COSMETIC BENEFITS OF NATURAL INGREDIENTS

Release/Most Recent Review Date: October 1, 2014
Expiration Date: September 30, 2015
Estimated Time to Complete This CME Activity: 1 Hour
Media/Method of Participation: Journal article, web-based post-test, and evaluation
Hardware/Software Requirements: Any web browser

Statement of Need

The use of products using natural ingredients for skin care have evolved significantly in recent years. Advances in the understanding of the mechanisms and biochemistry of natural ingredients has led to the development of new technologies and product formulations that provide benefits to the management of various cutaneous disorders as well as the natural aging process. Therefore it has become increasingly important for dermatology health care practitioners of all experience levels to have access to the latest evidence-based research on advances in the understanding of product containing natural ingredients and clinical experience in their application to the practice of dermatology.

Educational Objectives

This activity is designed to increase the knowledge of dermatology clinicians and residents on the latest research and new advances in skincare products with natural ingredients. The goal of the activity is to allow participants to explore emerging research on the intrinsic and extrinsic benefits of natural ingredients and their application in patient-care. Participants will gain information on how to practically apply this research and knowledge to real, day-to-day, patient encounters.

Upon completion of this enduring material, participants should be able to:

- Identify the active natural ingredients and their clinical uses in disorders of the skin
- Classify active natural ingredients and their cosmetic benefits in skincare products
- List key properties of natural ingredients and their relative usage in inflammatory dermatoses
- Review scientific efficacy, development, and clinical studies regarding the science of natural ingredients in skin care
- Recall the safety, stability, tolerability, and efficacy of natural ingredients

Target Audience

This activity is designed to increase the knowledge of dermatology clinicians and residents on the latest research and new advances in skincare products with natural ingredients.

Accreditation Statement

This activity has been planned and implemented in accordance with the essential areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the National Association for Continuing Education and the Physicians Continuing Education, Corporation. The National Association for Continuing Education is accredited by the ACCME to provide Continuing Medical Education (CME) for physicians.

Provider Contact Information

For questions about the CME activity content, please contact The National Association for Continuing Education at info@naceonline.com.

Privacy Policy

All information provided by course participants is confidential and will not be shared with any other parties for any reason without permission.

Credit Designation

The National Association for Continuing Education designates this journal-based CME activity for a maximum of 1 *AMA PRA Category 1 Credit*™. Physicians should claim only the credit commensurate with the extent of their participation in this activity.

How to Obtain CME Credit

You can earn one (1) *AMA PRA Category 1 Credit*™ by reading the CME article contained in this issue and completing a web-based post-test and evaluation.

Test is valid through September 30, 2015 (no credit will be given after this date).

To receive credit for this activity, please go to www.JDDonline.com and click on CME Activities under "Library." You will find instructions for taking the post-test and completing the program evaluation. You must earn a passing score of at least 70% and complete and submit the activity evaluation form in order to receive a certificate for *AMA PRA Category 1 Credit*™. There is no fee for this CME activity. Once you have completed the form online, you will be able to print your certificate directly. You can also receive credit for this activity by completing the post-test and evaluation at the end of this supplement and faxing or mailing it to JDD, 377 Park Avenue South, 6th Floor, NY, NY 10016; fax: 212-213-5435.

Faculty Credentials
Joseph F. Fowler Jr. MD FAAD (Division of Dermatology, University of Louisville School of Medicine, Louisville, KY)

Peer Reviewer Credentials
Perry Robins MD (Professor Emeritus, NYU School of Medicine, New York, NY)

DISCLOSURES

Policy on Faculty and Provider Disclosure: It is the policy of the National Association for Continuing Education (NACE) to ensure fair balance, independence, objectivity, and scientific rigor in all activities. All faculty participating in CME activities sponsored by the National Association for Continuing Education are required to present evidence-based data, identify and reference off-label product use and disclose all relevant financial relationships with those supporting the activity or others whose products or services are discussed.

