A SUPPLEMENT TO

JOURNAL OF DRUGS IN DERMATOLOGY

JDD

DRUGS • DEVICES • METHODS

The Biological Impact of Oats: Eczema and Beyond

ISSN: 1545 9616

October 2020 • Volume 19 • Issue 10 (Supplement)

This Supplement to the *Journal of Drugs in Dermatology* is funded by Johnson & Johnson Consumer Inc.

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The Biological Impact of Oats: Eczema and Beyond

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The objective of this Supplement is to highlight the data supporting the use of colloidal oatmeal in the treatment of atopic dermatitis and other skin conditions resulting from an impaired skin barrier or inflammation. Clinical efficacy and tolerance will be highlighted.

While colloidal oatmeal is the only ingredient in the skin protectant FDA monograph indicated for atopic dermatitis, there are still gaps in knowledge among professionals on the mechanisms of action that make this ingredient efficacious for conditions with impaired barrier function and inflammation. Upon completion of this Supplement, readers should understand the mechanisms of action of all components of oats that contribute to demonstrated efficacy in atopic dermatitis as well as other skin conditions and populations that have impaired barrier function and chronic itch associated with eczema/dry skin.

This Supplement contains two parts. Part I focuses on the history of oats, basic oat science, mechanisms of action, and research highlighting the efficacy of colloidal oatmeal in the treatment of atopic dermatitis. Part II features use in atopic dermatitis in special populations and clinical efficacy and tolerance beyond eczema.

Colloidal Oatmeal Part I: History, Basic Science, Mechanism of Action, and Clinical Efficacy in the Treatment of Atopic Dermatitis

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ABSTRACT

Colloidal oatmeal has a long-standing history in the treatment of dermatologic disease. It is composed of various phytochemicals, which contribute to its wide-ranging function and clinical use. It has various mechanisms of action including direct anti-inflammatory, anti-pruritic, anti-oxidant, anti-fungal, pre-biotic, barrier repair properties, and beneficial effects on skin pH. These have been shown to be of particular benefit in the treatment of atopic dermatitis. In Part 1 of this two-part series, we will explore the history of colloidal oatmeal, basic science, mechanism of action, and clinical efficacy in the treatment of atopic dermatitis.

J Drugs Dermatol. 2020;19:10(Suppl):s4-7

INTRODUCTION

History of Oatmeal

Oatmeal has a longstanding and rich history pertaining to its dermatologic use. The first documentation of oatmeal for skin health dates back as early as 2000 BC in Arabia and Egypt, where it was described as soothing and protecting in dry or itchy, inflamed skin.[1] Oatmeal flour was subsequently recognized as a topical therapy for a variety of dermatologic conditions in Roman medical literature.[1] The first scientific studies on the skin benefits of oatmeal appeared in the 1930s, including information about the cleansing properties of oatmeal, its role in relieving itch, and its function as a skin protectant.[2] In the 1940s and 1950s colloidal oatmeal became commercially available both in powder form and mixed with emollient oils, instigating medical studies examining the benefits of colloidal oatmeal baths in various xerotic dermatoses.[3] In 1989, the United States Food and Drug Administration (FDA) approved colloidal oatmeal as a safe and effective over-the-counter drug.[4] In 2003, the FDA noted that colloidal oatmeal could relieve irritation and itching due to a number of dermatoses, providing temporary skin protection.[5] Colloidal oatmeal is one of the few products that the FDA recognizes as a safe over the counter treatment. Today it is available in various forms including creams, lotions, shampoos, shaving gels, bath treatments, and body wash.

Basic Oat Science

Colloidal oatmeal is the powder obtained from the grinding and processing of whole oat grain. Under strict protocols established by the US Pharmacopeia, oat grain is ground and processed until no more than 3% of the total particles in the powder exceed 150 µm in size and no more than 20% exceed 75 µm in size.[6] The small size of the particles contributes to their ability to deposit on the skin and form an occlusive barrier when dispersed in water.

Oat is composed of various types of phytochemicals, which contribute to its wide-ranging function and clinical use. Colloidal oatmeal consists of sugars and amino acids (65%), proteins (15–20%), lipids (11%), and fiber (5%).[7] The most important groups of phytochemicals present in oats include phenolics, β-glucans, lignans, avenanthramides, carotenoids, vitamin E, and phytosterols.[7] Of the phenolics present in oats, ferulic acid and caffeic acid are strong antioxidants, and ferulic acid also has UV absorbing properties.[8] Flavonoids, a group of phenolic compounds present in oat, also are capable of absorbing ultraviolet A light from 320–370 nm.[9] β-glucans are polysaccharides of D-glucose monomers and have a high viscosity largely due to their β-(1–3)-linkages.[7] This viscosity contributes to the water-binding properties of oat. Oats also contain a wide range of minerals and vitamins, of which vitamin E is the most clinically relevant. Vitamin E is a naturally occurring antioxidant that protects against oxidative stress, inflammation, and photo-induced aging.[10]

