concentration in formulations.⁴² Furthermore, a cross-sectional study of pediatricians' treatment preferences for diaper rash revealed that 42.9% recommended a physician visit within 0-3 days. First-line treatments included moderate ZnO ($\leq 20\%$), panthenol/dexpanthenol, and *Hamamelis virginiana*, with significant variations in choices based on practice settings. In cases of non-response, pediatricians turned to antifungals, low-potency corticosteroids/high-concentration ZnO ($>20\%$).

Notably, 89.3% of pediatricians referred unresponsive cases to dermatologists for further management.⁴³ Supporting these findings, a study on 5% dexpanthenol and ZnO ointment in diarrhea-related DD showed a significant TEWL reduction on day 3 ($p=0.002$) versus an ointment base, though severity scores remained similar across days 1, 3, and 7. The ointment demonstrated better efficacy, especially in cases without prolonged diarrhea, with no adverse effects observed.⁴⁴ In the neurology ICU, a 40% ZnO cream with *Hamamelis virginiana* shows superior effectiveness in preventing pressure injuries (PIs) compared to barrier creams. This is evidenced by better pressure ulcer healing assessment scale (PUSH) scores and improved PI stages during hospitalization and at ICU discharge.⁴⁵ In a randomized study, topical ZnO 20% ointment achieved a 50% cure rate for warts, outperforming salicylic acid-lactic acid (42%), with no serious side effects.⁴⁶ Another study evaluated the efficacy of topical 15% ZnO ointment in reducing common wart size. After four weeks, ZnO significantly reduced the median surface area, suggesting its potential as an adjunctive therapy.⁴⁷

Table 1: Clinical efficacy of ZnO concentrations in skin rash management.

Indication	Age group (in years)	Concentrations of ZnO used	Key properties	Outcome
Diaper rash ⁴⁶	Pediatric	10% ZnO + tocopherol	Anti-inflammatory actions	Accelerates the healing process by reducing the rash size, thereby decreasing the severity of the DD and restoring the skin pH by the end of five days and can be considered in the treatment regimen for DD.
Diaper rash ¹⁵	Pediatric	5% ZnO	Physical barrier, antibacterial	Effective in reducing symptoms of diarrhea-induced DD.
Diaper rash ⁴⁷	Pediatric	Up to 20% ZnO + panthenol/dexpanthenol + <i>Hamamelis virginiana</i> extracts	Skin barrier function	Most preferred therapy in initial visits for DD.
Diaper rash ⁴²	Adults	7.5 and 40% ZnO in petrolatum/stearyl alcohol base	Anti-inflammatory, physical barrier	Significantly reduced barrier damage, as measured by TEWL and erythema
Pressure ulcer ⁴⁸	Adults	40% ZnO	Wound healing, tolerability	The results indicate that ZnO cream has more positive effects on preventing PIs than barrier cream in terms of PUSH scores and PI stages.
Burns ⁴⁸	Adults	20% ZnO and 80% petroleum	Antioxidant, physical barrier	More effective than silver sulfadiazine in treatment of burns, in terms of epithelialization, epidermal maturation, and scar formation.
Irritant DD ⁴⁸	Pediatric	5% dexpanthenol + 5% ZnO	Antibacterial, anti-inflammatory	Significantly decreased TEWL
Recalcitrant viral warts ⁴⁹	Adults	Topical ZnO 20% ointment	Antiviral, tolerability	50% of the patients showed complete cure from warts.
Warts ⁵⁰	Adults	15% ZnO ointment	Antiviral, physical barrier	Significantly reduced the size of common warts
In-contenance-associated dermatitis ⁴⁹	Adults	15.25% ZnO cream	Tolerability, anti-inflammatory	Tolerable and effective preparation for use in the management of incontinence-associated dermatitis.