Any real or apparent conflicts of interest have been addressed through a peer review process, as required by ACCME.

The faculty/authors have disclosed the following relationships with commercial interests:

Joseph F. Fowler Jr. has served as a consultant for Johnson & Johnson, Galderma, Innocutis, and Ranbaxy, and as a speaker for Galderma, Innocutis, and Ranbaxy, and has received research grants from Abbott, Allerderm, Allergan, Amgen, Astellas, Galderma, Genentech, Johnson & Johnson, Lilly, Medicis, Novartis, Qunnova, Taro, and Valeant.

The peer reviewers have disclosed the following relationships with commercial interests:

Perry Robins has no relevant conflicts of interest to disclose.

The planning committee of this activity, Caryn Cavallo, Assistant Editor, Dustin Harris, Designer JDD, Don Marcone, Continuing Education Grants Manager, Nick Gillespie, Assistant Publisher JDD, and Michelle Frisch, National Association for Continuing Education, have no relevant conflicts of interest to disclose.

Disclosure of Unlabeled Use: This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. The National Association for Continuing Education, *Journal of Drugs in Dermatology*, and the activity supporters do not recommend the use of any agent outside of the labeled indications. The opinions expressed in the educational activity are those of the faculty and do not necessarily represent the views of The National Association for Continuing Education, *Journal of Drugs in Dermatology*, and the activity supporters. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings.

Disclosure of Commercial Support: This CME article has been made possible by an unrestricted educational grant from Johnson & Johnson.

Colloidal Oatmeal Formulations and the Treatment of Atopic Dermatitis

Joseph F. Fowler Jr. MD FAAD
Division of Dermatology, University of Louisville School of Medicine, Louisville, KY

ABSTRACT

Colloidal oatmeal suspensions are currently available in bath soaps, shampoos, shaving gels, and moisturizing creams, and several studies have been conducted that demonstrate the efficacy and safety of colloidal oatmeal for the treatment of inflammatory skin conditions. The diverse chemical polymorphism of oats translates into numerous clinical utilities for atopic dermatitis (AD) and eczema. Avenanthramides are the principle polyphenolic antioxidants in oats, and they have been shown to assuage inflammation in murine models of contact hypersensitivity and neurogenic inflammation and also reduce pruritogen-induced scratching in a murine itch model. Moreover, avenanthramides are a potent antioxidant. This paper will discuss various studies that have found colloidal oatmeal compounds to be beneficial in the treatment of AD and also as adjunctive treatments for AD.

J Drugs Dermatol. 2014;13(10):1180-1183.

INTRODUCTION

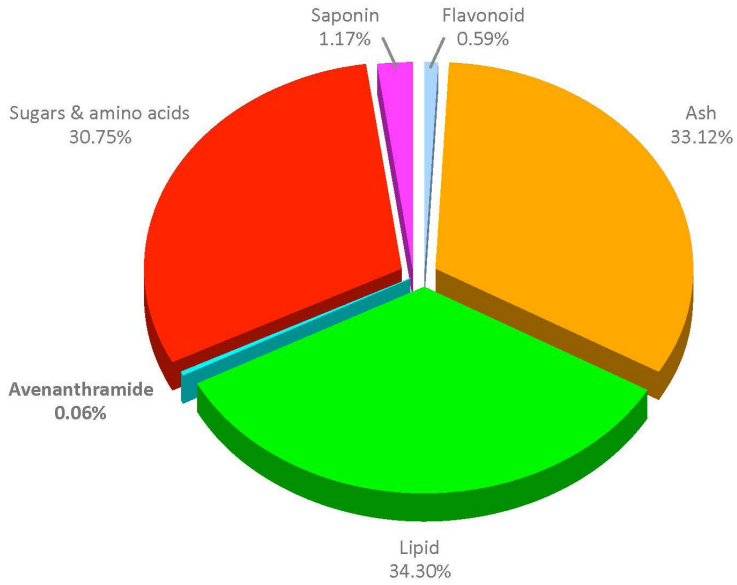
In 1945, colloidal oatmeal compounds became available for the treatment of inflammatory skin conditions.[1] In 1989, the Food and Drug Administration (FDA) recognized colloidal oatmeal as a safe and effective Category I ingredient, and it approved colloidal oatmeal as a skin protectant in 2003. Today, colloidal oatmeal suspensions are available in bath soaps, shampoos, shaving gels, and moisturizing creams.[1] Moreover, a wide range of studies have been conducted that evaluate the efficacy and safety of colloidal oatmeal as adjunct treatment in the management of atopic dermatitis (AD), and these studies have found that moisturizers and/or cleansers containing colloidal oatmeal significantly improved many of the clinical outcomes associated with AD.[2]

