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Mechanism of Action and Clinical Benefits of Colloidal Oatmeal for Dermatologic Practice

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ABSTRACT

Colloidal oatmeal has a long history of beneficial use in dermatology. It is a natural product that has an excellent safety record and has demonstrated efficacy for the treatment of atopic dermatitis, psoriasis, drug-induced rash and other conditions. In recent years, in vitro and in vivo studies have begun to elucidate the multiple mechanisms of action of naturally derived colloidal oatmeal. Evidence now describes its molecular mechanisms of anti-inflammatory and antihistaminic activity. The avenanthramides, a recently described component of whole oat grain, are responsible for many of these effects. Studies have demonstrated that avenanthramides can inhibit the activity of nuclear factor κB and the release of proinflammatory cytokines and histamine, well known key mechanisms in the pathophysiology of inflammatory dermatoses. Topical formulations of natural colloidal oatmeal should be considered an important component of therapy for atopic dermatitis and other conditions and may allow for reduced use of corticosteroids and calcineurin inhibitors.

INTRODUCTION

Colloidal oatmeal is a natural product with a long history of use in dermatology. Reports of the benefits of oats for skin span millennia. Today, colloidal oatmeal is still widely used in Europe for dermatologic indications and is one of the few natural products recognized by the U.S. Food and Drug Administration (FDA) as a safe over-the-counter (OTC) skin protectant.[1–3]

Indeed, contemporary scientific studies have begun to reveal the mechanisms by which oats act on skin, including anti-inflammatory and antihistaminic effects, among others.[4–8] Available formulations of colloidal oatmeal products have demonstrated efficacy in atopic dermatitis, drug-related rash and other dermatologic conditions.[7,9–11]

Although it is a natural product, colloidal oatmeal has been approved by the FDA in recognition that it is safe and tolerable for short- or long-term use. Products containing colloidal oatmeal represent a non-pharmaceutical option for acute or maintenance treatment of conditions such as atopic dermatitis and psoriasis. The adjunctive use of oat-containing products as an essential part of a basic skin care regimen may allow for reduced need for topical drugs such as corticosteroids or calcineurin inhibitors.

Colloidal Oatmeal: From Ancient Use to Modern Practice

The history of the human cultivation of oats dates to at least the Bronze Age, and the benefits of oats as a skin cleanser and treatment have been noted in the medical literature since Roman times.[1,12] In the modern age, colloidal oatmeal has been studied and proven for several indications. Early investigations of ready-to-use colloidal oatmeal described it to be a soothing, non-irritating and cleansing treatment for inflamed, itchy skin.[8,13–16]

Colloidal oatmeal is produced by grinding and processing dehulled oat grain. The fine milling process leaves a concentrated, starch-protein fraction of oat in the form of a powder. The composition of colloidal oatmeal consists largely of starch (65–85%), proteins (15–20%), lipids (3–11%), fiber (5%) and β-glucans (5%).[6] Each of these components contributes to the dermatologic properties of colloidal oatmeal as a cleanser, moisturizer, skin protectant and antipruritic. Formulations of colloidal oatmeal have been used for decades in Europe. In 1989, the FDA recognized the value of colloidal oatmeal as a safe and effective OTC skin protectant; this action was codified in 2003, when the FDA approved colloidal oatmeal as a monograph ingredient.[2,3] The formulations of colloidal oatmeal available today are multiple, including bath treatments, creams, lotions, body washes and other products.

Mechanisms of Action in Dermatologic Conditions

Although the use of colloidal oatmeal for dermatologic treatment spans thousands of years, the mechanisms by which oatmeal acts have begun to be uncovered only in the last half century. Mechanisms suggested by current evidence include anti-inflammatory and antihistaminic activity, enhancement of