Tolerability meets efficacy: a comparative insight

Topical ZnO remains the preferred treatment for diaper rash due to its well-established therapeutic profile and effectiveness. While corticosteroids are sometimes used in severe cases because of their potent anti-inflammatory properties, their prolonged and excessive use is associated with risks such as skin atrophy, pigmentary changes, suppression of the hypothalamic-pituitary-adrenal (HPA) axis, and bacterial resistance.^{18,20} In contrast, ZnO provides a protective barrier and soothing effect without these complications, making it a more tolerable for routine management and prevention of diaper rash.¹⁵ A randomized study comparing ZnO cream with talcum powder for preventing irritant diaper rash in infants found that ZnO was more effective in delaying the onset of diaper rash and reducing the overall risk. Both treatments were well tolerated, but ZnO provided superior protection by forming a durable barrier against moisture and irritants.⁵⁰ Similarly, a study comparing ZnO with rice-starch powder found that while the incidence of diaper rash was slightly higher in the rice-starch group, there was no significant difference in the time to onset or overall risk. Both treatments were well tolerated, but ZnO's enhanced barrier properties made it a more reliable choice for preventing skin irritation.⁵¹ In addition to its protective and soothing properties, ZnO has been shown to improve skin barrier function. A randomized trial evaluating the effectiveness of 5% dexpanthenol with ZnO ointment found that by day 3, TEWL was significantly reduced on the ZnO-treated side, suggesting improved skin integrity. Although further efficacy gains were observed by day 7, they were not statistically significant, indicating that ZnO's primary benefit lies in reinforcing the skin barrier rather than drastically altering severity scores.¹⁸ Beyond DD, ZnO has demonstrated benefits in managing other dermatological conditions, including stoutness-associated intertrigo, hemorrhoids, tinea infections, and axillary malodour.¹⁵ Its antimicrobial properties inhibit bacterial exoenzymes responsible for odor production, while its mild astringent action helps control moisture and irritation in the skin folds.¹²

RATIONALE FOR ZNO CONCENTRATIONS IN SKIN RASH MANAGEMENT

8.5% ZnO for infants and pediatric skin

Infants and young children have delicate, underdeveloped skin that is more susceptible to irritation, making lower concentrations of ZnO, such as 8.5%, particularly suitable.^{14,15} This concentration offers a balance between effectiveness and tolerability, leveraging ZnO's notable anti-inflammatory and barrier-protective properties to soothe and protect infant skin with minimal risk of side effects.⁴⁹ ZnO at lower concentrations has been associated with reducing TEWL, alleviating erythema, and promoting the resolution of DD, while being gentle enough for prolonged use on sensitive pediatric skin.⁵¹

15% ZnO for female intimate and friction-prone areas

In areas prone to frictional dermatoses, such as the female intimate region, 15% ZnO provides antimicrobial, soothing, and reparative benefits.²³ The concentration is optimal for reducing irritation, preventing secondary infections, and enhancing barrier recovery in delicate areas exposed to moisture and mechanical friction. Clinical studies have demonstrated the efficacy of ZnO preparations within this range in reducing erythema, improving skin barrier function, and managing conditions like intertrigo and irritant dermatitis, which frequently affect intimate skin folds.⁵²

25% ZnO for adults with incontinence-associated dermatitis

Adults, particularly those with incontinence or compromised mobility, often develop incontinence-associated dermatitis due to prolonged skin exposure to moisture and irritants.¹⁷ Higher concentrations of ZnO, such as 25%, offer robust barrier protection and anti-inflammatory action, effectively shielding the skin from irritants while promoting healing. Clinical data have shown that ZnO concentrations in the range of 25-40% significantly reduce TEWL and erythema, making them well-suited for managing IAD and preventing further skin breakdown in vulnerable populations.^{42,48}

GLOBAL REGULATORY LANDSCAPE OF ZnO IN OTC SKIN CARE

ZnO is approved by the U.S. FDA for use in over-the-counter (OTC) skin protectants, including diaper rash creams, anorectal skin protectants, and sunscreens. It is the broadest spectrum UVA and UVB reflector, acting as a physical blocker against harmful UV rays, preventing sunburn, premature aging, and skin cancer.⁴⁴ The FDA recognizes ZnO as generally recognized as safe and effective (GRASE) at concentrations up to 25% in sunscreens.⁵³ The European union allows ZnO as a colorant and a UV filter up to 25%, with the scientific committee on consumer safety (SCCS) confirming the tolerability of nanoscale ZnO (1-100 nm) for human use.⁴⁰ ZnO is available in 13 countries, including Abu Dhabi, Australia, Hong Kong, Ireland, Saudi Arabia, and the UK, in various forms like creams, ointments, and pastes. For skin protection in the U.S., ZnO is used in concentrations from 7.5% to 40%, with treatment durations ranging from 24 hours to four weeks. In wound healing, concentrations range from 3% to 32%, with treatment durations from 2 weeks to 9 months. ZnO also treats warts (15-20% concentration) over 4 weeks to 3 months and adenolymphangitis for up to 12 months.⁵² Clinical studies show no significant adverse effects from ZnO, even when applied under occlusion.⁴⁴ It is insoluble in water and biological fluids, minimizing systemic absorption.⁵³ The European commission supports the use of nanoscale ZnO up to 25% without safety concerns. This widespread regulatory approval underscores ZnO's efficacy and