Oats (Avena sativa) contain of a wide array of phytochemicals that include carbohydrates, proteins, lipids, flavonoids, avenanthramides, tocols, alkaloids, saponins, and sterols.[3] The diverse chemical polymorphism of oats translates into a myriad of clinical utilities for AD and eczema. The high concentration in starches and beta-glucan in oats provide protective and water-holding functions.[1] The saponins in oats are largely responsible for its cleansing activity.[1] The antioxidant and anti-inflammatory effect of colloidal oatmeal is due in particular to the presence of avenanthramides, vitamin E, ferulic acid and other antioxidants.[4,5] (Figure 1)

Avenanthramides are the principle polyphenolic antioxidants in oats.[4] Although avenanthramides represent only a small constituent of oats, they can have significant effects on the inflammatory processes typical of AD. Sur and colleagues found that avenanthramides at concentrations as low as 1 parts per billion diminished phosphorylation of the p65 subunit of nuclear factor kappa B (NF-kappaB).[6] Further, cells treated with avenanthramides showed a significant inhibition of tumor necrosis factor-alpha (TNF-alpha) and reduction of interleukin-8 (IL-8) release.[6] Moreover, topical application of 1-3 ppm avenanthramides has allayed inflammation in murine models of contact hypersensitivity and neurogenic inflammation and reduced pruritogen-induced scratching in a murine itch model. Sur and colleagues concluded that the avenanthramides found in oats proved to be potent anti-inflammatory agents.

Chen and colleagues assessed the pharmacokinetics and antioxidant action of avenanthramide A, B, and C in healthy older adults in a randomized, placebo-controlled, 3-way crossover trial.[7] Six subjects consumed 360 milliliters of skim milk alone (placebo) or containing 0.5 or 1 grams of an avenanthramide-enriched mixture extracted from oats. Plasma samples were collected over a 10-hour period, and the respective concentrations of avenanthramide A, avenanthramide B, and avenanthramide C in the avenanthramide-enriched mixture group were 154, 109, and 111 micromoles per gram. After consumption of 1 gram of avenanthramide-enriched mixture, plasma glutathione was elevated by 21% at 15 min ($P <$ or $= 0.005$) and by 14% at 10 hours ($P <$ or $= 0.05$). Thus, the investigators determined that oat avenanthramides are bioavailable and increase the glutathione antioxidant levels of healthy older adults.

FIGURE 1. The antioxidant and anti-inflammatory effect of colloidal oatmeal is due in particular to the presence of avenanthramides, vitamin E, ferulic acid, and other antioxidants.



Ceapro. Drago-Calm. Available at: http://www.ceapro.com/pdfs/dragocalm.pdf. Accessed July 11, 2007.

Atopic Dermatitis and hereditary eczema are characterized by erythema, pruritus, scaling, lichenification, and papulovesicles, and Schumaus and colleagues analyzed the efficacy of a proprietary formulation of standardized avenanthramide fraction isolated from oats in a topical suspension for ultraviolet (UV) radiation-induced erythema.[8] The study included 9 subjects who were given an erythema-inducing dose of UV light. The test areas of the subjects skin were treated 24 hours after irradiation with the standardized avenanthramide fraction, and the subjects' erythema was calculated relative to baseline. The 5ppm avenanthramides fraction produced a 75% reduction of histamine release in the irradiated areas of the skin, and a statistically significant (P<0.05) relief from erythema symptoms, such as itching, 30 minutes following its application. After one-hour, redness was reduced by more than 85% and after two hours the area of redness was reduced by 90%.

