# Avenanthramides: Oat Compounds With A Growing Role In Dermatology

**Therapeutic, nonnutritive, history of oats**

Cultivated oats have been part of the human diet since the Bronze Age, but the topical application of oatmeal preparations for skin care rather than nutrition was first described by the ancient Romans.[1,2] Medical texts by Pliny and other notables promoted the use of oatmeal flour for a variety of dermatologic conditions.[2] More recent centuries have found health benefits for both topically applied and orally ingested oat preparations. For example, in the early 1800's Henry Potter, a London pharmacist, produced a tincture of oats known as *Potter's Compound of Avena with Helionas Mixture No. 108A and Tonic No. 1*.[3] For the next hundred years, oats were regarded as so powerfully healthful that they were almost exclusively available at pharmacies.[4]

Oatmeal's ability to relieve itch and function as a skin protectant when formulated in facial masks and bath oils was first documented in the 1930's.[4] Initially, topical oatmeal preparations were homemade affairs that were soothing, but posed the unusual risk of clogging drains with the hydrated oat flour. Ready-to-use formulations simplified preparation and made it possible to conduct studies that showed colloidal oatmeal baths provided soothing treatment and nonirritating cleansing for inflamed skin associated with xerotic dermatoses.[5-9] By the end of the 20th century, the Food and Drug Administration (FDA) recognized colloidal oatmeal as safe and effective, and granted approval as a skin protectant in 2003, including colloidal oatmeal in the Final Monograph on Skin Protectant Drugs for Over-the-Counter Use.[10,11]

The range of dermatologic applications for colloidal oatmeal is extensive, most often as adjunctive therapy in pruritic skin conditions such as atopic dermatitis, allergic or irritant contact dermatitis, chicken pox, poison ivy, oak, and sumac, insect bites, winter itch, cercarial dermatitis, ichthyosis, prickly heat, hives, sunburn, and rashes.[5-9,12-17] Another application of oats that sparked extensive investigation decades later was their use as a commercial antioxidant in food and beverage products.[16,17] During the 1930's, foods that were sensitive to oxidation, such as milk, butter, and ice cream, were protected from spoilage by finely ground oats.[4]

**Active Oat Fractions: Phenolics and Avenanthramides**

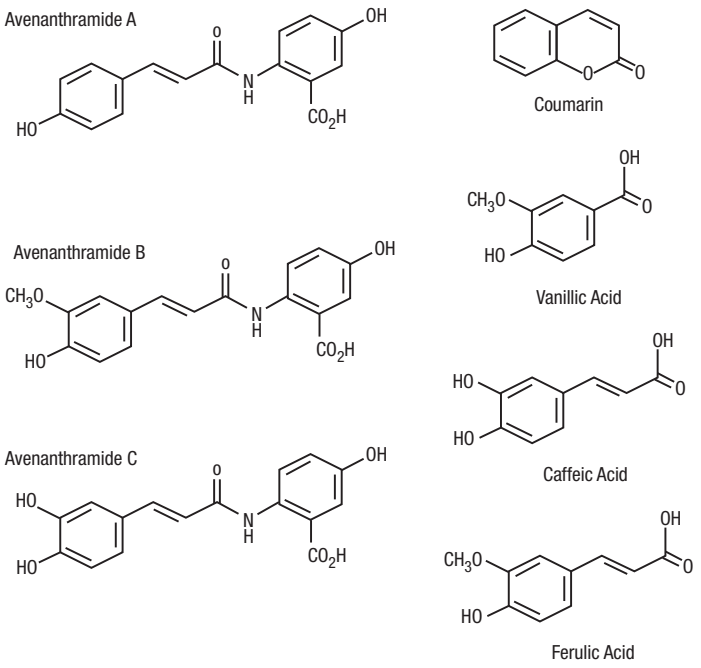
The recognized clinical benefits of finely ground oats are due to their remarkable chemical composition, and the fortunate coincidence that compounds essential for the natural development of oats may have beneficial effects on humans. Oats are generally regarded as having the highest protein and lipid content of any cereal grain, as well as a high fatty acid content.[4,17] Oat flour (prepared from finely ground oats) is predominantly composed of starches (65% to 85%), proteins (15% to 20%, including enzymes), fiber and beta glucans (5% each), small amounts of vitamins, and lipids (3% to 11%). The lipids are protected from oxidation by a variety of natural antioxidant compounds, most important of which is a group of phenolic compounds usually present at concentrations below 300 ppm.[17,18]

These phenolic compounds are part of a group of more than 5000 naturally occurring structurally and functionally related molecules. They are perhaps the largest group of phytochemicals with disease-preventing and health-promoting effects, and have been the focus of intense research because of their antioxidant activity.[19] Phenolics have a broad range of biologic activities including prevention of atherosclerosis, inflammation, and oxidation.[16] Oat phenolics may serve as potent antioxidants by scavenging reactive oxygen and nitrogen species and/or by chelating transition minerals.[16]

As a group, phenolics are the strongest antioxidants found in nature, yet within the group, individual compounds have characteristic biologic and antioxidant activity.[19] Oat phenolic compounds include simple forms with a single phenol ring, such as ferulic acid, caffeic acid, and vanillic acid; complex compounds with 2 or more rings such as coumarin; and the avenanthramides, a class of more than 40 phenolic compounds found only in oats (Figure 1).[18]