tolerability across various therapeutic and protective applications.⁴⁴

CONCLUSION

This comprehensive review underscores the multifaceted role of ZnO in both preventing and managing a diverse range of skin rashes across all age groups. ZnO's protective barrier, antimicrobial, and anti-inflammatory actions prove invaluable against DD, frictional dermatoses, and sanitary pad-related irritation. Concentrations between 5% and 20% are effective, promoting skin hydration, barrier repair, and wound healing. The higher prevalence of frictional and contact dermatitis in women, coupled with the vulvar skin's sensitivity, highlights the need for ZnO-based solutions. This comprehensive analysis reinforces ZnO's role in promoting skin health, reducing discomfort, and enhancing the quality of life across diverse patient populations. It particularly emphasizes the importance of hygiene and gentle skincare in managing moisture and friction-related rash. ZnO continues to stand as well tolerated, accessible, and essential component in dermatological care and management of many skin rashes.

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REFERENCES

- Skuhala T, Trkulja V, Rimac M, Dragobratović A, Desnica B. Analysis of types of skin lesions and diseases in everyday infectious disease practice-how experienced are we? *Life*. 2022;12(7):978.
- De Castro MC, Ramos-e-Silva M. The rash with mucosal ulceration. *Clin Dermatol*. 2020;38(1):35-41.
- Cleveland Clinic. Rashes (red skin). Cleveland (OH): Cleveland Clinic. Available at: <https://my.clevelandclinic.org/health/diseases/17413-rashes-red-skin>. Accessed on 9 February 2025.
- Dinulos JE, Dinulos JG. Present and future: Infectious tropical travel rashes and the impact of climate change. *Ann Allergy Asthma Immunol*. 2023;130(4):452-62.
- Hay RJ. Skin Disease in the Tropics and the Lessons that can be Learned from Leprosy and Other Neglected Diseases. *Acta Dermato-Venereologica*. 2020;100(9):adv00113.
- Woodhams L. The Knicker Study: a survey to determine the incidence of underwear rashes in hot and humid environments. *Aust J Dermatol*. 2011;52(4):A3.
- Ali M, Muazu L, Nas FS, Ibrahim YS. Dermatitis; Types, Causes, Symptoms and Management: A Review. *Dermis*. 2024;4(2):1-4.
- Lane AT. Diaper rash: causes and cures. *Patient Care*. 1988;22(3):167-73.
- Blume-Peytavi U, Kanti V. Prevention and treatment of diaper dermatitis. *Pediatr Dermatol*. 2018;35:s19-23.
- Klunk C, Domingues E, Wiss K. An update on diaper dermatitis. *Clin Dermatol*. 2014;32(4):477-87.
- Hebert AA. A new therapeutic horizon in diaper dermatitis: Novel agents with novel action. *Int J Women's Dermatol*. 2021;7(4):466-70.
- Foureur N, Vanzo B, Meaume S, Senet P. Prospective aetiological study of diaper dermatitis in the elderly. *Brit J Dermatol*. 2006;155(5):941-6.
- Permata AA, Rakhmani AN. Elderly Male with Ulcer and Diaper Rash Caused by Post-Stroke Immobilization with Hereditary Risk Factors, Uncontrolled Hypertension, Unstable Emotions, and Sleeping Difficulty. *J Ilmu Kedokteran Keluarga*. 2022;1(2):45-54.
- Giacomoni PU, Mammone T, Teri M. Gender-linked differences in human skin. *J Dermatol Sci*. 2009;55(3):144-9.
- Rahrovan S, Fanian F, Mehryan PP, Humbert P, Firooz A. Male versus female skin: What dermatologists and cosmeticians should know. *Int J Women's Dermatol*. 2018;4(3):122-30.
- Kawshar T, Rajesh J. Sociodemographic factors and their association to prevalence of skin diseases among adolescents. *Our Dermatol Online/Nasza Dermatologia Online*. 2013;4(3):281-6.
- Arora G, Khandpur S, Bansal A, Shetty B, Aggarwal S, Saha S, et al. Current understanding of frictional dermatoses: A review. *Indian J Dermatol Venereol Leprol*. 2023;89(2):170-88.
- Usatine RP, Riojas M. Diagnosis and management of contact dermatitis. *Am Fam Phys*. 2010;82(3):249-55.
- Gondokaryono SP, Nilasari H, Krisanti IA, Febrianti T, Purba H, Toyoshima H, et al. Efficacy of 3D-pore sanitary napkin on mild-to-moderate irritant contact dermatitis in the female genital area. *J General Procedural Dermatol Venereol Indonesia*. 2020;5(1):2.
- Ministry of Health and Family Welfare, Government of India. National Family Health Survey (NFHS-5), 2019-21.
- Woo J, Kim S, Kim H, Jeong KS, Kim E, Ha E. Systematic review on sanitary pads and female health. *The Ewha Med J*. 2019;42(3):25-38.
- Wakashin K. Sanitary napkin contacts dermatitis of the vulva: location-dependent differences in skin surface conditions may play a role in negative patch test results. *J Dermatol*. 2007;34(12):834-7.
- Cleveland Clinic. Chafing: Cleveland Clinic. Available at: <https://my.clevelandclinic.org/health/diseases/23517-chafing>. Accessed on 13 February 2025.