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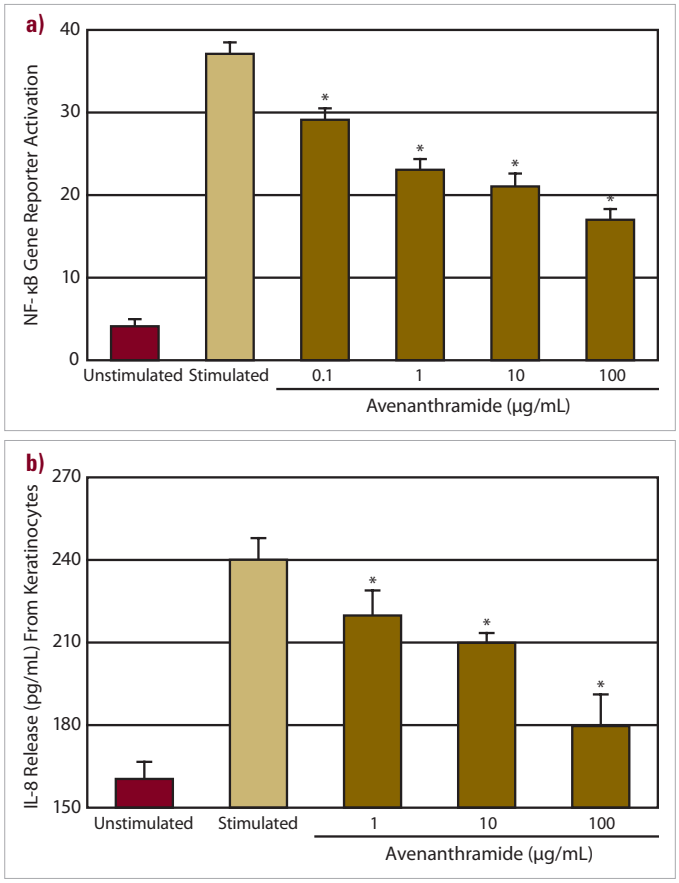
the skin barrier and other activities.[6–8,17] Among the more salient discoveries was the identification of the avenanthramides. These soluble phenolic compounds are a minor component of oats by weight (0.03%)[6] but have been the subject of intensive study because of their powerful antioxidative activity.[18,19]

Avenanthramides have been isolated from oat grain for use in dermatologic products and are often referred to as *Avena sativa* kernel extract. Recent in vitro work found that avenanthramides have anti-inflammatory and antipruritic properties, as evidenced by decreased activity of nuclear factor κB (NF-κB) in cultured keratinocytes.[6] In this study, treatment with avenanthramides was associated with decreased activation of NF-κB following induction by tumor necrosis factor-α (TNF-α), as well as reduced production of the proinflammatory cytokine interleukin 8 (IL-8). A similar, recent study evaluated the inhibitory effect of avenanthramide on tetradecanoylphorbol induction of NF-κB and IL-8 in cultured human keratinocytes.[7] The authors reported a significant, dose-dependent inhibition of NF-κB and IL-8 with avenanthramide (Figure 1). Similar data have been reported from studies of human vascular endothelial cells.[20]

Of particular relevance to clinical practice, Sur et al. also reported that the application of avenanthramides to skin significantly reduced oxazolone-induced contact hypersensitivity, resiniferatoxin-induced neurogenic inflammation and compound 48/80-induced, histamine-mediated itch (P<0.05 for all).[6] An in vivo study evaluated the effects of avenanthramides on histamine-induced itch and erythema.[17] Treatment with avenanthramides reduced itch compared to untreated control subjects. An in vitro component to this study demonstrated a significant reduction in histamine release from mast cells stimulated by substance *P*. Findings such as these suggest that avenanthramides represent a key active component of oats for dermatologic indications.

The multiple effects of avenanthramides are not the only mechanisms by which oats affect skin. Preservation of the skin barrier has also been proposed; barrier dysfunction contributes significantly to the pathology of various dermatologic conditions, in particular atopic dermatitis.[21] A study from the 1950s, for example, described the buffering characteristics of colloidal oatmeal.[8] This study demonstrated that treatment with colloidal oatmeal reduced the elevated pH of pathologic skin (e.g., eczematous or pruritic) or alkali-treated skin to within the normal range. This buffering capacity has important implications for preservation of skin barrier function. Other effects on the skin barrier include the formation of a protective moisturizing barrier over skin by the proteins and polysaccharides in colloidal oatmeal, reducing transepidermal water loss (TEWL), a key feature of barrier dysfunction. Colloidal oatmeal has also been shown to act as an emollient, humectant and occlusive.[7] An in vivo model of skin irritation, the sodium lauryl sulfate

FIGURE 1. a) Avenanthramide reduces nuclear factor-κB (NF-κB) activation and **b)** interleukin 8 (IL-8) release in a dose-dependent manner in cultured human keratinocytes.*indicates P<0.05.