Complex mixtures of phenolics can be isolated from oats by an ethanol-water extraction and have been further separated, identified, concentrated, standardized, and evaluated by in vitro and in vivo biologic models. They have been shown to inhibit oxidation of low-density lipoprotein; inhibit the autoxidation of linoleic acid and beta carotene; inhibit oxygen consumption following hemin-induced oxidation of

***Figure 1. Some of the many biologically active phenolic compounds in oats.***



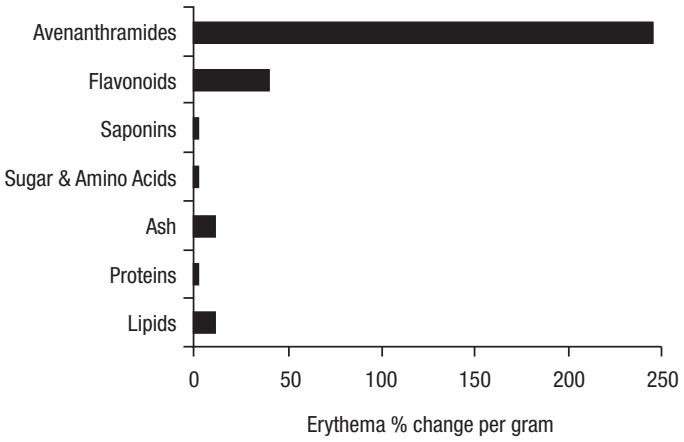

linoleic acid; inhibit collagen oxidation by peroxinitrite; and inhibit oat oil oxidation with activity comparable to commercial antioxidants like butylated hydroxytoluene and propyl gallate.[16-18,20,21]

## Avenanthramide biologic activity

Avenanthramides have 10 to 30 times the antioxidant activity of other oat phenolic compounds and are currently being studied to further characterize their biologic and chemical properties.[17] More than 25 years ago, ethanol–water extracts of oats (including avenanthramides and other phenolics) were evaluated for their effect on prostaglandin synthesis based on the observations that finely ground oat flour is useful for relieving itch, sunburn, and skin inflammation, and that prostaglandins are an important component of inflammation from burns, contact eczema, and exposure to radiation. Using an in vitro prostaglandin biosynthesis assay, the oat phenolic fraction (including avenanthramides) was found to inhibit prostaglandin biosynthesis nearly as well as the anti-inflammatory agent indomethacin.[22] Similar studies have shown avenanthramides to inhibit the release of the pro-inflammatory cytokine IL-8.[23]

More recently, separated oat fractions were tested in a skin erythema model to further explore the functional properties of various oat components. When compared to saponins, flavonoids, sugars and amino acids, ash, proteins, and lipids, the avenanthramide fraction was found to most effectively reduce UV-induced erythema 24 hours after dermal application.[24] A follow-up dose-response study of highly purified avenanthramides showed significant reduction in erythema at concentrations from 45 ppm to below 2 ppm.[24]

***Figure 2. Oat fraction erythema reduction. Avenanthramides were the most potent of 7 oat fractions at reducing skin redness 24 hours after application. In this trial, test sites were irradiated with 1.5 times the minimal erythema dose (MED) of ultraviolet light followed at 24 hours by application of 7 oat fractions. The change in skin color was measured 24 hours after samples were applied. The change in erythema was expressed relative to the dry weight of the applied sample.***




## Avenanthramide standardization

The key role of avenanthramides in the overall activity of natural oats provides an opportunity to standardize oat preparations to known concentrations of active ingredients.

***Table 1. Avenanthramide dose response for erythema-reduction. A purified avenanthramide fraction was prepared at concentrations of 45, 15, 5, 1.5, and 0.5 ppm and applied to skin 24 hours after exposure to 1.5 x MED; the change in skin color was measured 24 hours after avenanthramide application. Redness reduction was calculated relative to baseline skin color.***

| Avenanthramide Concentration, ppm | Erythema Reduction at 24 Hours, % |
|---|---|
| 45.0 | 18.7* |
| 15.0 | 18.4* |
| 5.0 | 19.4* |
| 1.5 | 14.0* |
| 0.5 | 7.1 |
| Untreated | 5 |

*P<.05, t-test

This is important because the chemical composition of oats varies with each species and subspecies and is further affected by soil type, growing conditions, and processing.[17,18,20] Although whole oat flour provides effective topical relief, the use of standardized oat extracts will help achieve predictable clinical benefit. Laboratory synthesis of individual avenanthramides is underway and will enable further characterization of each unique compound.

## Avenanthramide potential in skin care

The avenanthramide fraction of oats has been shown to be a highly effective antioxidant in a number of test systems. It has been demonstrated to perform as an anti-irritant and a skin protectant both in vitro and in vivo. The biologic and dermatologic applications of this activity have potential use in skin care for infants, people with sensitive skin, and for caring for sun-exposed skin. Because antioxidant activity is central to avenanthramide activity, these compounds will continue to contribute to improved outcomes anywhere reactive molecules play a role in disease processes.

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