24. Kurt AA, Aslan I, Duman G. Next-Generation Natural Baby Barrier Cream Formulations: Physicochemical Analysis and Safety Assessment. *J Cosmetic Sci.* 2021;72(2):173-88.
25. Blume-Peytavi U, Hauser M, Lünemann L, Stamatatos GN, Kottner J, Garcia Bartels N. Prevention of DDin infants-a literature review. *Pediatric dermatology.* 2014;31(4):413-29.
26. Dall'Oglio F, Musumeci ML, Puglisi DF, Micali G. A novel treatment of Diaper dermatitis in children and adults. *J Cosmetic Dermatol.* 2021;20:1-4.
27. 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.
28. Du Plessis S. The influence of different types of barrier creams on skin barrier function (Doctoral dissertation, North-West University). 2012.
29. Lachén EA, Martínez PH, Calzada YG. The most useful pharmaceutical formulations (individualized medications) in pediatric Dermatology: A review. *Actas Dermo-Sifiliográficas (English Edition).* 2021;112(4):302-13.
30. Kurt AA, Ibrahim B. Development and Microbiological Evaluation of Natural Diaper Rash (Diaper Dermatitis) Cream Formulations. *J Immunol Clin Microbiol.* 2024;9(1):1-1.
31. Shin HT. Diaper dermatitis that does not quit. *Dermatologic Therapy.* 2005;18(2):124-35.
32. Atherton DJ. A review of the pathophysiology, prevention and treatment of irritant diaper dermatitis. *Curr Med Res Opinion.* 2004;20(5):645-9.
33. Alvarez MS, Brown LH, Brancaccio RR. Are barrier creams actually effective? *Curr Allergy Asthma Rep.* 2001;1(4):337-41.
34. Schwartz JR, Marsh RG, Draelos ZD. Zinc and skin health: overview of physiology and pharmacology. *Dermatologic Surg.* 2005;31:837-47.
35. Sajjadian N, Hashemian F, Kadivar M, Sohani S, Alizadeh Tp. Efficacy of topical sucralfate versus topical Zinc oxide in diaper dermatitis: a randomized, double blind study. *Iranian J Dermatol.* 2012;15(3):85-8.
36. American Academy of Dermatology Association. How to treat diaper rash. Available at: <https://www.aad.org/public/everyday-care/itchy-skin/rash/treat-diaper-rash>. Accessed on 8 February 2025.
37. Nijhuis WA, Houwing RH, Van der Zwet WC, Jansman FG. A randomised trial of honey barrier cream versus Zinc oxide ointment. *Brit J Nursing.* 2012;21(20):S10-3.
38. Xhaufilaire-Uhoda E, Henry F, Pierard-Franchimont C, Piérard GE. Electrometric assessment of the effect of a Zinc oxide paste in diaper dermatitis. *Int J Cosmetic Sci.* 2009;31(5):369-74.
39. Baldwin S, Odio MR, Haines SL, O'Connor RJ, Englehart JS, Lane AT. Skin benefits from continuous topical administration of a Zinc oxide /petrolatum formulation by a novel disposable diaper. *J Europ Academy Dermatol Venereol.* 2001;15:5-11.
40. Mendes CR, Dilarri G, Forsan CF, Sapata VD, Lopes PR, de Moraes PB, et al. Antibacterial action and target mechanisms of Zinc oxide nanoparticles against bacterial pathogens. *Scient Rep.* 2022;12(1):2658.