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(SLS) irritation model reproduces elements of barrier dysfunction, including increased TEWL.[22] The application of oatmeal extracts to SLS-treated skin has been shown to significantly reduce irritation compared to vehicle (P<0.05), illustrating the anti-inflammatory effects of oats and suggesting potential benefits for the skin barrier as well.[23]

Other investigators have reported that oat extracts inhibited the phospholipase A2 (PLA2)-dependent mobilization of arachidonic acid from phospholipids in cultured human keratinocytes.[4] The oat extract used in this study also inhibited the formation of eicosanoids, expression of cytosolic phospholipase PLA2 and formation of metabolites of prostacyclin, all of which are implicated in the regulation of inflammation.[4] In a separate study, an oatmeal extract oligomer was shown to reduce vasodilation induced by vasoactive intestinal peptide in human skin samples.[5] Treatment with the oligomer significantly reduced edema (P<0.05) and mean surface of dilated vessels (P<0.05).

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Clinical Benefits of Colloidal Oatmeal for Dermatology

Several lines of evidence support the clinical efficacy of colloidal oatmeal for the treatment of common dermatologic conditions, such as atopic dermatitis and other inflammatory dermatoses.[7,9,10] First, early studies reported benefits of colloidal oatmeal for the management of dermatoses in pediatric[15,24] and elderly[8] patients, for whom the use of products with a well established safety record is of particular concern. More recent evidence describes the use of colloidal oatmeal body wash, creams and bath products in a broader population. One study of 21 subjects with mild-to-moderate atopic dermatitis involving at least five percent of the body surface evaluated once-daily use of an oatmeal-based body wash.[10] The subjects also applied an oatmeal-based cream to arms, legs, hands and torso twice daily. After two weeks of treatment, dermatologists' assessments of eczema activity were significantly reduced compared to baseline values; erythema also improved significantly within two weeks of treatment, and severity of itch and scaling improved significantly after just one week of treatment (P<0.05 versus baseline, all values). And finally, a four-week, single-blind, crossover study evaluated the safety and efficacy of a colloidal oatmeal bath in patients with a history of atopic dermatitis (n=25).[7] After treatment in the oatmeal bath for 20 minutes per day for seven days, scores for itching and burning were significantly reduced compared with baseline values (50% reduction in itching [P=0.01]; 67% reduction in burning [P=0.03]). Taken together, these studies demonstrate that topical treatment with colloidal oatmeal reduced the severity of symptoms associated with atopic dermatitis.

Use in Special Populations: Skin of Color and Adverse Drug Reactions

Treatment of dermatologic conditions in people of color often requires special consideration. For example, dry skin with an ashy appearance is common in individuals of color, with or without conditions such as atopic dermatitis. The use of a moisturizer containing colloidal oatmeal to treat dry, ashy skin was evaluated in subjects with Fitzpatrick skin types IV–VI in a two-week, single-blind trial.[9] Improvement in skin moisturization and brightness was noted within one day after initiation of the colloidal oatmeal product. The appearance of skin ash, flaking and dryness were also significantly improved within one day of use, as were subjects' assessments of skin texture, ash and scale (P<0.05 versus baseline, all values). Improvements were maintained throughout the course of the study.

Disorders such as postinflammatory hyperpigmentation (PIH) are more common in skin of color.[25] It is possible that the use of oatmeal-based products could reduce risk for PIH and similar conditions by reducing erythema. The relationship between conditions such as PIH and colloidal oatmeal remains to be evaluated. However, the use of oatmeal-containing products has been recommended for cleansing and moisturizing of dry, sensitive, or ashy skin in individuals of color.[26]

Colloidal oatmeal has also been used to treat rash associated with specific drug therapies. Inhibitors of the epidermal growth factor receptor (EGFR) and tyrosine kinase inhibitors (TKIs) are used to treat certain EGFR-positive cancers; unfortunately, 60–70 percent of patients develop an acneiform rash that can limit continuation of therapy.[11] Hand-foot syndrome is also a common, dose-limiting adverse effect of TKI therapy.[27] The treatment of these drug-related dermatoses with colloidal oatmeal lotion has been reported in the literature.[11,28] One study of 10 evaluable patients undergoing EGFR-inhibitor therapy and treated with an oatmeal-based lotion reported complete response in six patients and partial response in the remaining

TABLE 1.