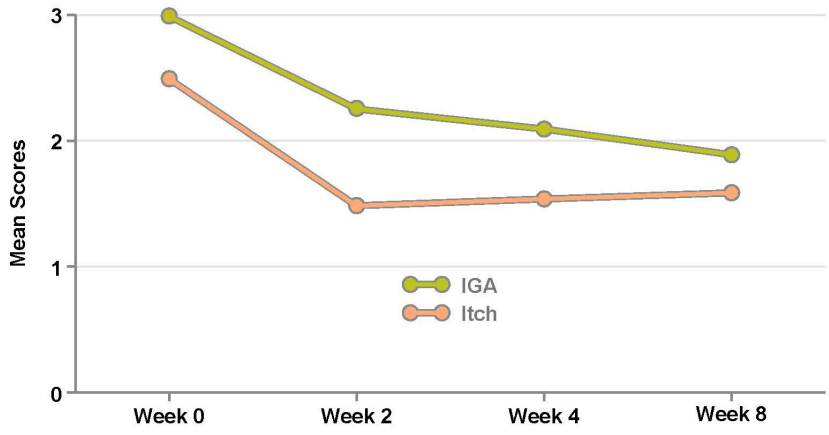
Oat colloidal suspensions have been used for decades as adjuncts in the treatment of AD, especially in the US, and Nebus and colleagues evaluated an oatmeal-based occlusive cream on subjects with AD.[9] Fifty patients between 12 to 60 years of age with mild to moderate AD, as measured by Hanifin and Rajka criteria, were enrolled into this multicenter, double-blinded, randomized clinical study. For 8 weeks, the patients used a daily skin care regimen consisting of twice a day application of an oatmeal-based occlusive cream (with vitamins and ceramides) and an oatmeal glycerin cleanser for moisturizing and body cleansing. Patients were also allowed to use their normal topical medications for their AD.

Independent dermatologist evaluations were performed at multiple time points throughout the study. The investigators found that the subjects who used an oatmeal-based occlusive cream and an oatmeal glycerin cleanser had significant improvements (P<.05) in the Eczema Area Severity Index (EASI) and Investigator's Global Assessment (IGA) scores after only 2 weeks of using the oat-based skin care regimen. Improvements in perceived itch (P<.05) were also noted at the 2-week time point. Patients provided positive feedback after using the regimen, and they perceived multiple skin benefits, including improved skin texture, decreased discomfort, and an overall improved look and feel. (Figure 2)

Goujon and colleagues assessed the risk of immediate and delayed allergic reactions to repeated and maximized applications of oat-containing cosmetics and oat extracts and their tolerance in cereal-sensitized adults with AD.[10] The 45-day, open-label pilot study included 12 cereal-sensitized atopic adults. The subjects were given repeated and maximized applications of oat-containing cosmetics at day 0, day 10, and day 31, and patch and prick tests were performed at day 7 and day 42. Goujon and colleagues found that oat-based cosmetics in cereal-sensitized atopic adults did not produce immediate or delayed allergic reactions and were well tolerated, and cereal sensitization does not increase the risk of allergic reactions to oat-containing cosmetics.