41. Gupta M, Mahajan VK, Mehta KS, Chauhan PS. Zinc therapy in dermatology: a review. *Dermatol Res Pract.* 2014;2014(1):709152.
42. Mirle N, Rajan A, Soans ST. A comparative study between local application of 10% Zinc oxide to a combination of 10% Zinc oxide and tocopherol in treating infant's diaper dermatitis. *Paediat Indonesiana.* 2024;64(2):113-9.
43. Yildiz I, Kizilca O, Haksayar A, HizliDemirkale Z. Pediatricians' knowledge, attitudes, and therapeutic approaches regarding diaper dermatitis: a common condition with many different practices. *Clin Cosmet Investigational Dermatol.* 2023;901-10.
44. Cosmetics Info. Zinc Oxide. Cosmetics Info. Available at: <https://www.cosmeticsinfo.org/ingredient/zinc-oxide/>. Accessed on 26 February 2025.
45. Koc F, Eren MG, Sert H. Comparing the efficacy of zinc oxide versus barrier creams for pressure injury prevention: a retrospective cross-sectional study. *Adv Skin Wound Care.* 2023;36(12):1-6.
46. Khattar JA, Musharrafieh UM, Tamim H, Hamadeh GN. Topical zinc oxide vs. salicylic acid-lactic acid combination in the treatment of warts. *Int J Dermatol.* 2007;46(4):427-30.
47. Songsantiphap C, Asawanonda P. Topical 15% zinc oxide ointment significantly reduces the size of common warts after four weeks: a randomized, triple-blinded, placebo-controlled trial. *J Clin Aesthet Dermatol.* 2019;12(9):26.
48. Wananukul S, Limpongsanuruk W, Singalavanija S, Wisuthsarewong W. Comparison of dexpantenol and zinc oxide ointment with ointment base in the treatment of irritant diaper dermatitis from diarrhea: a multicenter study. *J Med Assoc Thai.* 2006;89(10):1654-8.
49. Anthony D, Barnes E, Malone-Lee J, Pluck R. A clinical study of Sudocrem in the management of dermatitis due to the physical stress of incontinence in a geriatric population. *J Adv Nurs.* 1987;12(5):599-603.
50. Chaithirayanon S. Comparative Study between Talcum and Zinc oxide Cream for the Prevention of Irritant Contact Diaper dermatitis in Infants. *J Med Assoc Thai.* 2016;99:S1-6.
51. Samakayanusorn N, Chaithirayanon S, Chalermchai T, Ophaswongs S, Siriwat N, Udompataikul M. Comparison of rice starch powder and Zinc oxide cream for the prevention of irritant diaper dermatitis. *J Med Assoc Thai.* 2017;100(8):S1-6.
52. University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI), University of Maryland School of Pharmacy. Zinc

Oxide. Prepared for: US Food and Drug Administration. 2021.

53. U. S. Food and Drug Administration. Sunscreen drug products for over-the-counter human use: Amending OTC Monograph M020. Silver Spring (MD): FDA; 2021. Available at: <https://www.accessdata.fda.gov/scripts/cder/omuf/index.cfm>. Accessed on 12 February 2025.

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