Treatment of TKI- and EGFR Inhibitor-related Skin Toxicity With Colloidal Oatmeal Lotion: Patient Characteristics and Response to Treatment[11]

Patient No.	Cancer	Treatment	Skin Toxicity	Response to Lotion (d)	Onset of Response (d)
1	Colon	Cetuximab	Follicular pustular, erythema	CR	5
2	Colon	Cetuximab	Morbiliform	PR	7
3	Colon	Cetuximab	Follicular pustular, erythema	CR	9
4	RCC	Erlotinib	Follicular pustular, papular	PR	7
5	Pancreatic	Erlotinib	Follicular pustular, severe scaling and xerosis	CR	6
6	RCC	Panitumumab	Follicular pustular	PR	5
7	RCC	Panitumumab	Follicular pustular	CR	10
8	RCC	Sorafenib	Follicular pustular, erythematous	CR	5
9	RCC	Sorafenib	Erythematous, squamous	PR	6
10	RCC	Sorafenib	Follicular pustular hand-foot syndrome	CR	8

EGFR=epidermal growth factor receptor; CR=complete response; PR=partial response; RCC=renal cell carcinoma; TKI=tyrosine kinase inhibitor
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four patients (Table 1).[11] The authors noted that the lotion was not associated with any toxicity, unlike that observed with other available treatments. Other reports of the successful use of colloidal oatmeal lotion for EGFR-inhibitor skin toxicity have also been published.[28]

The Place of Colloidal Oatmeal in Dermatologic Practice

Although clinical evidence describing the use of colloidal oatmeal for dermatologic conditions remains limited, studies to date demonstrate its safety and efficacy for several indications. Preclinical work highlights multiple mechanisms of action, including anti-inflammatory, antihistaminic, antipruritic and other activities.

It must be emphasized that colloidal oatmeal, although recognized by the FDA, is a natural product, not a pharmaceutical. Indeed, clinical studies have reported no adverse effects associated with the use of oatmeal-based products. The use of such products may represent an alternative or adjunctive therapy for patients with dermatoses that require corticosteroid or calcineurin-inhibitor treatment. It may be possible to reduce exposure to these agents, which are currently the mainstay of treatment for atopic dermatitis and other common conditions.[29]

Reducing exposure to corticosteroids and other topical agents may be particularly useful in pediatric patients, especially those under the age of two years, for whom calcineurin inhibitors are not labeled.[28] Indeed, some physicians now use colloidal oatmeal products as a cornerstone of maintenance treatment for conditions such as atopic dermatitis.

CONCLUSION

Colloidal oatmeal is a safe, natural treatment for a variety of dermatologic conditions. Its safety and efficacy have also been recognized and approved by the FDA. Several evidence-based mechanisms of action have been established, including anti-inflammatory and antihistamic activities. Clinical studies also attest to its efficacy in the treatment of atopic dermatitis, ashy skin and EGFR inhibitor-associated rash. Early studies described its beneficial effects in particularly vulnerable subpopulations, such as pediatric and elderly patients. Future research opportunities include the treatment of pruritus and xerosis associated with chronic renal failure, senile pruritus, rosacea, acne and other common conditions. It is reassuring for both physicians and patients to acknowledge that colloidal oatmeal is a natural product that has been used for centuries, and no associated toxicities have been reported. Products containing colloidal oatmeal should be part of the first-line treatment of atopic dermatitis, psoriasis and other conditions and may allow for reduced use of corticosteroids, calcineurin inhibitors, or other topical agents.

DISCLOSURES

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Prof. Cerio discloses that he has received honoraria from Johnson & Johnson for serving on an advisory board (Berlin 2009).

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Dr. Downie discloses that she was a speaker, and has been compensated as a fee for service, by Johnson & Johnson, Allergan, Medicis, Galderma, Novartis, Intendis, Skin Medica, Stiefel and Merz. She is also a shareholder in Allergan.

Dr. Magina is on the advisory board and is a speaker for Pfizer, Schering-Plough and Abbott. She is a consultant for Johnson & Johnson. She has received honoraria from Pfizer, Schering-Plough, Abbott and Johnson & Johnson.

Dr. Stratigos discloses that he received honoraria from Johnson & Johnson for serving on an advisory board.

Dr. Dohil has no conflicts of interest to disclose.

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