Patients with AD are susceptible to allergens, and Italian investigators evaluated the allergic skin reactions of normal and

FIGURE 2. An 8-week monadic, blinded, clinical study was conducted to evaluate the tolerance and efficacy of an oat based skin care regimen in subjects with mild to moderate atopic dermatitis. Twenty-five subjects between 12 and 60 years of age (approximate mean age 30 years) completed the 8-week treatment, which consisted of 1) an oat-based body cream to be used twice daily, morning and night (or more often if needed) and 2) an oat-based body wash, used once a day in the shower or bath. Subjects were allowed to use their prescribed topical treatment as per their usual routine. Evaluations were performed at week 0, 2, 4, and 8. Evaluations included Eczema Area and Severity Index (EASI), investigator's global assessment (IGA), and subjective assessment so itching, burning and stinging (1–4 scale). Dermatologist evaluations showed a statistically significant (P<0.01) improvement in the IGA scores (green line) and in itch severity (orange line) at weeks 2, 4, and 8.



*Significant improvement (p<0.01).

IGA=Investigator's Global Assessment.

Nebus J, et al. Poster presented at: 67th Annual Meeting of the American Academy of Dermatology, March 6-10, 2009; San Francisco, CA.

atopic children to topical oat and rice colloidal grain suspensions with and without previous exposure to colloidal grain suspensions.[11] The double-blind, randomized patch study used two concentrations of oat and rice colloidal grains (0.007% and 0.7%) and applied them occlusively to the backs of 65 children living in Italy, whose ages ranged from 6 months to 2 years. Forty-three of the children had AD and 22 were normal.

The Italian investigators found that there was neither immediate urticarial nor allergic reactions in any of the 65 study subjects. Radioallergosorbent (RAST) tests were performed on 55 subjects. The negative RAST test results found in the nonatopic group correlated with their nonatopic status, but positive RAST tests were found in only 8 of 35 (23%) of the children with AD, and none of the sera from positive RAST scores corresponded to subjects with irritant patch reactions. So the data indicates that topical colloidal grains can be used as an adjunctive therapy in the management of mild AD in children under 2 years of age.

Grimalt and colleagues evaluated the effect of an emollient containing oat extracts on the quantity of topical corticosteroids used in infants with moderate to severe AD.[12] Over the course of 6 weeks, 173 infants under 12 months of age were treated for inflammatory lesions by moderate- and/or high-potency topical corticosteroids. The infants were randomly assigned to receive the emollient, and the infants who did not receive the emollient acted as a control group.The quantity of moderate- and high-potency corticosteroids used during the 6-week trial decreased by 7.5% (not significant) for the control group and 42% (P< 0.05) for the infants receiving the emollient. The investigators found that oat emollient significantly reduced the infants' corticosteroid use.

Although the vast preponderance of studies have concluded that oat-containing moisturizers and/or cleansers are safe and effective for the treatment of AD, one French prospective study found that some children with AD were susceptible to oat-induced allergic reactions. Boussault and colleagues conducted a prospective analysis of 302 children with AD referred for allergy testing between June 2001 and December 2004.[13] Atopy patch tests (ATP) and skin prick tests to oat proteins at concentrations of 1%, 3% and 5%, and the European standard series were performed on the children prior to oral food challenge and recurrent open application tests in the oat-sensitized group. In oat-sensitized children, the subjects respective oral food challenge and recurrent open application tests (ROAT) were positive in 15.6% of subjects (five of 32) and 28% (seven of 25) of subjects. Additionally, 32% of the children who used oat-derived topicals had oat-positive ATP tests compared to 0% in the children who did not use oat-derived topicals. The investigators concluded that oat sensitization in children with AD was higher than anticipated, and they suggested avoiding oat-containing proteins in children with AD.

As previously mentioned, the study of Boussault and colleagues was an anomaly when compared to other studies

assessing the safety and efficacy of colloidal oat compounds, but on closer scrutiny that study had methodological problems. A pair of the methodological flaws in the French study were that the investigators used oat pollen and not proteins found in colloidal oatmeal when conducting skin prick tests and IgE testing. Oat pollen is unlikely to contain the same proteins that are found in colloidal oatmeal, so an allergic reaction to oat pollen would not be a predictor of an allergy to proteins found in colloidal oatmeal.