Mechanism of Action

Colloidal oat has various mechanisms of action including direct anti-inflammatory, anti-pruritic, anti-oxidant, anti-fungal, pre-biotic, barrier repair properties, and beneficial effects on skin pH. Inflammatory skin disorders including psoriasis and atopic dermatitis (AD) exhibit high levels of arachidonic acid, eicosanoids, phospholipase A2 (the enzyme that mobilizes arachidonic acid), and leukotriene B4, which is a potent chemotactic factor that stimulates neutrophil degranulation and induces keratinocyte proliferation. Oat has been shown to inhibit phospholipase A2 in keratinocytes, thereby decreasing arachidonic acid release, which decreases pro-inflammatory eicosanoid formation.[11] The anti-inflammatory activities of oats have also been studied in the vasculature. Guo et al demonstrated that avenanthramides, specific polyphenols from oats, inhibit IL-1B induced NF-kB activation in endothelial cells.[12]

Avenanthramides have also been found to suppress IL-1β stimulated secretion of pro-inflammatory cytokines such as IL-6, IL-8, and MCP-1.[13] Taken together, these findings highlight the anti-inflammatory properties of oat and their role in alleviating inflammation in various dermatologic conditions.

Colloidal oatmeal also has anti-pruritic properties via the inhibition of neurogenic inflammation. In a murine itch model, mice were injected with compound 48/80, which leads to mast cell degranulation and histamine release, key mediators of itch. Those mice that were treated with avenanthramide itched 40.7% less than controls.[14] These findings in murine models have been evaluated further in clinical studies of patients who suffer from itch. In one clinical study, 139 patients with a variety of pruritic dermatoses were treated with colloidal oatmeal bath and cleanser for 3 months. More than 71% of patients achieved complete or near-complete relief of pruritus during the study period.[15]

In addition to anti-inflammatory and anti-pruritic properties, colloidal oatmeal also has anti-oxidant properties. Phenolic avenanthramides exhibit antioxidant activity in vitro. Phenols as a class of chemical compounds exert antioxidant activity through several mechanisms: some are hydrogen atom donors that inhibit the cascade of radical chain reactions, and others function as metal ion chelators.[16,17] The antioxidant properties of avenanthramides have been studied in detail. In one such study, eight avenanthramides identified in oat extracts were synthesized and assessed for antioxidant activity by determining reactivity toward 1,1- diphenyl-2-picrylhydrazyl and linoleic acid via the efficiency of hydrogen atom transfer from phenol to radical. Avenanthramides demonstrated higher antioxidant activity than other oat phenolic compounds, and authors hypothesized that it may be due to the resonance structure of its amide bond.[16]

Colloidal oatmeal also has anti-fungal and prebiotic properties. The *Pc*-2 gene in *A. sativa* plants confers resistance to *Puccinia coronate*, the crown rust fungus. Inoculation of oat plants with spores of *P. coronate*-induced avenanthramide production and inhibited further fungal growth.[18] Emerging evidence has also shown that colloidal oatmeal has prebiotic properties. Colloidal oatmeal is metabolized by and promotes the growth of bacteria that is commensal to the skin including *Staphylococcus epidermidis*, *Staphylococcus aureus*, and *Propionibacterium acnes*. In a study by Liu-Walsh et al, colloidal oatmeal increased the growth rate of *Staphylococcus epidermidis* significantly more than that of *Staphylococcus aureus*, suggesting a differential response of these organisms to oats.[19] Lactic acid and short-chain fatty acids are produced by microbes by fermentation, and have been shown to play an important role in the maintenance of gut and skin health. Lactic acid is also a known natural moisturizing factor and humectant. According to in vitro studies by Liu-Walsh et al, metabolism of colloidal oatmeal results in increased production of lactic acid by *Staphylococcus epidermidis* and *Staphylococcus aureus*. In the same study, six weeks of use of a moisturizing lotion containing 1% colloidal oatmeal significantly increased the level of lactate in vivo.[19]

