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.

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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]

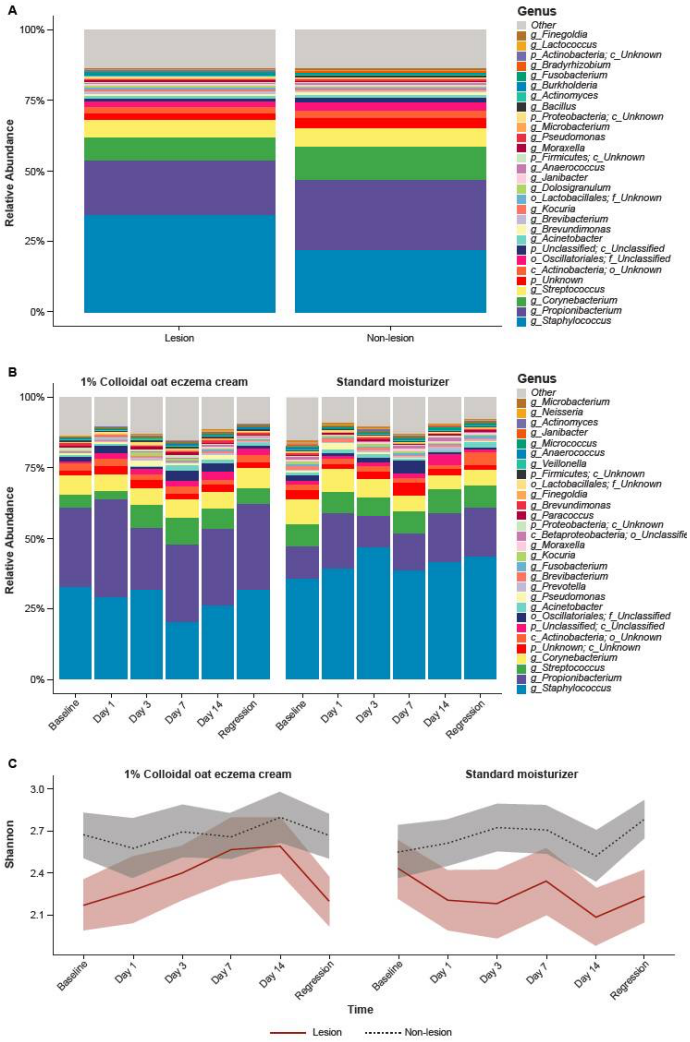
Colloidal oatmeal also has barrier repair properties. Lipids play a crucial role in the stratum corneum, particularly in its barrier function and ability to prevent excess loss of water. Stratum corneum lipids consist of an equimolar mixture of ceramides, cholesterol, and free fatty acids. Whole oat 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.

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