Boussault and colleagues also used ATPs at three different concentrations, but the investigators failed to report the subjects' reactions at the various concentrations, so clinical correlation of allergic reactivity and ATPs is uncertain. The ATP is neither routinely used, nor felt to be of clinical significance in the US. The ROAT was also problematic, because they were conducted in the subjects' home in an unsupervised manner. Moreover, only 25 of the original 302 subjects had a ROAT performed with an oat-based emollient and only 7 of the subjects had a "positive" test.

In conclusion, the FDA has acknowledged colloidal oatmeal to be a safe and effective skin protectant, and it has been used for decades to treat AD. In the treatment of AD, much of the recognized benefit of oats is derived from its phenolic components, especially avenanthramides, which have empirically demonstrated robust antioxidant and anti-inflammatory effects. Further, the majority of studies on oat-based products, either in atopics or non-atopics, show no propensity toward adverse events. And although rare cases of clinically relevant oat allergy may exist, oat-based products are safe and effective for the treatment of the vast majority of individuals, including pediatric patients.

DISCLOSURES

Joseph F. Fowler Jr. has served as a consultant for Johnson & Johnson, Galderma, Innocutis, and Ranbaxy, and as a speaker for Galderma, Innocutis, and Ranbaxy, and has received research grants from Abbott, Allerderm, Allergan, Amgen, Astellas, Galderma, Genentech, Johnson & Johnson, Lilly, Medicis, Novartis, Qunnova, Taro, and Valeant.

REFERENCES

1. Kurtz ES, Wallo W. Colloidal oatmeal: history, chemistry and clinical properties. *J Drugs Dermatol.* 2007;6(2):167-70.
2. Fowler JF, Nebus J, Wallo W, Eichenfield LF. Colloidal oatmeal formulations as adjunct treatments in AD. *J Drugs Dermatol.* 2012;11(7):804-7.
3. Camouse MM, Hanneman KK, Conrad EP, Baron ED. Protective effects of tea polyphenols and caffeine. *Expert Rev Anticancer Ther.* 2005;5(6):1061-8.
4. Saeed SA, Butt NM, McDonald-Gibson WJ, Collier HOJ. Inhibitor(s) of prostaglandin biosynthesis in extracts of oat (Avena sativa) seeds. *Biochem Soc Trans.* 1981;9:444.
5. Vie K, Cours-Darne S, Vienne MP, Boyer F, Fabre B, Dupuy P. Modulating effects of oatmeal extracts in the sodium laurel sulfate skin irritancy model. *Skin Pharmacol Appl Skin Physiol.* 2002;15(2):120-124.
6. 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):569-74.
7. Chen CY, Milbury PE, Collins FW, Blumberg JB. Avenanthramides are bioavailable and have antioxidant activity in humans after acute consumption of an enriched mixture from oats. *J Nutr.* 2007;137(6):1375-82.
8. Schumaus G, Herrmann M, Joppe H, et al. Oat avenanthramides: new actives to reduce itch sensation in skin. Paper presented at: 23rd Congress of the International Federation of Societies of Cosmetic Chemists; October 24-27, 2004; Orlando, Fla.
9. Nebus J, Skillman NJ, Nystrand G. A daily oat-based skin care regimen for atopic skin. Poster presented at: 67th Annual Meeting of the American Academy of Dermatology, March 6-10, 2009; San Francisco, CA. P1301.
10. Goujon C, Jean-Decoster C, Dahel K, et al. Tolerance of oat-based topical products in cereal-sensitized adults with AD. *Dermatology.* 2009;218(4):327-33.
11. Pigatto P, Bigardi A, Caputo R, et al. An evaluation of the allergic contact dermatitis potential of colloidal grain suspensions. *Am J Contact Dermat.* 1997;8(4):207-9.
12. Grimalt R, Mengeaud V, Cambazard F. The steroid-sparing effect of an emollient therapy in infants with AD: a randomized controlled study. *Dermatology.* 2007;214(1):61-7.
13. Boussault P, Léauté-Labrèze C, Saubusse E, et al. Oat sensitization in children with AD: prevalence, risks and associated factors. *Allergy.* 2007;62(11):1251-6.