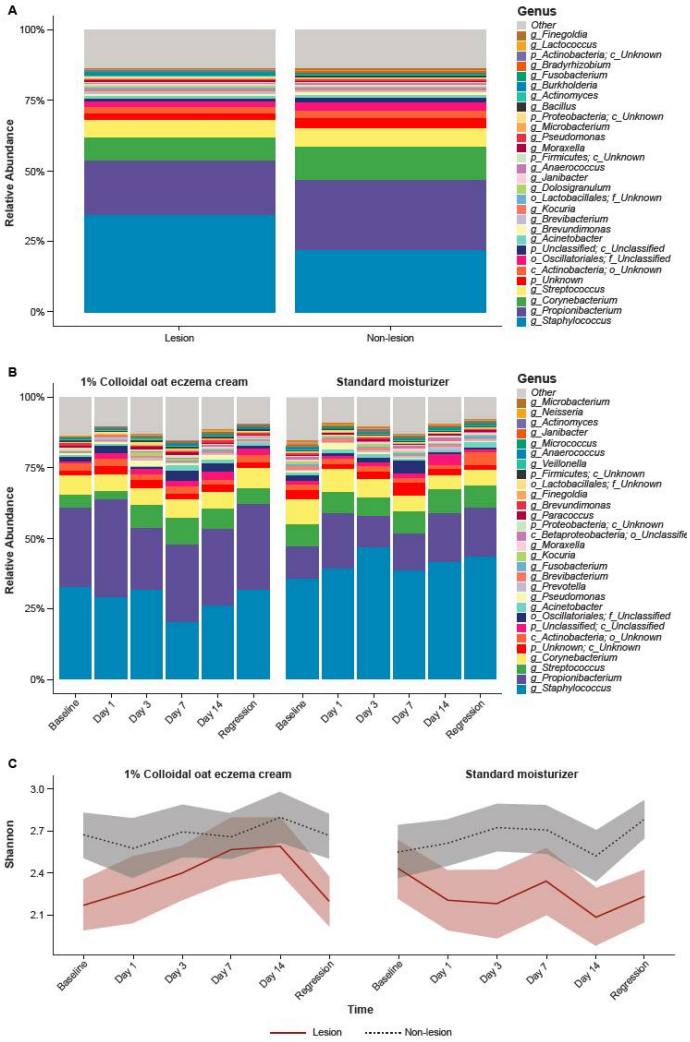
Colloidal oatmeal also has barrier repair properties. Lipids play a crucial role in the stratum corneum, particularly in its barrier function and ability to prevent excess loss of water. Stratum corneum lipids consist of an equimolar mixture of ceramides, cholesterol, and free fatty acids. Whole oat oil is rich in essential lipids including triglycerides, diacylglycerol, phospholipids, and free fatty aids. Oats also contain linoleic acid, which has been shown to be effective in reducing transepidermal water loss (TEWL) and restoring the permeability of the skin barrier.[20-21] The lipophilic molecules in oat also possess agonist properties towards various receptors and genes involved in epidermal differentiation, further lipid synthesis, and ceramide processing. Peroxisome proliferator-activated receptors (PPARs) are ligand-activated nuclear receptors that have been shown to induce both the expression of epidermal differentiation proteins and lipid synthesis in keratinocytes.[22] In in vitro cell and tissue culture studies, Chon et al demonstrated that lipophilic oat molecules possess dual PPARα and PPARβ/δ agonist activities. Oat oil treatment also resulted in a significant up-regulation of differentiation genes (including involucrin and transglutaminase 1) and ceramide processing genes (β-glucocerebrosidase, sphingomyelinases 3).[23]

Finally, topical application of oat extract has a beneficial effect on skin pH. The skin is a slightly acidic microenvironment with a pH of approximately 5.5.[15] This acidity enhances the barrier function of the skin, protecting against entry of pathogens, and assisting in maintenance of the integrity of the superficial keratin layer. Inflamed skin increases the pH of the skin from acidic to basic. Topical application of oatmeal extract has been shown to decrease the pH of the skin from a basic pH towards a normal physiologic pH, indicating that it can act as a restorative buffer.[15]

Use in Atopic Dermatitis

The clinical benefits of colloidal oatmeal have been demonstrated through extensive research across diverse patient populations, particularly in atopic dermatitis (AD). Atopic dermatitis is a common, relapsing inflammatory skin disorder with a complex pathogenesis. It is characterized by genetic abnormalities in the skin barrier via mutations in filaggrin, deficiencies in ceramides and cathelicidins, immunologic disturbances with a shift toward the Th-2 inflammatory pathway, and an elevation in serum immunoglobulin (IgE) levels. Topical agents are a mainstay of AD therapy regardless of disease severity. According to current clinical guidelines for the treatment of atopic dermatitis, the application of moisturizers should be an integral part of the treatment of patients with AD

FIGURE 1. (A) The microbiome diversity at lesion sites and adjacent sites changes overtime with 1% colloidal oat eczema cream. (B) The microbiome relative abundance of a standard moisturizer and 1% colloidal oat eczema cream. (C) Shannon diversity.



(based on level I evidence) and there is strong evidence that their use can reduce disease severity and the need for pharmacologic intervention.[24]

The use of colloidal oatmeal in the treatment of AD is ideal for several reasons. Both lesional and non-lesional skin in AD is characterized by xerosis, barrier abnormalities, and decreased content of ceramides. The disrupted skin barrier, as evidenced by increased transepidermal water loss, allows for penetration of irritants and allergens from the environment, subsequently leading to itch via cytokine release and inflammation.[25,26] Avenanthramides present in colloidal oatmeal can decrease inflammation and thereby have an anti-itch effect, as was previously discussed, via reducing the release of pro-inflammatory cytokines, and have been shown to significantly reduce scratching response by up to 40% compared with vehicle in murine models.[27] The lipids and fatty acids in colloidal oatmeal also offer barrier protection and help to replenish and supplement the stratum corneum in atopic dermatitis, which is known to be characterized by decreased ceramides (a vital stratum corneum lipid).

Several studies have examined the potential benefit of colloidal oatmeal as an adjunctive treatment in AD. In a study by Nebus et al, 25 patients aged 12–60 years with mild to moderate AD (by Hanifin and Rajka criteria) and at least 5% body surface area were enrolled in an 8-week study consisting of a topical regimen of twice daily application of an oat-based occlusive cream and once daily oat-based body wash. Patients taking systemic medications for eczema were excluded, but those using prescribed topical treatments were allowed to continue their medications. Investigator Global Assessment (IGA) scores, Eczema Area and Severity Index (EASI) scores, and itch severity were all significantly improved at weeks 2, 4, and 8.[28] An additional study with a younger cohort of 23 patients aged 3–5 months to 5 years-old examined the role of an adjunctive regimen of colloidal oatmeal cream twice daily with a colloidal oatmeal-based glycerin cleanser in conjunction with topical steroids. IGA and EASI scores were significantly improved from baseline at both week 2 and week 4, and Baby/Child Quality of Life Index was significantly improved at week 4.[29] In an international multicenter study conducted in Greece, Italy, and Portugal, 71 patients aged 6 months to >20 years with mild-to-moderate AD currently treated with or without topical steroids and/or immune modulators applied colloidal oatmeal twice daily. At 12 weeks, patients reported significant improvement in itch, erythema, and quality of life.[30]

Additional studies have compared the safety and efficacy of 1% colloidal oatmeal cream to prescription creams and emulsions in the management of mild to moderate atopic dermatitis. In a randomized, double-blind, two-arm trial by Lisante et al, 90 patients aged 6 months–18 years with mild to moderate AD were randomized to either use colloidal oatmeal cream or a standard, steroid-free prescription barrier cream twice daily. Patients using class IV–VII topical steroids were allowed in the study, those requiring systemic or class I–III steroids were excluded. At week 3, EASI scores showed that the colloidal oatmeal cream was non-inferior to the prescription cream.[31]

Atopic dermatitis is also characterized by a decreased microbial diversity with a disproportionate colonization and susceptibility towards *Staphylococcus aureus* pre- and during flares.[32] A controlled, multicenter, clinical usage study of patients aged 16–50 years with mild to moderate eczema examined the effect of twice daily use of 1% colloidal oatmeal cream on the skin microbiome. Compared to treatment with a standard moisturizer, treatment with 1% colloidal oat eczema cream was associated with trends toward lower prevalence of *Staphylococcus* species by day 7 and higher microbial diversity of lesional skin, approaching the level of diversity on

non-lesional skin. Similar improvement in microbial diversity was not observed with standard moisturizer. The authors posit that while unclear, the mechanism for increased microbial diversity may be through beneficial effects on skin pH and improvements in transepidermal water loss (See Figure 1).[33]

CONCLUSIONS

Oats have been used for centuries to treat a wide variety of dermatoses. In Part I of this two-part supplement, we have outlined the research and multifaceted benefits behind its use. Oat is composed of various compounds with a wide-ranging mechanism of action, possessing anti-inflammatory, anti-pruritic, anti-oxidant, anti-fungal, prebiotic, and barrier repair properties. These inherent characteristics of colloidal oatmeal lend to its function and effectiveness in the management of AD, a condition that is particularly burdensome and widespread. In the subsequent portion of this Supplement, we will continue to examine the clinical benefits of colloidal oatmeal in AD in special populations, and clinical efficacy and tolerance beyond eczema.

REFERENCES

1. Kurtz ES, Wallow W. Colloidal oatmeal: history, chemistry and clinical properties. *J Drugs Dermatol.* 2007;6(2):167-170.
2. Webster FH. Oat utilization: past, present and future. In: Webster FH, ed. *Oats: Chemistry and Technology.* St. Paul, Minnesota: American Association of Cereal Chemists, Inc; 1986:413-430.
3. Franks AG. Dermatologic uses of baths. *Am Pract Dig Treat.* 1958;9:1998-2000.
4. Skin protectant drug products for over-the-counter human use; proposed rulemaking for poison ivy, poison oak, poison sumac, and insect bites drug products. 54FR40808, 1989; October 3.
5. Skin protectant drug products for over-the-counter human use; final monograph. 68FR33362. 2003; June 4.
6. Colloidal Oatmeal. *The United States Pharmacopeia: The National Formulary.* Rockville, Maryland: United States Pharmacopeia Convention, Inc; 2006:591-592.
7. Health Benefits of Oat Phytochemicals. In: *Oats Nutrition and Technology.* Chichester, UK: John Wiley & Sons Ltd; 2013:171-194.
8. Graf E. Antioxidant potential of ferulic acid. *Free Radic Biol Med.* 1992;13: 435-448.
9. Collins FW. Oat phenolics: structure, occurrence and function. In: Webster FH, ed. *Oats: Chemistry and Technology.* St Paul, Minnesota: American Association of Cereal Chemists, Inc; 1986:227-291.
10. Nachbar F, Korting HC. The role of vitamin E in normal and damaged skin. *J Mol Med.* 1995;73:7-17.
11. Makdisi J, Kutner A, Friedman A. Oats and Skin Health. In: *Oats Nutrition and Technology.* Chichester, UK: John Wiley & Sons Ltd; 2013:311-331.
12. Guo W, Wise ML, Collins FW, et al. Avenanthramides, polyphenols from oats, inhibit IL-1B induced NK-kB activation in endothelial cells. *Free Radic Biol Med.* 2008;44:415-429.
13. Liu L, Zubik L, Collins F, et al. The antiatherogenic potential of oat phenolic compounds. *Atherosclerosis* 2004;175:39-49.
14. Sur R, et al. Avenanthramides, polyphenols from oats, exhibit anti-inflammatory and anti-itch activity. *Arch Dermatol Res.* 2008;569-574.
15. Grais M. Role of colloidal oatmeal in dermatologic treatment of the aged. *AMA Arch Derm Syphilol.* 1953;68:402-407.
16. Bratt K, et al. Avenanthramides in oats (Avena sativa L.) and structure-antioxidant activity relationships. *J Agric Food Chem.* 2003;51:594-600.
17. Dimberg L et al. Avenanthramides – a group of phenolic antioxidants in oats. *Cereal Chem.* 1993;70:637-641.
18. Miyagawa H. Induction of avenanthramides in oat leaves inoculated with crown rust fungus, Puccinia coronate f. sp. avenae. *Bio Biotech Bioch.* 1995;59:2305-2306.
19. Liu-Walsh F, Tierney NK, Hauschild J, et al. Fermentation of colloidal oatmeal by cutaneous bacteria results in enhanced production of lactic acid and short fatty acids. Poster 6639 presented at the *American Academy of Dermatology Annual Meeting*, 16-20 February 2018, San Diego, CA.
20. Ziboh VA, Miller CC, Cho Y. Metabolism of polyunsaturated fatty acids by skin epidermal enzymes: generation of anti-inflammatory and antiproliferative metabolites. *Am J Clin Nutr.* 2000;71 (suppl):361S-366S.
21. Potter RC, Castro JM, Moffatt LC, investors; Nurture, Inc. assignee. Oat oil compositions with useful cosmetic and dermatological properties. US Patent 5620692. April 15, 1997.
22. Chong HC, Tan MJ, Philippe V, et al. Regulation of epithelial-mesenchymal IL-1 signaling by PPARβ/δ is essential for skin homeostasis and wound healing. *J Cell Biol.* 2009;184(6):817-831.
23. Chon SH, Tannahill R, Yao X, et al. Keratinocyte differentiation and upregulation of ceramide synthesis induced by an oat lipid extract via the activation of PPAR pathways. *Exp Dermatol.* 2015;24(4):290-5.
24. Eichenfield, LF, Tom WL, Chamlin SL, et al. Guidelines for the management of atopic dermatitis. *J Am Acad Dermatol.* 2014;71(1):116-132.
25. Elias PM, Hatano Y, Williams ML. Basis for the barrier abnormality in atopic dermatitis: outside-inside-outside pathogenic mechanisms. *J Allergy Clin Immunol.* 2008;121(6):1337-1343.
26. Lebwohl M, Herrmann LG. Impaired skin barrier function in dermatologic disease and repair with moisturization. *Cutis.* 2005;76(6 Suppl):7-12
27. Sur R, Nigam A, Grote D, Liebel F, Southall MD. Avenanthramides, polyphenols from oats, exhibit anti-inflammatory and anti-itch activity. *Arch Dermatol Res.* 2008;300(10):569-574.
28. Nebus J, Nystrand G, Fowler J, et al. A daily oat-based skin care regimen for atopic skin. *J Am Acad Dermatol.* 2009;60:AB67.
29. Nebus J, Wallow W, Nystrand G, et al. Tolerance and efficacy of a colloidal oatmeal cream and cleanser regimen in babies and children with mild to moderate atopic dermatitis. Poster. 8th Annual Caribbean Dermatology Symposium. 20-24 January 2009. St. Maarten.
30. Lopes MJ. 11th Presentation at the European Society for Pediatric Dermatology Congress, 16-19 May 2012, Istanbul, Turkey. Presentation
31. Lisante TA, Nunez C, Zhang P. Efficacy and safety of an over-the-counter 1% colloidal oatmeal cream in the management of mild to moderate atopic dermatitis in children: a double-blind, randomized, active-controlled study. *J Dermatol Treat.* 2017;28(7):659-667.
32. Salava A, Lauerma A. Role of the skin microbiome in atopic dermatitis. *Clin Transl Allergy.* 2014;4:33.
33. Capone K, Kirchner F, Klein SL, Tierney NK. Effects of colloidal oatmeal topical atopic dermatitis cream on skin microbiome and skin barrier properties. *J Drugs Dermatol.* 2020;19(5):524-531.

 ORIGINAL ARTICLE Journal of Drugs in Dermatology

Colloidal Oatmeal Part II: Atopic Dermatitis in Special Populations and Clinical Efficacy and Tolerance Beyond Eczema

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ABSTRACT

Colloidal oatmeal has a diverse array of applications, clinical benefits, and uses beyond atopic dermatitis. First and foremost, it has been shown to be of benefit in the treatment of atopic dermatitis in skin of color. It has also been shown to be of benefit in the treatment of hand dermatitis, xerosis, psoriasis, skin manifestations of diabetes, and in the treatment of cutaneous adverse effects associated with oncologic therapies. In Part II of this 2-part series, we examine the efficacy, safety, and expansive clinical applications of colloidal oatmeal.

J Drugs Dermatol. 2020;19:10(Suppl):s8-11

INTRODUCTION

Atopic Dermatitis in Skin of Color

In Part I, we examined the ways in which colloidal oatmeal can be beneficial in the treatment of AD. Colloidal oatmeal has also been found to be of benefit in patients with skin of color and AD. An understanding of how colloidal oatmeal is of benefit in these populations begins with examining the structural and functional distinctions of skin of color.

Patients with skin of color encompass a wide range of racial and ethnic groups, including but not limited to persons of African, African American, Afro-Caribbean, Chinese, Japanese, Native American, Navajo Indian, Southeast Asian, Indian, Middle Eastern, and Latino descent and heritage. Racial and ethnic differences in skin color are directly related to variations in the number, size, and aggregation of melanosomes within the melanocytes and keratinocytes. In subjects with skin of color, there is a trend for melanosomes to be large with greater distribution throughout the epidermis.[1] Gunathilake et al demonstrated that dendrites from melanocytes of patients with Fitzpatrick skin type IV–V skin were more acidic than those from type I–II subjects, and that those in type VI–V skin also transfer more melanosomes to the stratum corneum, suggesting that melanosome secretion could contribute to the more acidic pH of type IV–V skin.[2] It has been well established that the stratum corneum functions best at a highly acidic surface pH, which is thought to serve an antimicrobial function, regulate barrier homeostasis and desquamation, and allow for optimal activity of the ceramide-generating enzymes sphingomyelinase and β-glucocerebrosidase.[2] There are conflicting data regarding racial differences in the structure of the stratum corneum. In one review article, it is argued that many of the studies cited in the literature have small patient populations and less-than-optimal study designs, which makes it difficult to draw definitive conclusions. In studies using tape-stripping techniques and microscopic visualization, patients with skin types V and VI were shown to have a stratum corneum with increased density but overall equal in thickness to types II and III. Taylor cites various studies, which posit that the increased density may be due to increased lipid content.[1]

As part of a larger trial comparing the efficacy of colloidal oatmeal with prescription barrier cream in the management of mild to moderate AD, 49 African American children aged 2–15 years were randomly assigned to twice-daily application of either colloidal oatmeal or prescription barrier cream. Colloidal oatmeal provided rapid improvement in baseline EASI score by day 7 (62.9% vs 53.7%) in addition to marked improvement in ratings of itch by day 7 (43.1% vs 33.3%) compared with prescription barrier cream.[3] Both treatments were clinically effective and well tolerated.

Clinical Efficacy and Tolerance Beyond Eczema

Colloidal oatmeal has been demonstrated to be effective in several clinical conditions aside from AD. Hand dermatitis is a common and widespread condition that disproportionately effects occupational groups exposed to irritants or allergens. Mainstays of therapy include avoidance of irritants or allergens and use of topical corticosteroids, although long-term use can lead to tachyphylaxis and steroid-sparing agents are

of benefit. In a randomized, double-blind placebo-controlled trial study with 6 weeks follow up, patients were randomized to two-week use of fluocinolone 0.025% followed by either 1% colloidal cream or base cream for 4 weeks as monotherapy. At the end of six weeks, patients randomized to use of 1% colloidal oatmeal had a statistically significant improvement in eczema severity and quality of life scores (HESI, Hand Eczema Severity Index; DLQI, Dermatology Life Quality Index) compared to the control group.[4]

Many studies have also evaluated the effectiveness of colloidal oatmeal in the treatment of moderate to severe xerosis, or dry skin. These studies have collectively demonstrated significantly greater improvements from baseline in skin barrier function (via corneometer measurements of transepidermal water loss), overall dryness, and itch, compared to either vehicle alone, similar ceramide cream, or prescription barrier cream.[5–7] Treatment with colloidal oatmeal lotion has also been found to have rapid and lasting efficacy, with a study by Nebus et al of thirty patients between the ages of 18 and 55 demonstrating significant improvement in measurements of transepidermal water loss and xerosis after only 4 days of use. Improvements were maintained after a 48-hour regression period.[8]

Psoriasis is a common, chronic skin disease affecting approximately 2% of the population that is characterized by dysregulation of the innate immune system and uncontrolled keratinocyte proliferation.[9] Patients often suffer from dryness and roughness, which leads to significant psychosocial distress. Colloidal oatmeal has also demonstrated benefit in patients with mild psoriasis. In a 4-week study of 60 adult females with psoriasis and self-reported sensitive skin, subjects were instructed to apply 1% colloidal oatmeal at least once per day to the whole body with a focus on dry patches. After 4 weeks of use, participants reported 45% improvement in itch and desquamation compared to baseline scores. 96% of patients reported that the 1% colloidal oatmeal lotion helped to reduce both the severity and number of appreciable patches.[10]

Successful treatment of mollucsum contagiosum (MC) with colloidal oatmeal has also been described. Molluscom contagiosum, a skin infection caused by a DNA poxvirus, is one of the most common viral skin infections seen in children. In an open study, 6 children aged 5–11 years with at least 10 cutaneous lesions of MC were treated with a zinc oxide cream containing colloidal oatmeal extracts (*Avena rhealba*). After 4 weeks of therapy, 4 of the 6 patients had complete resolution of their lesions and the 2 remaining patients had a >50% decrease in the total number of their lesions.[11] Pazyar et al posit that the antiviral properties of colloidal oatmeal extract are likely due to the inhibitory effects on eicosanoid formation, expression of cytosolic phospholipase A2, and arachidonic acid mobilization in human keratinocytes.[12]

Aside from its demonstrated benefit in a variety of dermatoses, colloidal oatmeal has also been continuously reported as safe and effective. Twelve independent studies evaluated irritant and allergic reactions via patch testing of various skin care products containing oatmeal in various formulations including lotions, creams, serums, and cleansers. Of the 2565 participants, only 20 subjects demonstrated transient low-level reactions such as faint erythema, and only 3 subjects demonstrated grade 1 reactions with edema.[13] Criquet et al further described two studies evaluating the ocular tolerance of a facial cleanser in 43 female subjects with normally sensitive eyes. Eye reactions were documented in only 3 subjects and confirmed by clinical opthalmologic evaluation.[13] In a total of 47 patients, clinical efficacy was demonstrated over the course of six weeks via skin hydration, reduced desquamation index, and subjective evaluation of signs of skin dryness after application. Dermatologist assessment demonstrated significant improvement of skin dryness, desquamation, and skin roughness in treated areas compared to controls.[13] Ultimately, the U.S. Food and Drug Administration generally recognizes colloidal oatmeal as safe and effective.

Systemic Conditions With Skin Manifestations

Colloidal oatmeal has been reported to be of benefit in the treatment of skin manifestations of systemic diseases. Diabetes mellitus is commonly responsible for skin changes including diabetic dermopathy and discrete to mild xerosis. Pierard et al describe a continuum between a sensation of dry skin, xerosis, and icthyosiform presentations of the shins and feet of diabetic patients.[14] In a study of 46 patients with diabetes and moderate dryness of the lower legs, twice daily use of an oatmeal lotion with avenanthramides and oat oil resulted in significant improvements in erythema, fissuring, scaling, and tactile roughness as early as 1 week into use. Improvements continued through 4 weeks of treatment.[15]

Dermatologic Side Effects Associated with Cancer Therapy

Oats have also been described in the literature to be of benefit in addressing skin toxicities associated with oncologic therapies. Targeted therapies, a newer genre of cancer treatment that specifically targets tumor cells, are well known for their significant dermatologic toxicities.[16] Over 50 distinct dermatologic toxicities have been reported in association with more than 30 anti-cancer agents, the most common of which include hand-foot skin reactions, nail changes, papulopustular (acne-like) eruptions, pruritus (severe itching), secondary malignancies, new neoplasms, and chemotherapy-induced alopecia (hair loss or spot baldness).[17–18] Of particular interest and study are epidermal growth factor receptor (EGFR) inhibitors and tyrosine kinase inhibitors, which are used to treat a broad range of solid organ malignancies. Treatment and optimal management of these cutaneous effects is important, as they can be severe enough to cause patients to discontinue treatment.

Among patients treated with EGFR inhibitors, up to 90% have experienced papulopustular eruptions.[19] The rash usually developed in the first 2–4 weeks after initiation of therapy as pruritic and tender erythematous papules and pustules on the scalp, face, neck, chest, and back.[20] Interestingly, there is a relationship between the development of the rash and the response to chemotherapy and ultimate survival.[21] Pruritus is another common adverse event with EGFRIs, affecting up to 54.9% of patients based on particular EGFRI treatment, and which can have a significant impact on quality of life.[22] Alexandrescu et al reported treatment with colloidal oatmeal of 11 patients with a rash induced by cetuximab, erlotinib, panitumumab, and sorafenib. Colloidal oatmeal was applied three times a day for 7 days. The overall response rate was 100%, with a complete response of 60%. The authors argue that the observed eruptions in these patients may represent an inflammatory reaction to EGFR inhibitors, thus explaining the response to colloidal oatmeal given its anti-inflammatory properties.[23] An additional study in Taiwan studied the benefit of colloidal oatmeal in a sample of 30 patients with dermatologic toxicities associated with EGFR inhibition. Patients applied colloidal oatmeal three to five times a day for 4 consecutive weeks. Dermatologic toxicity severity, body surface area involvement, and pruritus all improved at 4 weeks with no adverse events reported.[24] Unlike more potent topical treatments such as topical steroids, metronidazole, erythromycin, salicylic acid, and benzoyl peroxide, colloidal oatmeal is not associated with any toxicity.[23]

Radiation therapy is used in the treatment of various forms of cancer and is associated with acute and chronic skin changes. Early skin reactions usually occur within days to weeks, initially manifesting as transient to generalized erythema. If the cumulative radiation dose reaches 20 gray, dry desquamation can develop characterized by pruritus, scaling, and flaking of the skin.[25] Colloidal oatmeal has been studied as a treatment for radiation-induced skin reactions. In a study of 24 patients undergoing radical radiotherapy for anal cancer, patients were randomized to treatment with either colloidal oatmeal or aqueous cream. Skin reactions for both cohorts were comparable, but the colloidal oatmeal cohort had an appreciable response with regards to epidermal regeneration at follow up.[26] As treatments for cancer continue to evolve, so must treatments for their cutaneous adverse effects. Colloidal oatmeal has shown promise with an excellent safety profile.

CONCLUSIONS

In Part II of this two-part series, we examined the diverse range of clinical applications of colloidal oatmeal. Colloidal oatmeal has been shown to be beneficial in the treatment of atopic dermatitis in African American patients. It also has been shown to be of benefit in the treatment of hand dermatitis, xerosis, psoriasis, skin manifestations of diabetes, and in the treatment of cutaneous adverse effects associated with oncologic therapies. This wide-ranging efficacy and use is backed by proven safety and tolerability, making colloidal oatmeal an ideal treatment option in many case scenarios.

REFERENCES

1. Taylor SC. Skin of color: biology, structure, function, and implications for dermatologic disease. *J Am Acad Dermatol.* 2002;46(2):S41-S62.
2. Gunathilake R, Schurer NY, Shoo BA et al. pH-regulated mechanisms account for pigment-type differences in epidermal barrier function. *J Invest Dermatol.* 2009; 129(7):1719-1729.
3. Nunez C et al. A colloidal oatmeal OTC cream is as clinically effective as a prescription barrier repair cream for the management of mild to moderate atopic dermatitis in African American children. *J Am Acad Dermatol.* 2013;60(4):AB73. P6654.
4. Sobhan M et al. The efficacy of colloidal oatmeal cream 1% as add-on therapy in the management of chronic irritant hand eczema: A double-blind study. *Clin Cosmet Investig Dermatol.* 2020;13:241-251.
5. Nebus J, et al. Comparing the effectiveness of an oatmeal cream versus a prescription device cream in improving skin moisturization and barrier function in moderate to severe dry skin. *J Am Acad Dermatol.* 2011;64(2):S1, AB71.
6. Nebus J, et al. A 3-week moisturization study followed by a 2-week regression phase to evaluate the efficacy of a triple oat skin protectant cream versus a ceramide cream on moderate to severe dry skin. *J Am Acad Dermatol.* 2014;70(5):S1, AB61.
7. Kalaaji AN, et al. A randomized controlled clinical study to evaluate the effectiveness of an active moisturizing lotion with colloidal oatmeal skin protectant versus its vehicle for the relief of xerosis. *J Am Acad Dermatol.* 2015;72(5):S1,AB36.
8. Nebus J, et al. The rapid and lasting efficacy of an oatmeal lotion in improving the moisturization and skin barrier properties of extra dry, itchy skin. *J Am Acad Dermatol.* 2010;62(3):S1,AB56.
9. Nestle FO, et al. Psoriasis. *N Eng J Med.* 2009;361:496-509.
10. Nollent V, et al. Tolerance and Subject Satisfaction of an Over the Counter Colloidal Oatmeal (Avena Sativa) Lotion in Patients with Psoriasis and Sensitive Skin. Poster accepted for presentation. AAD Annual Meeting 2020.
11. Safa G, et al. Successful treatment of molluscum contagiosum with a zinc oxide cream containing colloidal oatmeal extracts. *Indian J Dermatol.* 2010;55(3):295-296.
12. Pazyar N, et al. Oatmeal in dermatology: A brief review. *Indian J Dermatol Venerol Leprol.* 2012;78(2):142-5.
13. Criquet M, et al. Safety and efficacy of personal care products containing colloidal oatmeal. *Clin Cosmet Investig Dermatol.* 2012;5:183-193.
14. Pierard GE, et al. Critical assessment of diabetic xerosis. *Expert Opin Med Diagn.* 2013;7(2):201-207.
15. Nebus J, et al. Safety and tolerance of skin protectant lotions with oatmeal in patients with diabetes. AAD Annual Meeting. 2008. AB P932.
16. Kao S, Friedman A. Supportive Oncodermatology: Addressing dermatologic adverse effects associated with oncologic therapies. *Oncology Issues.* 2018;33(6):64-75.
17. Balagula Y, Rosen ST, Lacouture ME. The emergency of supportive oncodermatology: the study of dermatologic adverse events to cancer therapies. *J Am Acad Dermatol.* 2011;65:624-635.
18. Osio A, Mateus C, Soria JC et al. Cutaneous side-effects in patients on long-term treatment with epidermal growth factor receptor inhibitors. *Br J Dermatol.* 2009; 161:515-21.
19. Perez-Soler R, Delord JP, Halpern A et al. HER1/EGFR inhibitor-associated rash: future directions for management and investigation outcomes from the HER1/EGFR inhibitor rash management forum. *Oncologist.* 2005;10(5):345-356.
20. Lacouture ME, Anadkat MJ, Bensadoun RJ et al. Clinical practice guidelines for the prevention and treatment of EGFR inhibitor-associated dermatologic toxicities. *Support Care Cancer.* 2011;19:1079-1095.
21. Saltz LB, Meropol NJ, Loehrer PJ et al. Phase II trial of cetuximab in patients with refractory colorectal cancer that expressed the epidermal growth factor response. *J Clin Oncol.* 2004;22:1201-1208.

22. Ensslin CJ, Rosen AC, Wu S et al. Pruritus in patients treated with targeted cancer therapies: a systematic review and meta-analysis. *Breast Cancer Res Treat*. 2012;135:347-354.
23. Alexandrescu DT, Vaillant JG, Dasanu CA et al. Effect of treatment with a colloidal oatmeal lotion on the acneform eruption induced by epidermal growth factor receptor and multiple tyrosine-kinase inhibitors. *Clin Exp Dermatol*. 2006;32:71-74.
24. Ke YT, Kuo CC. Effects of colloidal oatmeal lotion of symptoms of dermatologic toxicities induced by epidermal growth factor receptor inhibitors. *Adv Skin Wound Care*. 2017;30(1):27-34.
25. Hegedus F et al. Radiation dermatitis: an overview. *Int J Dermtol*. 2017;56(9):909-914.
26. Rudge R. Colloidal oatmeal emollient as an alternative skincare approach in radiotherapy: a feasibility study. *J Radiother Pract*. 2016;15(4):332-333.

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