AUTHOR CORRESPONDENCE

Joseph F. Fowler Jr. MD FAAD
E-mail:..... Fowlerjoe@msn.com

CME Post-Test: For fastest results, please complete this activity online by scanning the QR code below or visiting www.JDDonline.com in the Medical Education Library, where you will be able to receive your CME certificate immediately upon achieving the passing score. Successful completion of the Post-Test is required to earn *AMA PRA Category 1 Credit*™. You must earn a passing score of at least 70% and complete the activity evaluation form in order to complete the course, and receive a certificate for *AMA PRA Category 1 Credit*™. You can take the test online as many times as you require to achieve the passing score. Alternatively, you may select your best answer for each of the following questions and insert them into the Answer Grid found on the Evaluation/Certificate Request Form on page 1185, and return your completed Evaluation/Certificate Request Form to JDD by fax to (718) 407-0898, or by mail to 377 Park Avenue South, 6th Floor, New York, NY 10016.

1. What year did the Food and Drug Administration approve colloidal oatmeal compounds as skin protectants?

a. 2001

b. 2002

c. 2003

d. 2004

2. This polyphenol in colloidal oatmeal has robust antioxidant and anti-inflammatory properties:

a. Avenanthramides

b. Catechins

c. Theaflavins

d. Tannins

3. Colloidal oatmeal is associated with a reduction of the following cytokine:

a. Interferon-α

b. Interleukin-2

c. Interleukin-6

d. Interleukin-8

4. Colloidal oatmeal has been shown to increase plasma levels of this tripeptide that is a potent antioxidant:

a. Isoleucine-proline-proline

b. Leupeptin

c. Melanostatin

d. Glutathione

5. Grimalt and colleagues found that an oat-containing emollient had the following effect on infants with atopic dermatitis:

a. Decreased the quantity of topical corticosteroids used on the infants

b. Increased the quantity of topical corticosteroids used on the infants

c. Had no effects on the quantity of topical corticoste roids used on the infants

d. Enabled a cessation of the infants topical corticoste roids

Evaluation Form

Colloidal Oatmeal Formulations and the Treatment of Atopic Dermatitis

To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please take a few minutes to complete this Evaluation/Certificate Form. **For fastest results, please complete this form online at JDDonline.com** in the Medical Education Library. ***You must complete and submit this form or complete the CME activity online to receive credit for completing this activity. There is no fee for this CME activity.*** You must earn a passing score of at least 70% and complete the activity evaluation form in order to complete the course and receive a certificate for *AMA PRA Category 1 Credit™*. Alternatively, you may return this form to JDD by fax to (718) 407-0898, or by mail to 377 Park Avenue South, 6th Floor, NY, NY 10016.

Request for Credit

Name Degree

Organization Specialty

Address

City State ZIP

Telephone Fax

Email

Signature Date

I am registered on JDDonline.com
☐ Yes ☐ No

If yes:
User Name Password

Post-test Answer Key

1	2	3	4	5

☐ I participated in the entire activity and claim 1 *AMA PRA Category 1 Credit™*.

Please answer the following questions by circling the appropriate rating:

1 = Strongly Disagree	*2 = Disagree*	*3 = Neutral*	*4 = Agree*	*5 = Strongly Agree*

Was timely and will influence how I practice
1 2 3 4 5

Enhanced my current knowledge base
1 2 3 4 5

Addressed my most pressing questions
1 2 3 4 5

Provided new ideas or information I expect to use
1 2 3 4 5

Addressed competencies identified by my specialty
1 2 3 4 5

Avoided commercial bias or influence
1 2 3 4 5

Impact of the Activity

Name one new strategy you learned as a result of completing this activity:

Name one thing you intend to change in your practice as a result of completing this activity:

Additional comments about this activity:

Please list any topics you would like to see addressed in future educational activities: